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| **Medicine\_1999-** | |
| ID | 0561 |
| Biographical | In 1936, when I was born in the small Silesian village of Waltersdorf in the county of Sprottau in the then eastern part of Germany, now part of Poland, the fine structure of the cell was still an enigma. After 300 years of staring through light microscopes, essentially all that biologists had learned was that the cell was delimited by a plasma membrane and contained a nucleus. Staining procedures had revealed other distinct territories in the cytoplasm and in the nucleus, but their fine structure remained unknown. A dramatic revolution occurred in 1945, when Keith Porter, Ernest Fullam and [Albert Claude](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/index.html) at the then Rockefeller Institute for Medical Research in New York City introduced the electron microscope to look at cells. The first structure they saw was a lace-like network in the cytoplasm that they termed the endoplasmic reticulum. This discovery formed the foundation for my future scientific career.  1945 was also a turning point in my life. Until then my childhood was a perfect 19th century idyll. In the cold and snow-rich Silesian winters there were hour-long rides on Sundays in horse-drawn sleighs to my maternal grandparent’s farm to have lunch and to spend the afternoon. The house was a magnificent 18th century manor house in the nearby Altgabel with a great hall that was decorated with hunting trophies. In the summer, of course, horse-drawn landauers were used as means of transportation. The way to school was a long one. We went there on foot and as a pack, usually consisting of one or two of my seven brothers and sisters and of children from neighboring houses.  At the end of January 1945, we had to flee from the advancing Russian Red Army. My father, a veterinarian stayed behind for a few more days and left only hours before the Red Army moved in. My fourteen year-old brother, Reiner, drove my mother, my youngest brother, an older brother, the two younger sisters and me in a small automobile to relatives west of Dresden in Saxony. On the way there we drove through Dresden. We entered the city from the eastern hills. Its many spires and the magnificent cupola of the Frauenkirche (die Steinerne Glocke, the Stone Bell) were a magnificent sight even for the untrained eye of a child. Driving through Dresden, I still remember the many palaces, happily decorated with cherubs and other symbols of the baroque era. The city made an indelible impression on me. Only a few days, later, on February 13, 1945, we saw from a distance of about 30 kilometers a fire-lit, red night sky reflecting the raging firestorm that destroyed this great jewel of a city in one of the most catastrophic bombing attacks of World War II. It was a very sad and unforgettable day for me.  The months before and after the end of World War II were chaotic and miserable. None of my relatives had enough space to accommodate our large family leaving us divided among several relatives in different villages. There was no communication and little food. On September 9, 1945, we learned of the death of my beautiful oldest sister Ruth who, at age 19, was killed in an air raid on a train she was travelling in on April 10, 1945. She was buried in a mass grave near the site of the attack in Schwandorf, Bavaria. Ruth was born when my mother was just 20. The two had a sisterly relationship. My mother grieved over Ruth’s death until the end of her own life.  Fortunately, things took a turn for the better, when my father was able to continue his veterinarian practice in the charming medieval Saxon town of Freiberg. Most members of our family were reunited there by 1947. We lived in a nice villa surrounded by a large garden on the edge of town. My way to school was along the old medieval city wall. For only 40,000 inhabitants, Freiberg had a rich cultural life with a 175 year old theater. Most impressive were the musical performances in the magnificent gothic cathedral, the Dom, with the splendid great Silbermann organ. Each week Bach cantatas were performed. The great choral works of Bach, Mozart and Haydn were regularly performed and at the highest artistic level at the major religious holidays. I even participated in singing in the cantus firmus of Bach’s Matthäus Passion. So, it was almost like a 19th century idyll again, this time in a small medieval town instead of a country village.  However, there was now the ever more oppressive regime of East Germany to deal with on a daily basis. When I graduated from high school in 1954 I was not allowed to continue my education at a university because I was considered a member of the “capitalist” classes. Fortunately, at that time, i.e., before the Berlin Wall, it was possible to escape and to travel freely to West Germany. So, on August 28, Goethe’s birthday, I left Freiberg for Frankfurt on the Main in West Germany. The train left in the morning and in the afternoon it passed Weimar, where Goethe spent most of his life, and then Eisenach, where Bach was born and in the evening it arrived in Frankfurt, Goethe’s birthplace.  I studied medicine, beginning in Frankfurt and then in Kiel, München and Tübingen, graduating in 1960 from the University of Tübingen. Although I completed two years of internship in various small hospitals, I decided against continuing my medical training. I was much more fascinated by the unsolved problems of medicine than by practicing it. Fortunately, my oldest brother Hans had a similar experience in his field of study, veterinary medicine. He had obtained the prestigious Fulbright Fellowship to study in the U.S., continued his training there in microbiology and rapidly achieved the rank of full professor at the University of Wisconsin in Madison. He was extremely sympathetic to my dilemma and helped me to secure a graduate fellowship to study either with [Khorana](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1968/index.html) or with Van R. Potter. So, in 1962, I sailed to Montreal on a German steel freighter, and from there drove to Madison to arrive on a beautiful late day in May. Potter was a marvellous mentor, witty, energetic and stimulating. I graduated in November 1966, and decided to join [George Palade](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/index.html)‘s Laboratory of Cell Biology at the Rockefeller University (formerly the Rockefeller Institute). The revolution that began there in 1945, and that led to the discovery of all the major structures of the cell continued in the realm of relating cellular structures to specific cellular functions. My arrival there coincided with the end of this second phase and the exciting beginnings of a third phase, the molecular analysis of cellular functions (see below). I was fortunate enough in helping to initiate this third phase of analysis which is still in full swing.  George Palade has been my most influential mentor, a good friend and a wonderful colleague. He taught me how to conceptualize a collection of disparate facts, to formulate working hypotheses and to design experiments to test these hypotheses. I am greatly indebted to him.  In New York I married Laura Maioglio. Laura studied art history and, at her father’s death, took over Barbetta Restaurant founded by her father in 1906. Laura has introduced me to many artistic pleasures that I had not experienced before. She greatly encouraged me in my work and never complained about the many hours I spent in the laboratory.  In 1994, I founded Friends of Dresden, Inc., a charitable organization, with the goal to raise funds in the U.S. to help rebuild the Frauenkirche in Dresden. The rebuilding of many of the historic monuments of Dresden is one of the most exciting consequences of German reunification and the liberation from communism. It is a childhood dream come true.  It was one of the great pleasures of my life to donate the entire sum of the Nobel Prize, in memory of my sister Ruth Blobel, to the restoration of Dresden, to the rebuilding of the Frauenkirche and the building of a new synagogue. This donation also serves to express my gratitude to my fellow Saxons. They received us with open arms when we had to flee Silesia. I spent a wonderful period of my life there and they gave me a thorough and valuable education. A few thousand dollars will also be donated for the restoration of an old baroque church in Fubine/Piemonte/ltaly, the home town of my wife’s father, Sebastanio Maioglio. We have spent many happy summers there in the parental home of my wife.  *Günter Blobel died on 18 February, 2018.* |
| Autobiographica |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q83 | I wonder which factors have been of greatest importance for your career? |
|  | I was very fortunate to have been in the right environment and the right place at the right time, to have met the right teachers, and it started in elementary school, it went to the gymnasium I had wonderful teachers, in medical school I had wonderful inspiring teachers who always ask questions and stimulated us to think about things that weren’t known and so I was … When I did my medical doctorate I realised that many diseases are treated symptomatically and not in a causative manner and so I was very interested in learning more about diseases, the cause for diseases, this is why I went into research. I was very fortunate to meet [George Palade](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/palade-facts.html) who won the Nobel Prize in 1974, was a very stimulating man who shaped my career. So it was being in the right place at the right time and using the chances and the opportunities properly. |
| Q25 | And how important do you think the mentorship is? |
|  | Mentorship is very important because you have to learn how to formulate an idea out of the chaos of data that there is and out of the hints that there are that there may be a concept that you could distil out of this tremendous chaos of data and to integrate it into a new idea and that is something you have to learn. |
| Q25 | What comprises a good mentor? |
|  | A good mentor is a person who is not overpowering but is gently stimulating you and is opening up, helping you to open up a new world of ideas and that is what a good mentor is and who is passionate about what he or she is doing. That’s the most important thing, to be passionate, to be really involved in what you want to do. |
| Q8 | How come you decided to leave Germany and move to the United States? |
|  | I left Germany in 1962 and at that time Germany was still recovering from war and there were not too many research institutes available at that time and the opportunities were much more impressive in the United States, and I also wanted to have an American experience, I wanted to learn English, I wanted to be exposed to the American way of doing research and so this is why I went to the United States. Not with the intention to stay but actually to stay there maybe for one or two years and then come back to Germany but then I, for many reasons, I continued to stay there and I’m still there. |
| Q43 | Your work at Rockefeller University, there are many Nobel Laureates at that university. How does that come, what’s so specific or so special about Rockefeller University? |
|  | It is a fairly small place so that people know each other and you really … The administration of the place is not intrusive so that you have time to think about your research 24 hours a day. There’s only 150 students, graduate students and they’re very, very good graduate students with whom we interact on a more personal basis, there are something like 300 faculty and 150 students so the ratio is quite impressive and we know each other very well because it is a small place and we have time to think about research 24 hours a day, as I already said. |
| Q43 | Is it possible to create a creative environment? |
|  | It’s very difficult to do that, even at Rockefeller you have to constantly recreate this environment and the environment of course changes, it’s not something which is taken for granted. Another thing that Rockefeller is unique is it doesn’t have departments, it doesn’t have departmental boundaries so that you can create new disciplines by intermingling new ideas and you create just a new department or a new laboratory. You don’t have laboratories at the Department of Biochemistry, you can call your laboratory anything you want to, Laboratory of Cellular Biophysics for instance, if you were very interested in biophysics, you can also change the name again if you want to if you want to pursue something else and that gives you great flexibility. |
| Q12 | What would you … if I considered to go into medical research, what do you suggest that I should think of? |
|  | Now that the sequence of human DNA will be done within a short time, you will have a vast amount of information, we will have the Rosetta stone of human biology at least and that will give tremendous new opportunities for all disciplines, be it neurobiology, be it cell biology, be it pharmacology, immunology, everybody … All of the disciplines will benefit from this tremendous amount of information which is coming but now we need people who can digest this information and can distil it out into new concepts.  We have to learn how proteins work in the context of a cell and in the context of the organism. Just to give you an example, in *E. coli* we know, in the bacterium, we know the sequence for some time but we still don’t know what 50 percent of the proteins are doing in *E. coli* and *E. coli* is a much simpler organism than a human cell. So this is going to be a great challenge for your generation to really teach us what are all these proteins doing and how are they doing it in the context of a cell, not only of a cell but the entire organism.  And look for a good mentor.  Gunter Blobel: Look for a good mentor, somebody who’s passionate, somebody who really loves science and forgets about everything else, for the moment at least.  And how important is the environment?  Gunter Blobel: So the environment is very important, that you really can focus and concentrate on science and you’re not distracted by too many other things, teaching is very important but we do not have to teach undergraduates which saves us a lot of time. |
| Q23 | Let’s shift to something else. There are three key words in the will of Alfred Nobel. One is that the name of the prize is “Physiology or Medicine”, it’s not medicine which is physiology or medicine is a much broader field. The second thing is that the prize should be awarded for a discovery and it should be of greatest benefit to mankind. Of course the impact of these key words is consistently being discussed by the Nobel Assembly, but it is also now and then brought up in editorials in scientific journals. I don’t want you to judge the work that has been done by the Nobel Assembly but I would like you to put your work into these contexts in terms of discovery, in terms of benefit on mankind and physiology or medicine. |
|  | Well, first physiology or medicine. What we have worked on is the very basic aspect of how cells work, not a human cell only, but also all animal cells, plant cells even bacteria and all. Cell is a unit of life and how does it deal with organising itself. It is not just a mail to send something to this or this address but it is … because it also deals with how membranes are put together, it really deals with the structural organisation of a cell, how does it organise itself into the various compartments and how does it maintain this organisation and that is a very fundamental aspect about how all cells work. Now the medical benefits of that is that we for instance in the production of proteins that, let’s take insulin, which was formerly gotten from slaughterhouses and was extracted, can now be made in bacteria and you can use a zip code to get the insulin out of the bacteria and then can separate it from bacteria much easier.  … this is just what we have studied so far, it’s just the tip of the iceberg …  And there’s not only the insulin, there are many growth factors like erythropoietin of which last year $2 billion were sold alone, important for people who suffer anaemia due to kidney failure and dialysis patients in particular so there is a huge market of medicines which has been developed which is in part, in part based on the discoveries which were made and there will be many more. It will be very important in the understanding of diseases; we already know that some diseases are caused by miss-targeting of proteins or by improper traffic patterns in the proteins so this is just what we have studied so far, it’s just the tip of the iceberg, there will be many, many other diseases that will have as a cause irregular traffic patterns or inability of the cell to organise itself properly. |
| Q16 | So the benefit so far has mainly been to increase our knowledge but the benefit in terms of applications to treat the diseases will come later on? |
|  | In a way it, you know, the fact that you can now make recombinant proteins in bacteria and in yeast and you will be able to make many, not just insulin and erythropoietin, many other gross factors and you can easily purify it, you can make it in large quantities as a huge quantum term. The fact that you had to previously go and isolate them from slaughterhouse animals like this contamination, is a huge jump forward which will help all of medicine. Now it’s not only based on my discoveries obviously, it’s based on the fact that you can make recombinant DNA and that you can express recombinant DNA and bacteria and so on but we have learned how to get the protein out of the cell and therefore we can purify it much easier. That is a very, from a practical point of view.  I had lunch at Upjohn Pharmacia and they’re producing growth hormone and this is half a billion dollars’ worth of growth hormone that is being produced in bacteria, right, and they are making now factor VIII or they have already made factor VIII which is on the market which something to do with blood clotting and so therefore a large number, a whole repertoire of proteins will be produced in this way. You will, you may be able to engineer cells and to get certain proteins into certain organisms and make them more efficient and that may be very important for cell therapy in the future so there will be future benefits to come down the line as a result of understanding how the cell works.  But I would like to emphasise that we are far away from understanding the cell, I don’t like to give the impression that this now we understand the cell, we are very, very far away from understanding cells. We may never completely understand the cell, we may hit something like the uncertainty principle in physics where while we are trying to measure something in the cell we disturb something and therefore the measurement that we are getting is faulty. But we are not at that level yet, we still are trying to map out very basic functions of the cell and we will have to understand the entire repertoire of functions and what principles the cells use in order for instance to find out how is a normal cell distinct from a cancer cell, because at the moment we treat cancer cells and try to kill cancer cells but we don’t know the differences precisely and therefore we kill many normal cells too. So we have to learn about cells, cells is the unit, basic unit of life and we have to learn how they work and what we discovered is the common principle which works in all cells. |
| Q3 | You get very excited when you talk about this. Is excitement and curiosity the main driving force, why you have done all this? |
|  | I’ve always had fun, I mean I was, my entire research sort of was hypothesis driven therefore I always imagined how things would be and then some of my fantasies of course turned out to be wrong and one must not be wed to one’s fantasies, one must when data come which aren’t compatible with one’s fantasies, one must abandon them. There are beautiful hypothesis killed by ugly facts and so one has to, but one has to also pursue and see whether one can get evidence for or against it and it’s wonderful to take a phenomena and then think about them and then imagine how it could possibly work and then see whether one can provide some evidence for or against it. |
| Q34 | Yes, I wonder what consequence receiving the Nobel Prize have for your future. |
|  | I’ve noticed in this last eight weeks that a lot of people have asked me for my opinions and one thing I want to be very careful about, I don’t want to give opinions that are not based on facts, I don’t want to now discuss atomic disarmament and all sorts of other problems, societal problems, economic problems, other problems that we are afflicted with which I haven’t studied because I, also I like to hypothesise. In the end I would like to have facts and there are certain things that I would like to do, I would like to do things that interest me, like to do something for Dresden, I don’t want to go into the details why, I want to like to do something for understanding between people, peoples, I want to do something for humanity, I want to give something back of the wonderful education that I have received but I will more or less continue my research as long as I feel that I can do it. |
| ID | 0562 |
| Biographical | I was born in the lovely coastal city of Charleston, S.C. in 1916 and lived there until I was thirteen. In Charleston I first became enamored of “natural history” when I attended nature study classes and field trips to nearby beaches, marshes and woods, sponsored by the Charleston Museum. I became an avid shell collector and bird watcher (that was before the term “birder” was coined), and I still enjoy these hobbies. In 1929, my family moved from Charleston to Orangeburg, S.C., an inland, rural town of about 8,000 inhabitants, where my mother had grown up and still had some family. The reason for the move was that the Furchgott department store in Charleston, which had been started by my grandfather and was being run by my father and his two brothers, was unable to survive in the midst of the Depression, and my father decided to open a women’s clothing store in Orangeburg. So I spent my high school years in Orangeburg, enjoying small town life and competing with my first cousin Edwin Moseley for the highest grades in our class. He won.  Within the first couple of years of high school, I knew that I would like to be a scientist. My parents were encouraging: they gave me chemistry sets and a small microscope as presents. I liked to read popular books about scientists, although there were not many available at that time. My father subscribed to the Sunday New York Times, in which there was often a column on science that I found very exciting.  During the four years that I was in high school, my older brother Arthur was at the University of North Carolina at Chapel Hill. I wanted to attend college there also, but that was not possible when I finished high school in 1933 because tuition for me, as an out-of-state resident, was more than my father could afford at that time. So I spent my freshman year at the University of South Carolina, where my tuition was much less. However, by the summer of 1934, my father moved his business from Orangeburg to Goldsboro, N.C., where he felt that the local economy was better. So now, as a resident of North Carolina, I was able to register at the University at Chapel Hill as a sophomore majoring in chemistry.  At Chapel Hill, I had a number of excellent teachers in chemistry. During my junior and senior years, I had a small amount of financial support from an NYA job (NYA being the initials of the National Youth Administration set up by the federal government to help students during the Depression). In that job, I was a lab assistant in research to a junior faculty member working on the physical chemistry of solutions of cellulose. I had decided early in my college years that I would go on to graduate work in some branch of chemistry. My preference by the time I was a senior was physical organic chemistry. I sent letters to dozens of chemistry departments applying for a graduate fellowship or teaching assistantship. I had an excellent academic record, but by graduation time I still had no definite offer of a position for graduate training. I was almost resigned to taking a job in chemical industry, when around the middle of June while I was in Florence, S.C., where my parents now lived, an unexpected offer of a teaching assistantship came to me from the Physiological Chemistry Department of Northwestern University Medical School in Chicago. I was to be a graduate student of Dr Henry Bull, who had recently come to Northwestern, and whose research interests were physical chemical aspects of biochemistry.  Northwestern and Cold Spring Harbor (1937-1940) Before I went to Chicago, I worked for two summer months in 1937 for Eastern Airlines at the Philadelphia airport – a job which my older brother Arthur, who was employed by that airline, helped me obtain. The job allowed me to save some money and also allowed me free air travel to Chicago. That helped a lot since my stipend as a teaching assistant at Northwestern was only $50 a month for a nine-month academic year. When I arrived in Chicago, it had already been arranged for me to share a room with two more advanced graduate students. Living in Chicago was quite a change from living in the Carolinas. When I would walk to work in the winter from our rooming house, which was about a mile from the medical school, the chill wind whipping in from Lake Michigan along Chicago Avenue was quite an experience for a Southern boy.  My course work at Northwestern was partly at the medical school, and partly at the Evanston campus to which I would travel via the El. At the Evanston campus, my courses were mainly in physical chemistry under Dr Malcolm Dole, who was also on my PhD advisory committee. At the Chicago campus, I had to take physiology and bacteriology (along with medical students), Henry Bull’s course on physical chemistry in biochemistry, and some assorted graduate courses in physiology and biochemistry. The physiology course was under the direction of Dr Andrew Ivy, who had built up a sizeable physiology department faculty for those times. In contrast, the biochemistry faculty consisted only of the chairman, Dr Chester Farmer, Dr Bull and two part-time lecturers.  My laboratory work with Bull started out with the preparation of purified egg albumin. He was studying physical chemical changes in this protein after different methods of denaturation. He had begun to involve me in some of his studies when the summer of 1938 came along, and that turned out to be a special summer for me. Bull had been invited to present a paper on his work at the sixth Cold Spring Harbor Symposium on Quantitative Biology which was to take place at the Cold Spring Harbor Biological Laboratory of the Long Island Biological Association. The theme of the symposium, which was to run for five weeks in a leisurely fashion was the structure and function of proteins. Bull had obtained permission from the director of the Cold Spring Harbor Laboratory, Dr Eric Ponder, for me to attend the symposium, while earning my room and board by running the lantern slide projector at the lectures. The symposium was very exciting. I met many distinguished scientists. Ponder and a physician-scientist, Harold Abramson, arranged to have me assist in a research project at the laboratory for the rest of the summer after the symposium was over. The project was on the electrophoretic mobility of rabbit erythrocytes and ghosts, measured with the use of a microelectrophoresis cell and light- and dark-field microscopy.  By the end of the summer, I had become very interested in the physical chemistry of the red blood cell membrane. When I returned to Northwestern in the fall of 1938, Bull approved continuation of my research on red blood cells as a PhD thesis project. In particular, I was fascinated by the unexplained phenomenon of the transformation of mammalian red blood cells, suspended in unbuffered isotonic saline from discs to perfect spheres when a small drop of the suspension was placed between slide and coverglass. I discovered that the disc-sphere transformation depended on two factors. The first was a rise in pH to over 9.0 in the unbuffered suspension, as a result of the alkaline nature of the glass surfaces (pH being measured with a semi-micro glass electrode that I constructed). The second factor was the removal from the suspension of the red blood cells by adsorption onto the glass surfaces of the slide and coverglass of a substance in the suspension that prevented sphering on elevation of pH of the suspension. I demonstrated that this substance, which I termed the anti-sphering factor, was serum albumin which could not be effectively removed from the red cells simply by multiple washing and centrifuging. In addition to the work on shape changes in erythrocytes, my PhD thesis work involved additional studies on the electrophoresis of the cells under various conditions and on other aspects of the physical chemistry of erythrocyte membranes.  In the summer of 1939 at the invitation of Ponder, with whom I had extensive correspondence during the year and who had become in effect the major advisor for my PhD thesis research, I returned to Cold Spring Harbor to continue research on red blood cells. To earn my room and board, I waited on tables in the communal dining room. I also was able to attend the symposium talks of that year, which were on the subject of biological oxidations. There I first became aware of the new developments in oxidative energy metabolism and the importance of high energy phosphate compounds. Among the many outstanding biochemists attending were L. Michaelis, [Fritz Lipmann](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1953/index.html) and [Carl Cori](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html). Ponder and his young wife Ruth were very hospitable to me. I was much impressed with his skill in applying mathematics in his research, his facility in scientific writing, and his large collection of records of classical music.  I was able to complete and defend my thesis in time to receive the Ph.D. degree in June of 1940. Earlier that spring I had attended the annual meeting of the Federation of American Societies for Experimental Biology (FASEB) in New Orleans. I had fortunately been asked by Henry Tauber, an Austrian biochemist working for a pharmaceutical firm in Chicago, to share the driving in his car on the round trip to New Orleans as well as his room in a rundown hotel in New Orleans. Thus, I was able to attend this meeting at very little expense. At the FASEB meeting in New Orleans, where gatherings of participants were still called “smokers” and even a fancy meal was not more than two dollars, I had some interviews with persons about possible post-doctoral jobs. One of the interviews was with Dr. Ephraim Shorr, an Associate Professor of Medicine at Cornell University Medical School in New York City, whom I had met at Cold Spring Harbor the summer before. A few weeks later Shorr offered me a postdoctoral position in his laboratory. Although I was hoping to get a position which would allow me to continue work on physical chemistry of proteins or cell membranes, none came through, and I accepted the position with Shorr, with the understanding that I would begin in September.  The reason for waiting until September to begin work at Cornell was because I wanted to spend one more summer at the Biological Laboratory at Cold Spring Harbor. This time, however, I went there as an invited speaker at the symposium which that summer was on the topic of permeability of cell membranes. My talk was entitled “Observations on the structure of red cell ghosts.” At that symposium, there were again a number of established distinguished scientists like K.S. Cole, Robert Chambers and F.O. Schmitt; and in addition, a number of bright young scientists like Hans Neurath, who had also been at the 1938 symposium, Hugh Davson, who with Danielli had developed the lipid bilayer membrane model, and Benjamin Zweifach, with whom I was to collaborate later in research.  Cornell University Medical College (1940-1949) I stayed at Cornell University Medical College working in the laboratory of’ Ephraim Shorr for nine years. When I arrived, Sam Barker, a young research associate, was there to instruct me in methods and procedures they were using to study tissue metabolism (largely using Warburg manometers) and the turnover of rather ill-defined tissue organic phosphate fractions from canine cardiac muscle during incubations *in vitro.* For such studies the lab was one of the first to use radioactive phosphate, which we obtained from the cyclotron laboratory at Berkeley. Barker left toward the end of my first year at Cornell; and I was then responsible for running the laboratory for Shorr. Shorr himself, would sometimes take part in preparing tissue for the Warburg experiments. He was quite capable in the laboratory in addition to being a busy and excellent clinician.  During my first two years at Cornell, my major project was on phosphate exchange and turnover, using radioactive phosphate and slices of dog left ventricular muscle. A full paper on the work was published in the journal of Biological Chemistry in 1943. The methods and equipment we used in that work have long been superseded, but we did manage with chemical and some early enzymatic methods to show the extremely fast turnover of creatinine phosphate and the terminal phosphate of ATP in resting cardiac muscle.  The 1943 paper was my first full publication after three years of work at Cornell. One likely reason for sparse output was that the United States had entered World War II in December of 1941, and Shorr, like many others, began to undertake research that had more relevance to the war effort. With government and other support, he shifted the major research in the lab to circulatory shock – first on changes in tissue energy metabolism resulting from hypoxia associated with hemorrhagic shock, and then mainly on factors that might account for “irreversible” shock, the condition in which restoration of blood volume is no longer able to raise pressure and sustain life in the animal subjected to maintained low blood pressure as a result of controlled hemorrhage. To help in this new line of research, Shorr recruited Benjamin Zweifach, then a bright young physiologist who had trained with Robert Chambers and had developed a beautiful method for microscopic observation of blood flow in part of the mesentery (the “mesoappendix” area) of the anesthetized rat. In brief, the “rat mesoappendix test”, conducted by Zweifach and technicians whom he trained, produced evidence by 1944 for two vasoactive factors in circulatory shock. The first factor appeared in the plasma of dogs in the early reversible (by transfusion) stage of hemorrhage. Intravenous injections of this plasma increased the sensitivity of the small arterioles and pre-capillary sphincters to topically applied epinephrine in the mesoappendix test. This factor was termed VEM (for vasoexcitatory materials). As the irreversible stage of circulatory shock developed, VEM activity disappeared from the plasma and a new factor appeared which markedly decreased the sensitivity to epinephrine in the mesoappendix test. This factor was termed VDM (for vasodepressor material). We developed evidence, in part from *in vitro* experiments with tissue slices, that hypoxic kidney was the probable source of VEM and that hypoxic liver was the probable source of VDM. By late 1945, these developments led to a lead article in the journal *Science* by Shorr, Zweifach and myself.  During the war years, I was not solely involved in research on tissue metabolism and circulatory shock. In 1943, Eugene DuBois, chairman of the Department of Physiology at Cornell, arranged that I join his department as an instructor in order to replace a staff member lost to military service. Although I was teaching in physiology, I still spent most of my time in research in Shorr’s lab, which was partially funded by the federal Office of Scientific Research and Development. The work on VEM and VDM continued after the war ended. I had attempted to isolate the VEM-like material that accumulated in incubation fluid when kidney slices were incubated anaerobically. I was able to concentrate it somewhat and it appeared to be a labile dialyzable peptide, but I failed to isolate it. On the other hand, Abraham Mazur, a professor of biochemistry at the City College of New York who worked part time with us, purified a VDM-like material from liver which appeared to be ferritin. (Ferritin or not, we might now wonder whether VDM could somehow be related to nitric oxide!)  Unfortunately, the only bioassay procedure for detecting VEM and VDM activity was that involving changes in sensitivity to epinephrine in the rat mesoappendix test. Intravenous injections of solutions containing high levels of impure VEM or purified ferritin did not effect blood pressure in experimental animals. Attempts to develop an *in vitro* bioassay system also failed. These failures tempered my enthusiasm, and I think that of Zweifach, for the significance of VEM and VDM in the regulation of circulation. However, the failed attempts to develop an *in vitro* bioassay for VEM and VDM were very important for me for they introduced me to the pharmacology of smooth muscle, a subject that has been a major interest of mine ever since.  Two of the isolated smooth muscle preparations that I unsuccessfully tested for bioassay of VEM and VDM were a helically-cut strip of rabbit aorta, which responded with contraction to epinephrine, and a longitudinal segment of rabbit duodenum, which exhibited spontaneous rhythmic contractions that were inhibited by epinephrine and stimulated by acetylcholine. At that time, contractions of such smooth muscle preparations mounted in organ baths were recorded with isotonic levers on kymographs. One day in the course of making tests on segments of rabbit duodenum mounted in oxygenated Krebs solution, I was surprised to see that during the first hours of the experiment, contraction amplitude did not stabilize as usual but declined gradually and markedly even though the rhythmic frequency remained unchanged. I suspected that my technician had forgotten to add glucose to the Krebs solution. Adding glucose now quickly increased contraction amplitude to the normal level. This finding led to a simple procedure for finding out what sugars and fatty acids could be utilized for energy for contraction in the intestinal smooth muscle under aerobic and anaerobic conditions and to analyze the sites of action of metabolic inhibitors.  In the spring of 1949, 1 had two interesting offers at the assistant professorship level – one in physiology at Duke and one in pharmacology at Washington University School of Medicine. I decided on Washington University, partly because the new chairman there, Oliver Lowry, was someone I had known in the Enzyme Club in New York City and partly because I had begun to be very interested in pharmacology as a discipline. This was partly because of the studies I had begun on the effects of drugs and other agents on smooth muscle preparations *in vitro,* but also in large part because of my close friendship with Walter Riker, who was then a junior member in the Pharmacology Department at Cornell at the beginning of a distinguished career. His enthusiasm for research in pharmacology was contagious.  In the summer of 1949, my family and I drove from New York to St. Louis. My wife, Lenore, a native New Yorker, said she felt like she was going West in a covered wagon. By that time we had two daughters, ages four and one. Later we had a third daughter born in St. Louis. It might be noted here that none of my daughters became scientists. Instead, they all went into art (like my younger brother, Max). It might also be noted here that my wife Lenore died in 1983; and that now I have a new wife, Margaret (Maggie). I have been very fortunate in having wives who encouraged my work, even though it often reduced the time I could give to family matters.  Washington University (1949-1956) My seven years in the Pharmacology Department at Washington University were enjoyable ones. Oliver (Ollie) Lowry had been appointed chairman of that department a year or so before I came. He was already well recognized for his ingenuous methods involving enzymology , spectrometry and fluorometry in the quantitative analysis of important enzymes, substrates and products in extremely small amounts of tissue. He was very helpful in introducing me to enzymatic-spectroscopic methods (as developed by kalckar) for analysis of ATP, ADP and AMP. As a new chairman, Lowry inherited two faculty members, Helen Graham and Edward Hunter, and recruited two new ones, namely myself and Morris (Morrie) Friedkin. I had never had a course in pharmacology as a student, much less taught in one, and so I had to spend a lot of time during my first year in St. Louis keeping ahead of the medical students. Later, when I set up my own department in Brooklyn, I adopted for the pharmacology course there much of the lecture, laboratory and conference program that I had participated in at St. Louis.  Lowry’s department was a stimulating place for research. Over the years I was there, the departmental staff grew steadily. Lowry attracted outstanding postdoctoral fellows, such as Eli Robbins and Jack Strominger. We often joined the members of Carl Cori’s Biochemistry Department for seminars and journal club meetings.  My first research project at Washington University was a continuation of the work I had begun at Cornell on energy-metabolism and function of rabbit intestinal smooth muscle. I was able to obtain a small grant to support my research on smooth muscle, and to hire a technician, Marilyn (Wales) McCaman, who later became my first graduate student. By the middle of 1951, my favorite *in vitro* smooth muscle preparation had shifted from the rabbit duodenum to the rabbit thoracic aorta. I had found that the helical (spiral) strip of that vessel, properly cut and mounted in organ chambers for isotonic recording, gave very reproducible contractions to epinephrine and norepinephrine after equilibration in oxygenated Krebs bicarbonate solution. I had at first planned to study the effects of disturbances in energy-metabolism on these contractions, but I became much more interested in using the aortic strip for studies on drug-receptor interactions.  By 1953, I had published a paper entitled “Reactions of strips of rabbit aorta to epinephrine, isoproterenol, sodium nitrite and other drugs”. Among the other drugs was acetylcholine. I found that it only produced contractions, whether it was added to resting strips or strips precontracted with some other agent. That was a paradoxical response since acetylcholine was known to be a very potent vasodilator *in vivo.* Little did I suspect then what I was able to show many years later – namely, that relaxation of arteries by acetylcholine is strictly endothelium-dependent, and that my method of preparing the strips inadvertently resulted in the mechanical removal of all the endothelial cells.  In 1954, I published a paper on the use of dibenamine in differentiating receptors in the aortic strip, and in 1955 a review in Pharmacological Reviews on the pharmacology of vascular smooth muscle. In that review, I tried to develop receptor theory as a logical base for interpreting the responses of vascular smooth muscle to many neuro transmitters, hormones and drugs. In order to derive equations to account for the very slow onset and offset kinetics of competitive antagonists as compared to the fast kinetics of agonists, I developed a biophase model in which the agents moved between an aqueous extracellular phase and a lipid membrane phase containing the receptors. Although I paid homage in my review to A. J. Clark for his pioneering work in developing receptor theory, I took issue with his hypothesis that response of a tissue to an agonist is proportional to the fraction of receptors occupied by the agonist. Our results with dibenamine, which behaved as an irreversible competitive blocking agent of adrenergicalpha-receptors, had indicated that with a strong agonist like epinephrine, one could still achieve well over half of the maximum contraction when only a small fraction of receptors were still active. This was the beginning of my interest in the concept of “receptor reserve” or “spare receptors.” (A year later, R.P. Stephenson published his classic paper on the subject in which he introduced the concepts of efficacy, full agonist and partial agonist.)  In the review of 1955, I also briefly reported on a newly discovered phenomenon – namely, that strips of rabbit aorta undergo reversible relaxation when exposed to light of proper wavelength and intensity. This photorelaxation was an accidental discovery that came from the observation that in one experiment active contractile tone of two strips in one pair of organ chambers fluctuated with time, whereas that of two strips in another pair of chambers remained steady. The two strips showing fluctuations did so synchronously. Those two strips, but not the other two, were in organ chambers near a window through which they were exposed to skylight. Suspecting that the fluctuations in tone were due to fluctuations in light intensity on the strips near the window (it was a cloudy-bright day), I closed the shade on the window and both strips increased in tone. I opened the shade and both decreased in tone. From that point on, we never allowed our strips to be exposed to direct skylight. (The usual overhead fluorescent lights do not produce photorelaxation.) Some studies on the characteristics of photorelaxation were begun in St. Louis, and then extended when I moved to Brooklyn.  In addition to working on *in vitro* smooth muscle preparations at Washington University, I also began what became many years of research on the pharmacology of an *in vitro* cardiac muscle preparation – namely the isolated electrically-driven right atrium of the guinea pig. In starting that work, I had the assistance of a very able technician, Taisija De Gubareff. Using chemical and enzymatic methods for analysis of creatinine phosphate, ATP, ADP, and AMP, we showed that neither development of “experimental failure” *in vitro* (a steady loss of contractile force over hours) nor recovery from failure on addition of a cardiac glycoside was due to changes in concentration of these high-energy phosphates. We also reported on the effects of anaerobiosis and of a number of positive and negative inotropic agents. We collaborated with my good friend William Sleator of the Physiology Department in the study of changes in cellular action potentials (measured with intracellular microelectrodes) associated with the changes in contractility of the guinea pig atrium in response to epinephrine and acetylcholine, and a number of other inotropic agents.  Suny Medical Center in Brooklyn (1956-) In 1956, I accepted the position of chairman of the new Department of Pharmacology at the State University of New York (SUNY) College of Medicine at New York City (actually in Brooklyn, and later changed in name to SUNY Downstate Medical Center and more recently to SUNY Health Science Center at Brooklyn). The department had previously been part of a joint physiology and pharmacology department headed by Chandler Brooks but with the opening of a new, relatively huge (for the time) basic science building for the medical school and with good financial support from the State University, there was ample room and resources for a separate department. From the former joint department, I inherited Julius Belford as an associate professor and Bernard Mirkin as an assistant professor. For additional faculty, I recruited Kwang Soo Lee, Leonard Procita, Lowell Greenbaum, Walter Wosilait and Arthur Zimmerman, all in time for them to teach our first course for medical students. The following year C. Y. Kao joined the staff. Also during the first year, we accepted our first graduate students, namely Maurice Feinstein, who worked with me, and Arnold Schwartz, who worked with Lee. During that year I didn’t do much bench work in the research lab since most of my time was spent organizing the department and learning how to be a chairman. (I never became a well-organized administrator and was always poor at delegating authority.)  In Brooklyn, I continued research on photorelaxation of blood vessels, factors influencing contractility of cardiac muscle, peripheral adrenergic mechanisms, and receptor theory and mechanisms. Then, about twenty-three years after moving to Brooklyn, the research in my laboratory largely shifted to endothelium-dependent relaxation of blood vessels. For convenience, I shall divide the discussion of research in Brooklyn into subsections corresponding to the areas that I have listed.  *Photorelaxation of Blood Vessels* Helping with this research were Eugene Greenblatt, my first postdoctoral fellow, and Stuart Ehrreich, my third graduate student. Among other things, we were able to obtain an accurate action spectrum (with a peak at 310 nm) for the photorelaxation. Later we observed that addition of sodium nitrite to the bathing medium greatly sensitized the rabbit aortic strip to photorelaxation and shifted the peak of the action spectrum to about 355 nm. Ehrreich and I found that many other smooth muscle preparations (from stomach, intestine and uterus) which did not ordinarily relax in response to radiation did so in the presence of inorganic nitrite. Percy Lindgren, a visiting faculty member from the [Karolinska Institute](http://www.nobelprizemedicine.org/), also worked with us for a while on photosensitization by nitrite.  Many years later in the early 1980’s, after the discovery of endothelium-derived relaxing factor (EDRF), I again began research on photorelaxation. Although photorelaxation did not depend on the presence of endothelium on the strip or ring of rabbit aorta, we found many similarities between it and endothelium-dependent relaxation (as produced by acetylcholine or A23187). Not only was photorelaxation, like endothelium-dependent relaxation, causally dependent on the elevation of cyclic GMP as a result of stimulation of guanylate cyclase, but both were inhibited by hemoglobin and by methylene blue. This work was carried out with Desingarao Jothianandan, who has been a most helpful research associate in my lab over the past seventeen years. Then, after EDRF was identified in 1986 as nitric oxide, Kazuki Matsunaga (a postdoctoral fellow) and I reinvestigated the potentiation of photorelaxation by sodium nitrite. Using a cleverly designed perfusion-bioassay type apparatus, Matsunaga clearly demonstrated that the potentiation was due to the photoactivated release of NO from nitrite. It is tempting to hypothesize that light (in the absence of added nitrite) produces relaxation of vascular smooth muscle by photoactivating the release of NO from some endogenous compound in the muscle cell.  *Factors Influencing Contractility of Cardiac Muscle* My first graduate student in Brooklyn, Maurice Feinstein, did his Ph.D. thesis research on the effects of experimental congestive heart failure, asphyxia and ouabain on high energy phosphates and creatine content of the guinea pig heart. My second graduate student, Albert Grossman, who began work in 1957, did his thesis research on the effects of frequency of stimulation, extracellular calcium concentration and various drugs on calcium exchange and contractility of the guinea-pig left atrium. Grossman and I published three papers based on his thesis research, which was one of the first attempts to determine the rates of exchange of calcium (using 45Ca) between extracellular fluid and various intracellular “pools” of calcium in cardiac muscle under various conditions affecting contractility. We showed that the positive inotropic effects of norepinephrine and strophanthin-K were correlated with an increase in rate of exchange of calcium in an intracellular pool associated with the contractile process and that the negative inotropic effects of acetylcholine and adenosine were correlated with a decrease in rate of exchange in that pool.  We also continued work with ryanodine, which produced a negative inotropic effect on the guinea-pig atrium and actually changed the force-frequency effect from a positive to negative staircase (mimicking the normal staircase in frog heart). Sleator, De Gubareff and I had shown that the decrease in force with ryanodine (unlike that with acetylcholine or adenosine) was not associated with a decrease in duration of the action potential. The thesis research of Grossman and a few years later that of another graduate student, Peter Wolf, also using 45Ca to measure effects of ryanodine on calcium exchange, led to a hypothetical model that fits fairly well with more recent work of others on the reactions of ryanodine with “receptors” involved with calcium transport in the sarcoplasmic reticulum.  *Peripheral Adrenergic Mechanisms* In writing the 1955 review on the “Pharmacology of vascular smooth muscle,” I had become very interested in the mechanisms by which sympathetic postganglionic denervation and certain drugs like cocaine markedly potentiate the response of effector organs to epinephrine and norepinephrine, yet markedly reduce the response to the sympathomimetic tyramine. My second postdoctoral fellow, Sadashiv (Sada) Kirpekar, was assigned to work in this area. He proved to be a gifted investigator, and we published a number of papers together on work carried out between 1959 and 1962. In one paper, with the running page heading of “the cocaine paradox,” we presented evidence that in aortic strips of rabbit and isolated electrically-driven atria from guinea pig and cat, cocaine potentiated responses to norepinephrine and inhibited those to tyramine by blocking one and the same site on adrenergic nerve terminals. Blockade of this site inhibited the neuronal uptake of no repinephrine from the region of the adrenergic receptors, thus potentiating its action; however, blockade of the site also inhibited uptake of tyramine, whose sympathomimetic action depends on release of norepinephrine from neuronal storage sites, thus inhibiting its action. The site, which we called the “transfer site” later became known as the uptake-1 (UI) site. In the same paper we showed that reserpine, which depleted neuronal storage granules of norepinephrine, did not interfere with activity of the uptake site. In addition to Kirpekar, Peter Cervoni came in as a postdoctoral fellow to work on peripheral adrenergic mechanisms. Both he and Kirpekar later became faculty members in the department with Kirpekar staying on and becoming a stellar figure in the field of adrenergic mechanisms before his untimely death in 1983.  In 1960, I was invited to present a paper on some of my studies on receptors for sympathomimetic amines at a CIBA Foundation conference on Adrenergic Mechanisms held at CIBA House in London. It was the occasion for my first trip abroad and was very exciting. Among the many distinguished pharmacologists at the conference were Sir Henry Dale, Sir John Gaddum and J.H. Burn. Burn at that time was pushing his “cholinergic-link” hypothesis for norepinephrine release at adrenergic nerve terminals. I felt strongly that he had misinterpreted the experimental results which had led to the hypothesis and in the discussion sessions I presented our own results with isolated atria which indicated that there were nicotinic cholinergic receptors on adrenergic nerve terminals which when stimulated by nicotine or acetylcholine triggered a transient release of norepinephrine, but which played no role in release of norepinephrine on electrical stimulation of the nerve.  In 1962-63, 1 spent a sabbatical year in the Department of Physiology of the University of Geneva, where Jean Posternak was chairman. Although I did some research and teaching there, I spent most of my time writing papers on research that my colleagues and I had completed during the preceding few years and on a review on receptor mechanisms (see below). I also visited a number of laboratories in Europe where outstanding research on adrenergic mechanisms was in progress. Among these were the laboratories of [S. von Euler](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1970/index.html) in Stockholm, E. Muscholl in Mainz and John Gillespie in Glasgow.  Between 1965 and 1970 I was fortunate in having a number of very competent coworkers in research on peripheral adrenergic mechanisms. In addition to Kirpekar, there were Pedro Sanchez-Garcia, (a visiting research associate who later became a leading pharmacologist in his native Spain), Jerome Levin (a postdoctoral fellow) and Arun Wakade (a graduate student who later became a faculty member).  In early 1971, I began my second sabbatical leave, this time at the relatively new medical school of the University of California at San Diego (located in La Jolla). I became a visiting professor in Steve Mayer’s Pharmacology Division of the Department of Medicine. One reason for this choice of a sabbatical site was that I wanted to learn the method for analysis of cyclic AMP that Mayer had developed (this was before the development of radioimmunoassays for cyclic nucleotides). However, I did not do a lot of research at La Jolla, partly because a fair amount of my time that year was devoted to duties as president of the American Society for Pharmacology and Experimental Therapeutics.  On returning from La Jolla to Brooklyn in 1972, I continued research on the role of receptors located on prejunctional terminals (varicosities) of adrenergic nerves. I collaborated with Kirpekar in an attempt to characterize the inhibitory prejunctionalalpha-adrenergic receptors on the nerve terminals in cat spleen. At the same time, one of my graduate students, Odd Steinsland, was conducting a very exciting thesis project on cholinergic receptors on prejunctional adrenergic nerve terminals in the isolated, perfused central ear artery of the rabbit. He first pharmacologically characterized with the use of various muscarinic agonists and antagonists the prejunctional receptor through which acetylcholine produces a marked inhibition of norepinephrine release (monitored by both the degree of vasoconstriction and [3H]norepinephrine release). He then went on to study the release of norepinephrine from the adrenergic neurons in the ear artery by cholinergic agonists acting on prejunctional nicotinic receptors. At the same time I was continuing studies, with the assistance of Taruna Wakade, on the pharmacology of cholinergic nicotinic receptors on adrenergic prejunctional terminals in the guinea-pig left atrium.  *Receptor Theory and Mechanisms* When I first gave a course on receptor theory and mechanisms to graduate students in 1957-1958, the literature on the subject was relatively sparse: papers by Clark, Gaddum, Schild, Ariëns, Stephenson, Nickerson and myself. I became interested in developing suitable theory (occupation theory) and *in vitro* procedures for differentiating and characterizing receptors. In particular, I concentrated on receptors for adrenergic and cholinergic agents using as test tissues the rabbit aortic strip, duodenal segment, and stomach fundus muscle, and the guinea-pig electrically driven left atrium and tracheal ring.  In 1963, toward the end of my sabbatical year at the University of Geneva, I completed a review on “Receptor Mechanisms” for Volume 4 of the Annual Review of Pharmacology. In it, I took the opportunity to stress the importance of Stephenson’s ideas on efficacy and spare receptors. In 1965 at a symposium on receptor mechanisms at Chelsea College in London, I presented a paper on the use ofbeta-haloalkylamines, as irreversible receptor antagonists, in the differentiation of receptors and in the determination of dissociation constants of receptor-agonist complexes. Using a slightly modified form of Stephenson’s equations and introducing a term,epsilon, for intrinsic efficacy, I derived a simple equation that predicted that the slope and ordinate intercept of a double reciprocal plot of equiactive concentrations of an agonist before and after irreversible inactivation of a fraction of its receptors, could permit the determination of both the fraction of receptors still active as well as the dissociation constant (KA) of the agonist-receptor complex. For different agonists acting on the same receptor, one could calculate from the KA values the fractional occupation by each to obtain the same standard response before receptor inactivation, and thus obtain relative efficacies. Using this approach, Paula (Bursztyn) Goldberg (a graduate student) and I compared the dissociation constants and relative efficacies of agonists acting on muscarinic cholinergic receptors of isolated strips of rabbit stomach fundus muscle; and later John Besse (a postdoctoral fellow) and I compared the dissociation constants and relative efficacies of agonists acting onalpha1-adrenergic receptors of rabbit aorta. In light of what is now known about receptor signalling pathways through G-proteins, it is probably better to admit that the pharmacological procedure which we developed for obtaining agonist-receptor dissociation constants can only give approximate relative values. Nevertheless, the procedure has proven useful in a number of studies.  In 1972, I published a review entitled “The classification of adrenoceptors (adrenergic receptors). An evaluation from the standpoint of receptor theory”. In it I attempted to formulate the methods and necessary conditions for the classification and differentiation of receptors by pharmacological procedures designed to give accurate dissociation constants of competitive antagonists, acting on a given receptor, and accurate relative potencies and, if possible, dissociation constants of agonists acting on the same receptor. In particular, I attempted to point out pitfalls in such procedures and how to avoid them. For example, I derived theoretical equations to illustrate how removal of the agonist from the region of the receptor by active uptake or enzymatic destruction could markedly alter the slope of a Schild plot for competitive antagonism from the theoretical slope of 1. Later, Aaron Jurkiewicz, a visiting research associate from Sao Paulo, Niede Jurkiewicz and I successfully used these theoretical equations in the analysis of propranolol antagonism to isoproterenol in guinea-pig tracheal strips before and after blockade of removal of the agonist by active uptake.  In 1977, I organized for the annual FASEB meeting a symposium on receptors. By then binding of radioligands (usually 3H-labelled competitive antagonists) had been used for several years for quantifying specific receptors in membranes from homogenized cells and for determining the dissociation constants of competitive antagonists and agonists for those receptors. Most of the papers at the symposium were reports of studies with radioligands (e.g., R. J. Lefkowitz on bothalpha-andbeta-adrenergic receptors; P. Seeman on dopamine receptors; S. Snyder and colleagues on serotonin receptors and opiate receptors). My paper at the symposium was partly a discussion of how pharmacological procedures for differentiating and characterizing receptors based on occupation theory were still very useful in conjunction with the exciting new developments in receptor research being made with specific radioligands.  Also, I reviewed work that had been carried out in my laboratory onbeta-adrenergic receptors mediating relaxation of guinea-pig tracheal smooth muscle, and presented results of pharmacological experiments that showed that this smooth muscle did not have exclusively the2-type of thebeta-adrenergic receptor, as dogma of that time would have it, but had an admixture of thebeta1-type as well – usually as a small fraction of the total ofbeta-receptors, but, depending on the guinea-pig used, sometimes much more.  *Endo Thelium-dependent Relaxation* Having obtained pharmacological evidence that guinea-pig tracheal smooth muscle sometimes has a sizeable fraction of thebeta1-type adrenergic receptor along with thebeta2-type (see above), I decided that it would be well to reexamine the smooth muscle of rabbit thoracic aorta to see if it also might have varying amounts of thebeta1-type receptor mixed with thebeta2-type. However, in the very first experiment designed for this new study in May 1978, an accidental finding as a result of a technician’s error completely changed the course of research in my laboratory. The accidental finding was that on the preparation of rabbit aorta being used in the experiment, the muscarinic agents acetylcholine and carbachol induced relaxation rather than the expected contraction. Why this accidental finding was so exciting, how it led to our discovery of the endothelium-derived relaxing factor (EDRF), and how that factor was eventually identified as nitric oxide will not be discussed here since those matters will be considered in detail in my Nobel Lecture.  In 1982, I resigned from the chairmanship of the Department of Pharmacology at the SUNY Downstate Medical Center, but continued as a professor. In 1989, I retired from my professorship (receiving emeritus status), so that I now was free of teaching duties and committee work related to the medical curriculum but could still continue research in the department. My retirement also now allowed me to spend about three and a half months each winter as an adjunct Professor in the Department of Molecular and Cellular Pharmacology of the University of Miami School of Medicine. Most of my time there I have spent trying to catch up on the writing of manuscripts and on the reading of the burgeoning literature in the field of nitric oxide research – an impossible task these days! During the winter sojourns in Miami, I keep in touch with what is going on in my research laboratory in Brooklyn by means of an occasional visit, but mainly by frequent fax and telephone communications with my one or two coworkers there. I consider myself very fortunate in having this Brooklyn-Miami arrangement. Of course, an additional advantage for my wife Maggie and me is that the arrangement allows us to enjoy the very pleasant winter weather in Miami and some of the outdoor activities that it fosters (golf, for instance, in my case).  From 1982 until the present writing, I have been the recipient of a number of honors and awards for my research. Naturally, I have been very pleased to be the recipient. Yet, in thinking back about what aspects of my research have given me the greatest pleasure, I would not place the honors and awards first. I think that my greatest pleasure has come from each first demonstration in my laboratory that experiments designed to test a new hypothesis developed to explain some earlier, often puzzling or paradoxical finding, have given results consistent with the hypothesis. It is not just the immediate pleasure of obtaining such results but also the anticipated pleasure of discussing the results with others doing research in the same area – obviously an ego supportive aspect.  I still enjoy doing bench work in the laboratory with my co-workers. The research still is rather “old fashion” pharmacological research. I was very lucky to stumble on unexpected results in 1978 that led to the finding of endothelium-dependent relaxation and EDRF, and eventually to NO; for if I had not, I would probably have still concentrated on research on receptor theory and mechanisms, and been left far behind by others in that field who have so brilliantly and successfully developed and used molecular biological and other advanced methodologies in their research. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
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| Biographical | The first two decades of my life were spent in the New York City area, where the families of both my parents had settled in the 1920s after immigrating from Italy. My father had been a ship builder in Naples but my mother was still a young child when she came from Sicily. They met for the first time in Brooklyn, New York in the 1930s, were married, and then moved to the nearby coastal city of Long Beach. I was born on May 31, 1941 in Brooklyn and my brother, Angelo, followed on January 10, 1944. My father worked as a carpenter, whereas my mother elected to bring up her two sons at home.  Long Beach was a beautiful town, about 25 miles east of New York City located on the south shore of Long Island. We had a lovely home within walking distance of the beach along the Atlantic ocean. I can still recall walking to the beach and going for a swim nearly every day in the summer. My greatest joy each morning was building gigantic sand castles using dripping sand wetted by the incoming tide. All my friends believed and predicted that I would grow up to become an architect or engineer. This view was reinforced by my eagerness even as a young child to disassemble anything I could find and put it back together again. The joy of discovering that I could actually get the object to function again was quite rewarding and satisfying. But my greatest joy came when I was 8 years old. To my surprise and delight, mother and father finally responded favorably to my relentless request to have a chemistry set, and bought me one. I can recall vividly following every step of every experiment and becoming overjoyed at the success of each one. This was much more fun than building sand castles on the beach. My inquisitiveness drove me to the library to study more applied aspects of chemistry. Soon after completing dozens of additional experiments and going through several larger chemistry sets, I realized that what I really wanted to accomplish was to build a bomb and to send up a rocket. After about one year of experiments, I finally achieved those goals, albeit at the expense of numerous horrified reactions from the neighbors.  My interest in chemistry remained strong at Central Grade School and Long Beach High School, which led me to apply to Columbia University in New York City to study chemistry and pharmacy. I was especially pleased when I learned that I had been accepted to the freshman class at Columbia. I wanted to attend a university that was within commuting distance of home because I did not want to leave my family and friends in Long Beach. During my high school years I had developed a great interest in playing ball and racing cars, and I did not want that to come to an end, at least not just yet. My favorite sport was one-on-one stickball, the New York City sport of sports, where a “bouncy” rubber ball is thrown by the opponent pitcher against a brick or cement wall on which is drawn a “strike zone”. The batter uses a stick conveniently detached from a suitable broom or mop to hit the fast pitched ball. When I was not playing stickball I was building and racing cars at the West Hampton Drag Raceway. I guess I could never get away from taking things apart and putting them back together again. Indeed, I spent many long hours thinking about whether I should study chemistry or open up my own drag racing shop out on Long Island. Well, chemistry it was. I took dozens of chemistry courses, but a course in pharmacology, although poorly taught, really caught my attention. I studied the subject well beyond the course requirements and tried to hang around the pharmacology laboratories as often as I could. The result of this was my application to graduate school in pharmacology upon graduation from Columbia University in 1962.  I was delighted to be admitted to the pharmacology program at the University of Minnesota in Minneapolis, which was considered to be one of the best departments of pharmacology in the nation at that time. Actually, I had applied to the University of Wisconsin in Madison, where the department was located when I first applied. But for one reason or another, the entire department was relocated from Madison to Minneapolis just after I had been accepted in Madison. A bit confused, I reported to Minneapolis in September of 1962 to study pharmacology. At first, things were difficult for me because I had left my family, friends, stickball, racing cars and the beach behind. And then things got even worse when I experienced my first winter season of -40°F with winds of 30 mph. But I survived my first winter and went on to enjoy the upper midwest and the “Big Ten” college football games.  My studies in graduate school involved developing a better understanding of why and how neurons of the sympathetic nervous system innervate the heart and produce and release norepinephrine. I spent three of the most intense years of my life in the laboratory, where I was determined to unravel every bit of information possible within the time frame allotted to me to satisfy the research requirements for the PhD degree in pharmacology. My research was different from most in that it required, in addition to pharmacology, a great deal of knowledge in several other distinct disciplines such as physiology, biochemistry and anatomy. My major, of course, was pharmacology and I selected cardiovascular physiology as my minor. But that was insufficient, so I took several additional courses in biochemistry and anatomy. The most demanding course I took was enzymology, taught by [Paul Boyer](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1997/index.html), who was awarded the Nobel Prize in Chemistry last year (1997). I have not stopped using enzymology in my research since taking that course. My research turned out to be acceptable to my committee, chaired by the late Frederick E. Shideman, MD, PhD, who was also Chairman of the Department of Pharmacology at the University of Minnesota. He decided that I should write four separate manuscripts on my thesis research and that we should submit them to the Journal of Pharmacology and Experimental Therapeutics. The editors of the journal accepted all four papers and published them back-to-back in one issue of the journal, a feat never again repeated either by the journal or by me.  After Minneapolis, I accepted a postdoctoral position at the National Institutes of Health in the Laboratory of Chemical Pharmacology in the National Heart, Lung and Blood Institute. My mentor was Elwood Titus, a brilliant scientist who was able to mix chemistry and pharmacology with the greatest of ease. I tried to learn as much as I could from him in two years. Perhaps I tried a bit too hard. For example, he asked me to study the chemistry of beta adrenergic receptors and I decided that I was going to isolate, characterize and elucidate the chemical structure not only of beta but also of alpha adrenergic receptors, all in two years. Having published four consecutive papers in a distinguished journal on my first try, I thought that my research career was going to be a breeze. The N.I.H. proved to me that this was not going to be the case, and it was not. My work resulted in only one publication, but the agony of frustration caused me to mature quickly. The atmosphere of the N.I.H. was highly conducive to learning science and I had the opportunity to discuss my work and research in general with Bernard Brodie, Jim Gillette, [Julius Axelrod](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1970/index.html) and other distinguished scientists.  My first real job after my research training was with the drug industry. Geigy Pharmaceuticals recruited me in 1968 with an attractive package including the responsibility of heading the biochemical and antiinflammatory program. Although this was an entirely new research topic for me, I accepted the position because of the enormous responsibility that would suddenly be mine. The work was quite satisfying in that I became a part of a larger group whose efforts led to the development and marketing of a new nonsteroidal antiinflammatory drug (diclofenac). About half way through my career at Geigy, my daughter, Heather, was born. I recall that day vividly (January 10, 1970) because I had to rush my wife to the nearby hospital in the midst of a snow storm. But all turned out well and I found myself devoting a great deal of time to something other than my own research. With the birth of Heather came a move from a small apartment in Hartsdale to a much larger unit in Irvington on the Hudson. This was a lovely neighborhood in which to raise a child.  In addition to my work on drug development, Geigy allowed me the freedom to pursue basic research in biochemical pharmacology, which led to my interest in studying the relatively new cyclic nucleotide, cyclic GMP. Although I enjoyed my work at Geigy Pharmaceuticals, when the company merged with Ciba Pharmaceuticals I decided to try my hand at academic research and teaching. In January of 1973, I accepted the position of Assistant Professor of pharmacology at Tulane University School of Medicine in New Orleans. I chose to go to Tulane because I wanted to continue my research on cyclic GMP, and there was a young pharmacologist at Tulane with the same interest. We moved to New Orleans, where we bought our first home in Terrytown, an attractive nearby suburb.  My interest and motivation in studying the possible physiological significance of cyclic GMP grew and grew during my first two years at Tulane. Thanks to my own laboratory and those of other interested collaborators, we made many significant contributions to the field of cyclic GMP and cyclic nucleotide research in general. My early work with cyclic GMP involved leukocytes and the heart, but this eventually led to an interest in blood vessels. I recall reading an interesting paper by [Ferid Murad](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1998/index.html)‘s group in 1977, in which nitric oxide and various nitro compounds were shown to activate the cytosolic form of guanylate cyclase and to elevate cyclic GMP levels in various tissues. Nitroglycerin was one of those nitro compounds that Ferid had studied and speculated might release nitric oxide which then activated guanylate cyclase. It occurred to me that nitric oxide might account for the vascular smooth muscle relaxing action of nitroglycerin and that cyclic GMP might be the second messenger responsible for mediating the vasorelaxant effect of nitric oxide. In 1979 we published the first account of the capacity of nitric oxide to relax vascular smooth muscle. We purchased a small cylinder of nitric oxide gas, made a dilution in nitrogen (nitric oxide is very unstable in the presence of oxygen), and injected a fine stream of gas bubbles into an organ bath in which was mounted a strip of bovine coronary artery precontracted by addition of phenylephrine. The result was a rapid and profound relaxation of the coronary artery strip. This vasorelaxant effect of nitric oxide was blocked by addition of hemoglobin, which promotes oxidation of nitric oxide, and methylene blue, which had been known to inhibit guanylate cyclase. And so we knew right away that nitric oxide was probably responsible for the vasorelaxant effect of nitroglycerin and that cyclic GMP was the likely ultimate mediator of relaxation, just as Ferid Murad had predicted.  We wondered whether the platelet antiaggregatory action of certain nitrovasodilators could also be attributed to nitric oxide and cyclic GMP. A relatively straightforward experiment was conducted with human platelet-rich plasma, in which we examined the influence of added nitric oxide on ADP-induced platelet aggregation. The results were dramatic. Nitric oxide potently inhibited platelet aggregation and actually reversed aggregation once it had occurred. This effect was mediated by cyclic GMP. Thus, at least two biological actions of nitric oxide were clear from these early studies. Nitric oxide is a vasorelaxant and inhibitor of platelet aggregation, and both effects are mediated by cyclic GMP.  The next step was to elucidate the mechanism by which nitroglycerin is converted to nitric oxide by vascular smooth muscle. After reading nearly every paper in the field of organic nitrate esters and their vasodilator effects, I was motivated by the work of Phil Needleman, who showed that the vasodilator action of nitroglycerin and other organic nitrate esters was dependent somehow on the presence of thiols. A long and tedious series of experiments in my laboratory led to the discovery that thiols were required for the activation of guanylate cyclase by nitroglycerin and related nitrovasodilators. Interaction between thiols and nitro compounds led to the formation of intermediate S-nitrosothiols, which were chemically unstable and decomposed to liberate nitric oxide gas. Depletion of tissue thiols resulted in diminished vasorelaxation by nitroglycerin because nitric oxide could no longer be generated. Moreover, tolerance to the vasodilator action of nitroglycerin appeared to be due to thiol depletion, which could be reversed by adding back thiols in order to generate more nitric oxide. This work was published in 1981 in the Journal of Pharmacology and Experimental Therapeutics.  Having elucidated the mechanism of action of nitroglycerin as a vasodilator, the next step was to understand how nitric oxide activates guanylate cyclase. An elegant series of experiments was published in the late 1970s by Patricia Craven and Fred DeRubertis, showing that activation of guanylate cyclase by nitric oxide might require the presence of heme. This made sense to me because heme iron had long been known to have a high binding affinity for nitric oxide. Suppose guanylate cyclase had a heme prosthetic group that bound nitric oxide and somehow became activated to generate more cyclic GMP from GTP? In 1981 we set out to purify and characterize guanylate cyclase from bovine lung. A young biochemically trained postdoctoral fellow from Yale University, Mike Wolin, joined my laboratory to tackle this project. After an incredibly long and tedious series of experiments, each often lasting for 96 consecutive hours, we found the heme in purified guanylate cyclase. Subsequent experiments revealed that the presence of enzyme-bound heme was an absolute requirement for guanylate cyclase activation by nitric oxide. We went on to propose that nitric oxide reacts with heme iron to alter the configuration of the catalytic binding site for GTP and promote the conversion of GTP to cyclic GMP and pyrophosphate. In conducting these experiments, we discovered that the non-nitric oxide containing substance, protoporphyrin IX, activated heme-deficient guanylate cyclase by kinetic mechanisms that were indistinguishable from the mechanism by which nitric oxide activates heme-containing guanylate cyclase.  Although the above observations were exciting, they were also puzzling because it was unclear why mammalian cells were so sensitive to nitric oxide. Why do we have receptors for nitric oxide, an air pollutant and a metabolite of nitroglycerin? Was it possible that our own cells actually produced nitric oxide or nitroglycerin but we were unaware of it? In 1983, my laboratory set out to determine whether or not mammalian cells can produce either nitric oxide or a nitro compound that could be metabolized to nitric oxide. A separate project in the laboratory was to study endothelium-dependent vasorelaxation and to attempt to identify the mysterious “EDRF” (endothelium derived relaxing factor) discovered three years earlier by [Robert Furchgott](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1998/index.html). Both research projects came together in 1984 when we suddenly realized that EDRF and nitric oxide possessed similar pharmacological and biochemical properties. EDRF and nitric oxide were both chemically unstable and both activated guanylate cyclase and elevated tissue levels of cyclic GMP. The cyclic GMP elevating and vasorelaxant effects of both EDRF and nitric oxide were inhibited by addition of methylene blue to organ chambers. These findings, reported in 1984, prompted me to ascertain whether EDRF, like nitric oxide, required bound heme on guanylate cyclase in order to activate the enzyme and stimulate cyclic GMP formation. I can recall vividly the positive results of the first experiment, and I knew we had it. EDRF must be nitric oxide. I first reported these findings in the summer of 1986 at a vascular conference held at the Mayo Clinic in Rochester, Minnesota. Unexpectedly, at least to me, my colleague Robert Furchgott presented his own evidence that EDRF might be nitric oxide. I presented additional evidence a few months later at the fall American Heart Association meeting in Dallas and at the spring FASEB meeting in Washington, DC in 1987. So now it was clear why nitric oxide is such a potent vasorelaxant. This small lipophilic chemical is produced by vascular endothelial cells and functions to decrease vascular smooth muscle tone and to inhibit platelet aggregation.  The frenzy and excitement of these times in the mid-1980s was stalled at times by my divorce and my decision to leave Tulane University and begin a new personal life and academic career at UCLA School of Medicine. I moved to Los Angeles in May of 1985 and bought a small home in Encino, just 12 miles from the UCLA campus. My daughter, Heather, joined me in 1988 and attended California State University at Northridge. As a result of witnessing her dad’s commitment to many long hours of research and teaching, Heather chose to major in radio, film and television. At first, her decision to shy away from a career in science concerned me, but then I realized how talented she was and how successful she would become.  The discovery that EDRF was nitric oxide led to an avalanche of studies that created an exciting new field in biological research. New physiological and pathophysiological roles for nitric oxide were being discovered on a weekly basis. In record time, several prominent laboratories elucidated the biochemical mechanisms involved in the synthesis of nitric oxide by various cell types. While studying the relaxant effects of nitric oxide on vascular and nonvascular smooth muscle from corpus cavernosum erectile tissue, we realized that the naturally occurring physiological neurotransmitter involved in the erectile response in mammals was unknown. John Garthwaite had just reported that nitric oxide was a neuro transmitter in the brain, and we wondered whether or not nitric oxide could be the neurotransmitter in the so called nonadrenergic noncholinergic neurons that were known to innervate the corpus cavernosum smooth muscle. After all, nitric oxide released from such nerves would be expected to diffuse into the nearby vascular and nonvascular smooth muscle and cause relaxation. Such an effect could account for the marked relaxation of both vascular and nonvascular smooth muscle that accompanies the erectile response and allows for the engorgement of blood in the sinusoidal or trabecular network of blood vessels in the corpus cavernosum. The first carefully designed experiment was successful. Electrical stimulation of strips of rabbit corpus cavernosum caused a transient but marked smooth muscle relaxation that was prevented by addition of a nitric oxide synthase inhibitor and enhanced by addition of a cyclic GMP phosphodiesterase inhibitor. Addition of authentic nitric oxide to organ chambers mimicked the effects of electrical stimulation. A subsequent experiment revealed that electrical stimulation results in the production of nitric oxide in the corpus cavernosum. Further studies using human tissue showed that patients with impotence suffer from an impaired nitric oxide cyclic GMP pathway in the erectile tissue, and this work laid the foundation for the development by others of a drug that proved to be effective for the treatment of impotency in humans. Sildenafil (ViagraR) promotes the erectile response by inhibiting a specific isoform of cyclic GMP phosphodiesterase and allowing cyclic GMP to accumulate when guanylate cyclase is activated by nitric oxide released from the nerves innervating the erectile tissue.  In the fall of 1994, I met Sharon Elizabeth Williams, a lovely and charming medical student here at UCLA. Sharon had been a nurse anesthetist for several years and then decided to obtain an M.D. degree in order to practice anesthesiology at a more professional level. After graduating from UCLA, Sharon moved to the east coast to begin her internship and residency at Johns Hopkins University. Shortly after her move, we started dating by long distance and were married in July of 1997. A year later, in the spring of 1998, Sharon transferred back to UCLA to continue her residency in anesthesiology. Finally, we were together. During the week we reside in an apartment adjacent to the UCLA campus in Westwood and we spend our weekends in my home in Malibu.  As a result of my work during the past decade, many investigators jumped in to extend our findings. This led to the development of close collaborations with numerous laboratories and the formation of close and genuine friendships in many different parts of the world. I treasure these friendships even more than the awards I have received for my research accomplishments. I also realize that these accomplishments would not have been possible without the interest, hard work, and commitment on the part of my technical assistants, graduate students, postdoctoral fellows, medical fellows, visiting scientists, research collaborators at home, and collaborators at other institutions.  Another rewarding development has been my discovery that I also have a real knack for and love of teaching what I know to medical and graduate students. I have consequently made teaching a regular part of my schedule since I came to UCLA and I cherish the Golden Apple teaching awards I have won from my classes. I trust that I have helped guide at least some of these young people toward careers that will be a blessing to them and to humanity. In my own case, the combination of biomedical research and teaching continues to provide me with an exciting and useful life, and I am exceedingly grateful. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q1 | Ferid Murad, welcome to this interview with Nobelprize.org. Could we begin by you telling us a little about how you became a scientist in the first place? |
|  | Ferid Murad: Thank you, I’m pleased to be here. I had a knack as a youngster for mathematics and science, I really enjoyed it, starting in the third and fourth grade. I found that those classes were so much more fun and appealing than some of the other classes, the English classes and the government classes and so forth. Some of the science teachers I had along the way were very encouraging and that helped to have the mentors there at the right time. When I was about 10 years old, I thought I was going to go into medicine. How I decided that I don’t know. My parents had very little education but I’d recognised the importance of education because of them. I thought my first choice would be medicine and my second choice would be teaching, perhaps mathematics or chemistry and my third choice was pharmacia or pharmacology. I’ve found that those goals haven’t changed. I think it’s because I really enjoyed science and mathematics, I had a knack for it and I did very well with it.  The humanities in school were not quite as exciting to me but I did it. I learned how to memorise, I played mathematical games in my mind. I’d walk down the street and memorise licence plate numbers, things like that. I developed lists of random numbers and tried to learn them all and memorise them. It was great preparation for medical school but because of the knack in science, I thought that what I should do is go into medicine. I also, because of teachers, thought teaching was a possibility. One summer, I was interested in butterflies with a friend, I was a youngster and we were catching butterflies. I didn’t want to touch them with my fingers as I mounted them with pins in this cloth or frame that I constructed, so I went to the local pharmacist and asked them if I could have some cyanide, potassium cyanide and hydrochloric acid and he gave it to me, today that wouldn’t happen.  Those were the days.  Ferid Murad: But that got me interested in chemistry and I also was thinking about the possibility of pharmacia or pharmacology and in eight grade we were asked to write a paper, an essay about career choices: What do you want to be when you grow up? My first choice was medicine and my second was teaching, being a professor, and my third choice was a pharmacist or pharmacologist. I’ve become all three of those. I guess I knew what I wanted to do and I had goals and worked very hard for it, but what really influenced the whole process so much was the recognition, the encouragement from so many mentors, high school teachers, college teachers and certainly graduate school and medical school. When I decided, instead of going to medical school, to go into an MD PhD programme which was a brand new, spanking new programme in Cleveland, had just gotten started.  That was the programme that [Earl Sutherland](https://www.nobelprize.org/prizes/medicine/1971/sutherland/facts/) began.  Ferid Murad: Earl Sutherland began that programme in Cleveland in 1957, a couple of years after he went there as chairman of the pharmacology department. Earl was an MD who was a clinician in the army and subsequently went back to St Louis and trained with [Carl Cori](https://www.nobelprize.org/prizes/medicine/1947/cori-cf/facts/) in biochemistry and got interested in glucagon metabolism and phosphorylase and then as a very young man, went to Cleveland as chairman of pharmacology. A couple of years later he hired a young assistant professor, Ted Rall who was a biochemist and Ted looked after his laboratory as Earl did his administrative things, as the departmental chair, but Earl had an incredible vision as a physician and as a scientist, he could put it all together. Ted had the skills of how to do that right experiment and make it work, he had the hands for the laboratory and he insisted on all kinds of controls, so I was fortunate to have worked with both of them.  Earl had this incredible vision about how biology should work or did work, and Ted taught me how to do the experiments so that you would believe your data. Ted would ask for so many controls that, as an MD PhD student I kept flipping back and forth between medical school and graduate school because it was not a federally funded programme at the time, it was all pieced together with some of Earl’s donations from some /- – -/ companies for his interests with glucagon with Lilly, a training grad that he had and his research grads. In order to get my stipend, I had to spend so many months a year in the graduate programme, otherwise I’d have to forfeit my stipend, so I was flipping back and forth between medical school and graduate school and that was exciting and the curriculum was quite unusual. It was the first school, not only to create the MD PhD programme because of Earl, but also to teach in a different fashion with the working systems, it was a very integrated approach to teaching. One lecture would be anatomy and the next would be physiology and the next would be biochemistry and the next would be clinical applications, so you learned how to put it all together very quickly. Having worked with both Earl and Ted, who were quite different and having this curriculum, I just got really turned on and when I decided to go into this programme, instead of going to medical school, my parents were rather disappointed.  I can imagine, because you were taking a step away from a traditional career.  Ferid Murad: My parents wanted me to become a doctor and go home and practice in a small town on the south side of Chicago, Whiting, Indiana, and I didn’t know what to say to them. I looked at them and I said, If I become a doctor and come home and practice, in my entire lifetime maybe I can help 2 or 3,000 people, but if I go into research and if I’m lucky and find something important, I’ll be able to help a lot more. They then understood it and it made sense to them. I really got turned on, both in medicine as well as laboratory, got married, had quite a few children, we had four children when we finished that seven-year programme …  … and you needed a job to pay for them.  Ferid Murad: … and I wasn’t ready for a job, I wanted some more training, so I decided to take an internship of residency and went to Mass General and that’s where I got to meet [Mike](https://www.nobelprize.org/prizes/medicine/1985/brown/facts/) and [Joe](https://www.nobelprize.org/prizes/medicine/1985/goldstein/facts/) and a lot of other wonderful people. |
| Q11 | Tell me about the beginning of Mike Brown and Joe Goldstein’s relationship, because you were there at the start. |
|  | Joe came from Dallas, he had gone to medical school at South Western and Mike came from Pennsylvania, University of Pennsylvania, and they were both brilliant students. The whole group, there were only 12 interns in their class and I think all of us were the top one or two students in our classes, so we were all very bright people, but only a couple of us had experience in a laboratory. I was one, Tony Gotto was another with a PhD and the rest hadn’t had much experience in a laboratory, but that class turned out a lot of academicians and scientists, a stellar group: Tom Smith who became Head of Cardiology at the Brigham and Ed Scolnick who became President of Research at Merck and myself, it was really quite a group.Mike and Joe have had this extraordinary relationship of working so closely together for 35 years, did they recognise it immediately when they started?  Ferid Murad: No, I think they became friends initially, like we were all really good friends and colleagues. There wasn’t much free time in this process, we worked 100 hours a week and whenever you had a little bit of free time, we’d go to somebody’s house for a party. We’d steal some lab alcohol and make some punch and that was entertainment for a weekend. I think their relationship grew when they got to NIH. They worked in different laboratories, but I think their relationship was fostered and promoted. Then what happened was that Mike, after NIH, went to Dallas to do a fellowship in gastroenterology with Dan Foster, I believe, and Mike went to Seattle to do a fellowship in genetics.  Yes, Joe went to Dallas and Mike went to Seattle.  Ferid Murad: No, Mike was in Dallas and Joe went to Seattle.  Oh, really, okay.  Ferid Murad: Then Joe was recruited back to Dallas as a young faculty member and that’s when their collaboration began. It was probably, let me guess, I would say the early or mid-1970s, early 1970s probably. They were now both on the faculty, seeing each other and their relationship really took off, with genetic approaches lipid metabolism, that’s how it got fostered. |
| Q18 | Yes. One thing that you seem to emphasise when you talk about science is the amount of work that’s required and you just referred to 100 hour weeks. Is that something that came out of your background? |
|  | Ferid Murad: My parents worked very hard, my father was an immigrant, he was an Albanian from Macedonia, he came to the US when he was young, 19. My mother he met later, she was American. Both came from very poor backgrounds, little or no education, they ended up in a family restaurant business, putting in long, long hours, 14-, 16-hour days. I grew up in that environment and although they had hadn’t had much education, they really encouraged their three sons and I was the oldest of three, to go on to school. If we were going to have a different lifestyle, we had to get an education and that was apparent and a lot of folks coming into the restaurant, this was a family restaurant where the workers and teachers and bankers were coming in for lunch, many of them became mentors and advisers and they kept encouraging me as well. My parents gave me an awful lot of freedom, they told me how important education was, I recognised how important it was and if I was going to have a lifestyle different than theirs, I had to have an education, but I saw the work ethic that was necessary to accomplish what you wanted to do. I was a bright kid, I had a pretty decent IQ I think, but I’m not brilliant and I made up for it with a lot of extra hard work and I think you can do that, so I’ve always, I think my whole life, worked 70, 80, 90, 100 hours a week. I still work 70, 80 hours a week.  That’s a message worth spreading.  Ferid Murad: You do it if you enjoy it, it’s not painful to do it, it’s fun to do it. It’s fun to go to work and solve problems. |
| Q3 | Another thing I think you stressed in some of your writings was the need for competition, the importance of competition. |
|  | Ferid Murad: I think competition is important. I competed with my brothers, I competed with classmates in school, it was fun, we had a great time. One of my best friends I met in kindergarten, we’ve known each other ever since, he became an aeronautical engineer, he was on some of the projects with Boeing that built the Stealth Bomber, very talented aeronautical engineer. I went the medicine route but when we see each other, in the past we would compete with chess or we would compete with whatever and we still compete, but it’s fun.  Okay.  Ferid Murad: I say competition is very healthy, it motivates you, it drives you. It’s got to be friendly competition, it can’t be horribly aggressive competition, but it’s most fun when you win.  Yes, that’s true. I suppose that it’s a fine line to tread between friendly competition and unfriendly competition.  Ferid Murad: Correct. |
| Q25 | When you think of mentorship, what characterises a good mentor? |
|  | Ferid Murad: It’s like raising a family, you want to encourage your trainees or children, you want to provide everything they need, the resources, the space, the equipment, ideas, but you expect them to contribute as well and what I enjoy is having, not arguments but discussions about my ideas versus theirs. I want them to be open and straightforward and tell me what’s on their mind, tell me when I’m wrong and I’ll do the same with them and that’s an interesting interaction and dialogue. There are lots of educationaI systems that don’t work that way, where the trainees feel suppressed, afraid to test the boss, ask questions and I think that’s wrong, that inhibits creativity, I think.  I suppose classically, medical training fits into that.  Ferid Murad: Exactly. |
| Q26 | When you recruit students to work in your lab, what do you look for in them? |
|  | Ferid Murad: I have a lot of international students. Of the 130 or so trainees I’ve had, probably ⅔, ¾ are foreign, from all over the world and the others are American, I mix them up. The trainees have backgrounds in genetics, molecular biology, biochemistry, pharmacology, physiology, cell biology and I put them all together and they all teach each other something. They end up collaborating. They all have their separate projects and when they come to start working in the laboratory, I offer my ideas but I want them to meet everybody and come back with some of their own ideas and they will settle in on a project. They each have a project to work on, but all of the projects intermingle and overlap to some extent, resulting in collaborations and assistance from other people in the laboratory, so they’re all learning something. I learn a lot. |
| Q13 | How do you organise a lab where people are working on different projects, with different skill sets and yet you need them to interact? |
|  | Ferid Murad: We have lots of meetings, lab meetings weekly, where three or four of them will present their work over the last month or so, so over the course of a month, basically everybody has an opportunity to present what they’re doing. It’s an opportunity for others to see what they’re doing, learn about new techniques and ideas, opportunities to collaborate. I’m there to orchestrate, I’m there to provide the resources, test some of the ideas, offer ideas but not inhibit experimentation. I never ever tell a person not to do the experiment, I say if that’s important for you and interesting enough for you, you do it, even if it means doing it on your own time, you do it. I think it’s good and healthy for a trainee to discover something themselves and when they do, they really get into it, they really have ownership of that. |
| Q56 | We’re a bit jumping out of temporal sequence, but when you found yourself in industry in the 1980s and 1990s, were you able to apply the same principles to allowing people to do their own experiments? |
|  | My laboratory, when I went to industry, was different than the other laboratories. It’s only because I went into the industry in a very senior position, with a lot of authority and a lot of resources and they weren’t hiring me to run a laboratory. They were hiring me to be an executive to run RND, but I said, If I’m coming into industry, the only way I will come is with my own laboratory, post-docs and grads, because I want to continue doing my own thing in the midst of all of this. They agreed to that, they didn’t want to lose me as a candidate, but once I got in the system, then they said, You’re really an executive, why are you running this laboratory? I said, I’m running the laboratory because I love it and how can I manage research if I don’t do it myself? You have to be able to do it and you have to be an example. I’ve always thought that, as an administrator – and I’ve become more and more of an administrator over the years – that I have to do better and more research and more funding than anybody else to be a leader. If I can’t do that, I shouldn’t be a leader, so I work very hard at it. |
| Q38 | Were you able to have any influence over the way that Abbott [Laboratories], as a whole, did its research? |
|  | I influenced a lot of projects. I terminated some that I didn’t think were going to be successful. It’s very difficult to do that, you have to do it slowly and it’s not easy and created a lot of new projects. I think I was having a lot of fun at Abbott, learning an awful lot about the pharmaceutical industry, about toxicology and formulation and marketing and acquiring a lot of skills, that I hadn’t had from academics, but what disturbed me was my senior managers. There were about three people above me in the company, were marketing sales types, they were not scientists and their philosophy and notion about science was quite different. They thought that you could open the spicket and turn it off at will, they didn’t realise that you had to have a programme going on for some five or ten or 15 years sometimes before you saw a product come out of it and that you couldn’t just stop it all of a sudden for fear that you’d chase off a lot of talented scientists. I was also concerned that their investments in RND were not sufficient compared to their investments in sales and marketing. The sales marketing budgets were twice the RND budgets and that didn’t make sense to me for a technology-based company.  Is that still the case?  Ferid Murad: Yes, it is, in fact it’s getting worse and I think that’s why the pipeline in large multinationals is drying up. |
| Q23 | We’ll return to that theme in a little while. I wanted to focus on the discovery that in particular led to the award of the Nobel Prize, together with [Robert Furchgott](https://www.nobelprize.org/prizes/medicine/1998/furchgott/facts/) and [Louis Ignarro](https://www.nobelprize.org/prizes/medicine/1998/ignarro/facts/) in 1998. You found that nitroglycerin, which had been around for 100 years and used to relieve chest pain and angina, works by the release of nitric oxide which is an unusual signalling molecule because it’s a gas and the question that seems to be begging is how come nobody had found this for 100 years? |
|  | If you went looking for a gas or a free radical as a messenger, it would be an impossible project and the way we discovered it was really through the back door, through another avenue. I grew up in Cleveland working with Sutherland and Rall, interested in cyclic AMP. How do hormones regulate cyclic AMP and what are the biological effects of cyclic AMP to regulate glycogen metabolism, fat metabolism etc?  Cyclic AMP being the first second messenger.  Ferid Murad: The first intra-cellular second messenger and then in the mid-1960s, cyclic GMP was discovered by some chemist. I kept an eye on the field because I was intrigued with that notion of another messenger molecule and over the next few years, a couple of messengers started popping up. Calcium came along, prostaglandins were looking promising, d*iacylglycerol was looking* promising, cyclic GMP started looking promising and when I left my training in NIH to go to my first faculty position at Virginia in 1970, I said, I’m going to switch from cyclic AMP to cyclic GMP. As a young faculty member, I saw a lot of activity in the field of cyclic AMP research, a lot of laboratories were now working with this. In 1971, Earl Sutherland got the Nobel Prize for that, so that attracted even more people and I didn’t want to compete with these big factories as a young faculty member. I thought there was a lot of high risk to that and I saw cyclic GMP as a new emerging field where I could take my information and ideas from the cyclic AMP field and work in another direction, so I made the switch to cyclic GMP. I wanted to figure out how hormones and drugs regulated cyclic GMP production and what are some of the biological effects of cyclic GMP, those were unknown at the time.  In our very first experiments we found that tissue extracts contained not just one enzyme to make cyclic GMP but at least a couple, a soluble activity and a particulate activity. With some biochemical studies we thought they were different isoforms, one had cooperativity with substrate, the other did not and I thought, wouldn’t it be interesting, whereas adenoid cyclase at the time appeared to be a single isoform in the membranes. We now know they’re mini-isoforms but in those days we thought there was just one and for guanylate cyclase, it’s cousin, to now have multiple isoforms. I thought wow, this is interesting, they’re different compartments in the cell, perhaps they are different hormones and mechanisms to regulate each of these enzymes. There will be different pools of cyclic GMP in the cell, perhaps with different functions and wouldn’t that be an interesting complicated problem to tackle? We went after it, it turned out hormones wouldn’t activate the enzyme in cell free preparations, which was one of our goals, we wanted to figure out how hormones worked, how did they couple to the cyclase regulation? They didn’t work in cell free systems and because we thought we had different isoforms, I thought maybe different hormones would work on each isoform differently. Ultimately we had to purify those isoforms and clone them and express them but that took a long time, that took 12 years probably, so I took a shortcut and threw in the kitchen sink. I knew that you can’t trust kinetic data in crude preparations room for a lot of artefacts. Our preparations had nucleotidases, phosphatases, phosphodiesterases, competing for substrate, competing for a product that we were measuring, so what we were seeing could have been spooky and erroneous…  Artefactual, yes.  Ferid Murad: I took a shortcut and made a cocktail of all sorts of inhibitors like you pull off the shelf, to inhibit nucleotidases, phosphatases, phosphodiesterases, pyrophosphrate, fluoride, azide, hydroxalamine, methylzanthines.  As you say, everything that was on the shelf.  Ferid Murad: Everything I thought would inhibit this pathway and re-examine the kinetics and accidentally found that some of these compounds activated the enzyme. Azide, hydroxalamine and sodium nitrate and that was an important lead. As a student, I recognised the importance of fluoride activation about doing cyclase. We had another small molecule in the cyclic AMP system, that turned out to be very valuable in understanding the role of adenoid cyclase regulation and the role of G proteins.  So you were pre-warned to look for small molecule activation.  Ferid Murad: Yes, there was a precedent for it and now we stumbled into another class of small molecules that did it with guanylate cyclase and I said, Maybe these will be hormone surrogates that are bypassing the system. Obviously the hormone receptor binding at the cell surface is not communicating to the cyclase. In a cell free preparation we’re missing something but these are activating, maybe they’ll help us figure out what we’re missing and that’s what led us in the nitric oxide, we took these compounds and we put them in the tissues and they raised cyclic GMP levels in lots of tissues, including smooth muscle. I thought cyclic GMP in smooth muscle would cause contraction. As a student I knew that cyclic AMP caused relaxation, I thought they would antagonise each other.  But no?  Ferid Murad: That’s not what we saw, they caused relaxation and once we saw that we said, What do other smooth muscle relaxants do? What does nitroglycerin do and what does nitroprusside do? We put them in and sure enough, they elevated cyclic GMP levels and I don’t mean intact cells but in broken cells. Now we ended up with a family of molecules that were capable of increasing cyclic GMP levels in intact cell cultures and slices and tissues, as well as activating the soluble isoform of guanylate cyclase. Then it became a mystery story for a couple of years. What is this intermediate, they’re all pro drugs and an important lead for us was the discovery that some tissues did not respond to azide. That’s because they possessed inhibitors and we purified those inhibitors and they were haemoglobin and myoglobin, so we knew that haem proteins could somehow interfere with the activation. We had a long list of we call nitro vasodilators, they were all nitrogen containing, some were nitrose, nitrosos, hydrazines, whatever. We said, Could the intermediate by nitric oxide? because in the literature, we found papers with a very high affinity of nitric oxide for the haem prosthetic group of these proteins …  Okay, so it was binding nitric oxide.  Ferid Murad: … and we said, Let’s see if it’s nitric oxide, and sure enough it was. That’s how we found it. It was accidental, some biochemical you know, rationalisation, serendipity, it happened that we had to have smooth muscle in the lab at the time.  Yes, many things coming together and above all, a preparedness to look at the data in a particular way.  Ferid Murad: We were approaching it from a very biochemical direction but I thought in a very meaningful, logical, sequential fashion. The big mystery is, how do we jump from all these nitro vasodilators, which we thought were pro drugs to the activator of G cyclase. We stumbled with it for a couple of years and then finally we realised there could be nitric oxide and made it and sure enough it worked. |
| Q57 | Have you pondered whether there were people out there in previous decades who were close to the possibility of solving this problem? |
|  | Yes, there some other laboratories, one that I remember quite well. A fellow up in Minnesota, Nelson Goldberg who was also interested in cyclic GMP, trying to figure out what regulated this production, what were some of its functions? He was working with lymphocytes and a lot of other systems. Nelson was really a very aggressive, hustling, clever scientist, however Nelson, although he was a good friend, we were fierce competitors and a lot of stuff that he did I didn’t believe. I could never tell whether Nelson did the experiment once or a dozen times and Nelson had the preconceived notion of this is what cyclic GMP should do, it should antagonise cyclic AMP. He came up with yin yang hypothesis, one goes up, one goes down, this was all nonsense in my opinion, because we couldn’t see any of that sort of stuff, but what it did for us is motivated us to work harder. We were trying to be number one and Nelson was very close, he could have, had he not forced his data to his preconceived notion of how things worked, he probably could have found before us, but he was forcing all the data to fit what he believed should be and I think that’s always a bit mistake in science. Instead of really saying, this didn’t work the way I thought it would work, maybe something else is going on. That’s what Ted Rall taught me to do. Earl Sutherland taught me to be as imaginative and free associating as you can be, just pluck it out of here and there and try to figure out how to put them together, his mind was incredible. Ted taught you how to pigeonhole all of it into a spot and do the experiment in such a way that it was either right or wrong. So it was fun to have had that experience working with both of them.  Yes, you got the air and the land right there.  Ferid Murad: Yes, when we did an experiment and I got a result, I knew I could believe it and if it didn’t fit my ideas, I said, Something else is going on, let’s go think about this now.  Following up on the story, you then had Furchgott discover quite rapidly that there was this thing, EDRF, Endothelium-derived relaxing factor, and that that was the mechanism of action of certain drugs action on the smooth muscles surrounding blood vessels, but it took another six years or so for the connection between nitric oxide and EDRF to be made. Lookingback, it seems perhaps to students …  Ferid Murad: For some people it took six years.  Oh right, oh okay.  Ferid Murad: I’ll tell you this story.  Yes, please tell me the story because it seems, looking back, that it might have been an obvious …  Ferid Murad: Robert Furchgott was a vascular biologist, pharmacologist for many, many years. I met him as a student in Cleveland when I was a graduate student. Earl Sutherland would bring dignitaries through for seminars and I got to meet Furchgott very early on, in the days where he was looking at receptor theory and receptor abundance and excess receptors in vascular preparations. It had been known for a long, long time that some agents, acetylcholine, histamine, others would lower blood pressure in animals or man, they were hypertensive vasodilators, but they would never work in the laboratory and that’s because the integrity of the endothelium was destroyed in the process of making those preparations. One day, Bob gave an experimental protocol to his technician and instead of making strips where they would take a muscle and open it up and put it on their finger and clean off the tissue and mount it on the hooks, in the process what you’re doing is touching the endothelium and destroying it. His technician took a short cut and just like the salami, whacked off rings and hung them up and now they caused relaxation. It was a different preparation with the endothelium intact and Bob is so meticulous and clever that he realised the difference. He said, My goodness, now we have the endothelium and here we didn’t.  Now the other tip-off: one day their chambers were near a window and they had a shade and somehow they put up the shade or put it down, one or the other, and they noticed that when they opened the shade, the muscles relaxed, when they closed the shade, they contracted – he had light induced relaxation. When we found nitric oxide activation of guanylate cyclase, I was very excited to find a free radical activating enzyme, that was a precedent and it had never been shown before. I thought perhaps other free radicals might regulate other enzymes and I knew that there was a lot of free radical chemistry and photo chemistry, so we’d drink cocktails with riboflavin and other goodies in our preps and would shine light on them and try to activate the enzyme. On one occasion we were successful, but we could never repeat it, but when it worked once, I knew it had to work, but we couldn’t repeat it, something was different the next time we did it. Again, it reflects Ted Rall’s assistance in how to design an experiment, if you’ve got your data, you can believe it, but if you can’t reproduce it, it doesn’t mean it doesn’t work, it means you’re doing it differently, but we could never get it to work. When Furchgott found this factor coming out of endothelial cells that caused relaxation of smooth muscle, he came through Charlottesville to give a seminar, all excited about these endothelial dependant vasodilators and EDRF. This was in the spring of 1980, before his *Nature* paper. After his seminar, I buttonholed him and took him off to my office and I said, Bob, EDRF with a short half-life of several seconds is a reactive species, it’s probably a free radical or some other reactive molecule and I think it’s going to work through cyclic GMP and it might be something like nitric oxide or a complex, let’s collaborate and figure this out. We agreed to do that. It turned out that in that trip to Charlottesville, his wife fell, broke her hip, turned out she had metastatic breast cancer in her hip, they returned to New York and he was so distracted with her breast cancer. Shortly after that I started looking at Stanford, we moved the lab out to California, so we never collaborated, I wish we had.  Yes, that’s a missed opportunity.  Ferid Murad: Yes, we lost about a year or so because we hadn’t collaborated because of his experience and hers, but then we got out to Stanford, I moved in the summer of 1981, about a year after his visit. Michael Peach, a pharmacologist from Virginia and a colleague and a vascular biologist, interested in prostaglandins but also following the EDRF story, came to visit and consult for syntax across the street from the VA where my office and labs were. He came over one afternoon, we were chatting and he said, What are you doing with EDRF? and I said, Mike, we’re waiting for samples from Furchgott, we’re going to collaborate and see if it works with cyclic G, I think it will, but we never gotten any samples from him, as far as I know. I said, Let me call the post-doc in who was going to do the experiment. I called in Robert Rappaport who was with me at the time and I said, Robert, have you ever gotten samples from Furchgott’s lab? He said, No, and then he smiled. I said, Robert, what’s going on? Sheepish smile. He said, I’ve been stashing samples away that I’ve been doing in the Revco. I said, Robert, this is an example of a trainee who’s inquisitive enough to take the time to do it, but he’s afraid to tell the boss, but he’s doing the right thing. How can you ever inhibit that sort of activity, behaviour? You don’t want to do that. I said, You better go back to the lab and get all those azides and sure enough it worked and we then showed that EDRF worked through cyclic GMP. That was a nice follow-on story to Bob’s work. Shortly thereafter, he and Ignarro and even Muncada started saying the EDRF might be nitric oxide and I said, No it’s not. I said, Maybe you’re making nitric oxide but what is in that interstitial space regulating the smooth muscle, has got to be something else.  Why did you think it had to be something else?  Ferid Murad: Because NO’s a free radical and is going to collide with all sorts of stuff and it won’t survive, it has a short half life, a few seconds. To this day, I believe that the enzyme, nitric oxide synthase makes NO, no doubt about that, we’ve purified most of them, it doesn’t have others, but I think that Furchgott’s EDRF is a family of molecules. NO is a candidate, nitrosothiols, nitrosamines, nitros of fatty acids. All of those are EDRFs, as defined by Furchgott.  How generally accepted would that view be now?  Ferid Murad: Nobody wants to accept it. I’ve been saying that since about 1988 or 1989. |
| Q63 | I remember in the late 1980s, people sitting around in the coffee room in the pharmacology department in Oxford, disbelieving the possibility that EDRF could be NO. |
|  | Ferid Murad: The enzyme makes NO, NO certainly gets through the lipid bile air. It can go one or 200 extra from studies now with electrodes and other methodologies, but I think it’s a family of molecules and all of those are capable of delivering NO as NO donors to activate G cyclase.  Is the hypothesis testable, is there any way that you could actually …?  Ferid Murad: I don’t think so with current technology. I think the concentrations of EDRFs in that interstitial space are so low that we just don’t have methods to identify them and isolate them and mass spec them or whatever we’re going to have to do. I think that they could well be several or a family of molecules, all of which are capable of relaxing smooth muscle. If you look at Furchgott’s definition, which is sort of a loose definition, all it is, is a substance with a short half-life that relaxes smooth muscle. That can be a lot of things. The enzyme no doubt makes NO, NO comes out, that’s been measured with electrodes and with theoretical calculations, distances of 100 to 200 microns are possible, so for small vessels there may be enough, for big vessels, I’m not sure it gets that far, but how do you determine what it is, it’s going to take some new approaches.  Apart from the basic interest of knowing that EDRF would be a family rather than a single entity, are there practical applications?  Ferid Murad: I don’t know. That’s something that’s been pointed out to me, does it really matter? If NO is made and NO activates the enzyme and is responsible, does it matter what’s in between? Probably not, but as a scientist you like to know.  Yes, it’d be nice to know.  Ferid Murad: I think if you knew some of the substances that were in between, perhaps the chemists and the pharmacologists could in the future design molecules to either protect or scavenge them in some way and that might lead to a new approach for drug development.  It would seem to offer the possibility of more cell activity.  Ferid Murad: Maybe. |
| Q38 | You did find yourself in industry for a few years and then you returned to Houston, to the lab. Did the sojourning industry change your approach to the way you ran your lab, did experiments? |
|  | My laboratory in industry was an academic laboratory, it was no different than what it was at Virginia and Stanford. We turned out to be a resource for reagents for other laboratories. Other laboratories were becoming interested in cyclic G, in phosphodiesterases in other words. We had reagents, antibodies, whatever, that we were supplying other laboratories. But we were sort of an island in the midst of the company really and I think the laboratory was viewed differently by other scientists and perhaps favoured by me, which I’d hope was not the case, that we had more freedom, our own grant money and post-docs, things that other people in the company didn’t have. It made for a little discomfort in the company. There was pressure on me to give it up, I refused to do that. The reason I gave it up is because I was concerned about some of the decisions being made by senior management. We had some problems where drugs should have been pulled from the market and weren’t. We had situations where they would not pursue directions for research that I thought were important. One of the examples, in Virginia I collaborated – about the time we discovered NO actually – with an Infectious disease faculty member, Dick /- – -/ who was interested in third world diarrhoeal disease, particularly Bangladesh at the time, he had been in the Public Health Service for a while. He had a strain of E-coli that produced a heat stable endotoxin that caused diarrhoea. He had worked previously at Hopkins showing with Bucky /- – -/, the /- – -/ toxin increased cyclic AMP production toxin and he thought that perhaps this toxin would do the same, increase cyclic AMP and cause diarrhoea. I said Ok, we’ll help you work out the mechanism, but I want to look at cyclic G also.  Sure enough, this toxin activated the particular isoform guanylate cyclase and it was a new novel pathway for diarrhoea. It turns out both cyclic AMP and GMP activated the inappropriate kinase in the intestinal mucosal epithelial cells. Those kinases which you’re going to hear from [Edmond Fischer](https://www.nobelprize.org/prizes/medicine/1992/fischer/facts/) this week, phosphorylate, the cystic fibrosis transmembrane conductance channel, the chloride channel. When it’s phosphorylated, chlorine comes out the cell as does sodium, water and that’s the mechanism of diarrhoea. I’ve always wanted to find a compound that would block that pathway and I wanted to work on it at Abbott, because it was such a simple, straightforward problem and we had the resources to find it pretty quickly, I think, but I wasn’t permitted to work on. I didn’t understand why and one day my president said, It’s a third world disease, we’re not interested in third world disease, there’s no profit. |
| Q63 | Given the current antagonism towards the pharmaceutical Industry that this is a generic problem for them, one would have thought that such PR exercises at the very least would be |
|  | If it were Merck, with Roy Vagelos, he would probably have said, Go chase it, Ferid, but Abbott and others wouldn’t have done that. What has happened is, I left Abbott for a variety of reasons. I learned as much as I could about the industry, I was a little concerned about how things were going, a little bit concerned about the lack of freedom to work on things that I thought were important. We had compounds that could have been very effective in a lot of infectious diseases in AIDS patients, they didn’t want to chase it. Ultimately they did but they wouldn’t listen to me. I was the senior scientific officer, I felt it strange that they wouldn’t listen. I said, Okay, time to go back to academics and I went to Houston, I looked at some other opportunities and chose Houston, but now we have found such a compound and I’m really excited about it. I’ve screened the library, we have a hit, a lead, we’ve got a compound that not only blocks guanylate cyclase activation by E-coli heat stable enterotoxin, but it blocks G cyclase activation by guanylin in intestinal peptide. It blocks /- – -/ toxin activation by adenoid cyclase, it blocks /- – -/ and epinephrine activation of adenoid cyclase, it blocks atriopeptin activation of guanylate cyclic. This is a marvellous compound, I think it’s going to be universally effective in all the diarrhoeal diseases.  Where is it now, the compound?  Ferid Murad: Right now we’ve patented it, we’re trying to do some initial chemistry to make some analogues. We know it works *in vivo*, in animal models, it does block diarrhoea due to toxin, it blocks anthrax, it really is marvellous. Now the problem is to move it forward into toxicology, medicinal chemistry, analogues, formulation and then the clinic and that’s tough to do in academics.  Yes, you need a trustworthy partner in industry.  Ferid Murad: I can do it, if I had the resources and money, I could do it because I’d have the experience, I know how to do it. It’s easier to do in industry, where the resources exist and the money exists, but I’ll find it and one way or another I’ll find it. I’m really anxious to get this into some clinical trials.  It matters but it’s tough.  Ferid Murad: I know. I figure it’s going to take me five or six million dollars to get it into clinical trials and at that point we’ll stir up some interest. I think it may also work in inflammatory bowel disease and that’s where the interest will come. If we can get it to work in inflammatory bowel disease, the big companies will be interested and hopefully they’ll give it away to WHO for third world diarrhoea or something.  Yes, otherwise one goes the route of finding Gate’s money or something.  Ferid Murad: I’d try all the avenues I can at the moment. I’ve told people I’m going to sell my house if I have to. |
| Q4 | I wish you a lot of a luck with that. That’s a tremendous project. I think to finish, I’d like to just discuss a little bit more about what it is that you think is most important for medical students now to understand. You yourself had training and very novel training in the 1950s based on basic research and medical training combined and of course MD PhD programmes are very popular now, but the majority of medical students don’t go through this. |
|  | I think there are in the US, I believe, out of the 126 medical schools, probably about 30 or 40, maybe a little more with MD PhD programmes and typically they only have a handful of students, although some programmes like Washington University and a few others are much larger, but typically less than 5 or 10% of the class is MD PhDs. They’re always very good students. The programme is designed to, in my opinion, train academics to come back and do research, either in a clinical department or a basic science department, one or the other. If you look at the spread, people have done both, people have gone into clinical departments to research or basic science departments to research. Some of us have done clinical training, ended up in clinical departments and then switched to basic science departments, as I have. Others have not done clinical training and gone into basic science departments. I don’t think it matters. I think the programme is designed to train academics to come back and teach and do research. The difficulty that we’re having, certainly in the US and I’m sure it’s true here in Europe as well, is that for the clinical faculty member to do research today is becoming extremely difficult because of managed healthcare. You have to spend so much of your time seeing as many patients as possible to satisfy the budgets and financial justification of the programmes, that there’s no time left for research. For many, many years, I have always believed that you have to emphasise one or the other, it’s wonderful if you can do everything, I wish I could, I tried for some time, but after a period I had to decide whether I was going in for science clinical medicine and teaching or research. I chose the research track, but I always tried to do research in a clinical department, so I could impact and influence the clinical faculty and collaborate with them.  Today, it’s very, very hard to do both. You can only be an expert if you spend most of your time doing one thing, whether it’s research or patient care. If you’re doing patient care and it’s part-time, you’re not going to be the pro, an expert, you’re not going to get the referrals from your colleagues. They’re going to send them to the person who’s doing it full-time. If you’re not doing research full-time, you’re not going to get the grants. Now it doesn’t mean 100% of the time but certainly more than 50 or 60 or 70%. You’ve got to choose, it doesn’t mean that you can’t be concerned about the other and participate to some extent, but to be the triple threat and be the perfect teacher and clinician and scientist, that’s not feasible these days. It’s going to be frustrating for students, more so than it was for me, to make those choices. I took it all, I absorbed it all because I enjoyed it all, but at some point I realised I’ve got to emphasise one thing or the other. I think it’s going to be a little harder for people to make those choices. Educational costs are escalating through the roof, people can’t take the long training programmes that I went through. I trained for 12 years after college, let me think, is that right? Yes, 12 years. It’s hard to do and I did it with a family, with five kids, it was very hard to do.  You’d have to go into practice after that these days, just to pay for it.  Ferid Murad: Exactly, well that’s what’s happened. I have a son-in-law who’s a cardiologist and another son-in-law who’s a neuroscientist, one’s a PhD. and one’s an MD. The MD has done a lot of research, cancer research, cardiovascular research, he’s probably spent about four or five years in the laboratory. He got himself an American heart fellowship and the whole bit. He grew up in California, he wanted to go back to California. To afford housing in California and pay off all of his debts, he had to go into practice, so now he’s a cardiologist in California to pay all of his past loans and move into a house. He’d loved being an academic but I don’t think he can afford to do it, which is sad.  Yes, so now it’s a case of do one thing and do it well.  Ferid Murad: Yes.  On that note, I guess we should stop. Thank you very much indeed for taking the time to talk to us.  Ferid Murad: I think the important message for young people … When I was a student, I absorbed everything, I never cut a single class in my career because I thought everything was important. I couldn’t determine what was important and what wasn’t, therefore I learned it all. In our faculty we’d say, half of what I’m going to tell you is true and real and the other half is not, but I can’t tell you which half, so I would learn it all. Today that’s different and I think that education is so costly that you can’t afford not to take advantage of it, the opportunity and what you’re learning may not be applicable later on, but it prepares you to learn it later and you’ve got to do what you enjoy doing. It doesn’t matter what you do, as long as you enjoy it and do it very, very well, the best you can be. |
| ID | 0565 |
| Biographical | My history is not atypical of many Americans: born in the midwest, educated in the East, and now living in the West. My early years were shared between Des Moines, Iowa and Cincinnati, Ohio. Shortly after I was born on May 28, 1942 in Des Moines, my father, Lawrence, was drafted into the United States Navy. I was named for my father’s younger brother who died of Hodgkin’s disease at the age of 24. We moved to Boston briefly where my father enrolled in Naval officer training school before being sent to the south Pacific. He served as a communications officer for the remainder of World War II on an island called Eniwetok where the first hydrogen bomb was detonated a decade later.  During my father’s absence, my mother, Miriam, and I lived in Cincinnati where her mother, Mollie Spigel, also lived. Prior to moving to Cincinnati, Mollie had lived in Norfolk, Virginia, where she raised three children after her husband Benjamin was killed at age 50 in a traffic accident. Besides many special memories of my maternal grandmother, I have many fond reminiscences of my paternal grandfather, Ben, who emigrated to the United States in 1896 as a young boy from Moscow. He grew up in Sioux City, Iowa, as did my father with many other Russian Jews. Shortly after the end of World War II, we returned to Des Moines where I attended primary school and my brother, Paul, was born. In 1952, we moved back to Cincinnati with the hope that my father would be able to find a much better job as an architect. In Cincinnati, he practiced architecture for the next 25 years, which enabled him to provide a very comfortable home for his family.  During my time at Walnut Hills High School, I studied Latin for five years, which was to help me immensely later in the writing of scientific papers. But I found high school rather uninteresting and was most fortunate to be accepted by the University of Pennsylvania where I majored in Chemistry.  The intellectual environment of the University of Pennsylvania was extraordinary – there were so many internationally renowned scholars who were invariably receptive to the intrusions of undergraduate students even before the days of student evaluations of the faculty. The small size of the undergraduate student body undoubtedly contributed to the accessibility of the faculty. Besides numerous science courses, I had the opportunity to study philosophy, the history of architecture, economics, and Russian history in courses taught by extraordinarily knowledgeable professors. Although I was among the smallest of the heavyweight crew team members and thus had no chance of rowing in the varsity boat, I greatly enjoyed the many hours that I spent at this wonderful sport.  During the summer of 1963 between my junior and senior years, I began a research project on hypothermia in the Department of Surgery with Sidney Wolfson. I quickly became fascinated by the project and continued working on it throughout my senior year. I decided to remain at Penn for Medical School largely because of the wonderful experience of doing research with Sidney Wolfson. During the second year of medical school, I decided to ask Britton Chance if he would allow me to study the surface fluorescence of brown adipose tissue in Syrian golden hamsters as they arose from hibernation. Chance had reported that the surface fluorescence of other organs reflected the oxidation-reduction state of those tissues. As anticipated, large changes in the fluorescence of brown fat were found during non-shivering thermogenesis.  My research on brown fat allowed me to spend much of the fourth year of medical school at the Wenner-Gren Institute in Stockholm working with Olov Lindberg on the metabolism of isolated brown adipocytes. This was an exciting time and I began to consider seriously a career in biomedical research. Early in 1968, I returned to Philadelphia to complete my medical studies and to contemplate my options. The previous spring, I had been given a position at the NIH once I completed an internship in medicine. It was the height of the Vietnam war with 500,000 young Americans trying to control the spread of Communism in southeast Asia. But I was facing an internship at the University of California San Francisco (UCSF) that would require me to work every other night for an entire year, a prospect about which I was not enthusiastic. The privilege of serving in the US Public Health Service at the NIH clearly outweighed the unpleasant prospects of an internship. Although the workload was awesome, I managed to survive because San Francisco was such a nice place to live. During that year, I met my wife, Sandy Turk, who was teaching mathematics to high school students.  At the NIH, I worked in Earl Stadtman’s laboratory where I studied glutaminases in *E. coli.* My three years at the NIH were critical in my scientific education. I learned an immense amount about the research process: developing assays, purifying macromolecules, documenting a discovery by many approaches, and writing clear manuscripts describing what is known and what remains to be investigated. As the end of my time at the NIH began to near, I examined postdoctoral fellowships in neurobiology but decided a residency in Neurology was a better route to developing a rewarding career in research. The residency offered me an opportunity to learn about both the normal and abnormal nervous system.  In July 1972, I began a residency at the University of California San Francisco in the Department of Neurology. Two months later, I admitted a female patient who was exhibiting progressive loss of memory and difficulty performing some routine tasks. I was surprised to learn that she was dying of a “slow virus” infection called Creutzfeldt-Jakob disease (CJD) which evoked no response from the body’s defenses. Next, I learned that scientists were unsure if a virus was really the cause of CJD since the causative infectious agent had some unusual properties. The amazing properties of the presumed causative “slow virus” captivated my imagination and I began to think that defining the molecular structure of this elusive agent might be a wonderful research project. The more that I read about CJD and the seemingly related diseases – kuru of the Fore people of New Guinea and scrapie of sheep – the more captivated I became.  Over the next two years I completed an abbreviated residency while reading every paper that I could find about slow virus diseases. In time, I developed a passion for working on these disorders. As I plotted out a course of action, the task became more and more daunting. The tedious, slow, and very expensive assays in mice for the scrapie agent had restricted progress and I had no clever idea about how to circumvent the problem. I did think that after working with the scrapie agent for some time that I might eventually be able to develop such an assay.  Since both Sandy and I liked living in San Francisco, I accepted the offer of an assistant professor position from Robert Fishman, the Chair of Neurology, and began to set up a laboratory to study scrapie in July 1974. Although many people cautioned me about the high risk of studies on scrapie due to the assay problems, such warnings did not dull my enthusiasm. To gain a base of research support from the NIH, I initially wrote grant proposals on glutamate metabolism in the choroid plexus. Such proposals were dull but were readily funded because I had worked on glutaminases earlier. Eventually, I managed to gain modest NIH support for my scrapie studies but this was not without considerable difficulty. To rebut the disapproval of my first NIH application on scrapie, I set up a collaboration with William Hadlow and Carl Eklund who were working at the Rocky Mountain Laboratory in Hamilton, Montana. They taught me an immense amount about scrapie and helped me initiate studies on the sedimentation behavior of the scrapie agent.  I had anticipated that the purified scrapie agent would turn out to be a small virus and was puzzled when the data kept telling me that our preparations contained protein but not nucleic acid. About this time, I was informed by the Howard Hughes Medical Institute (HHMI) that they would not renew their support and by UCSF that I would not be promoted to tenure. When everything seemed to be going wrong, including the conclusions of my research studies, it was the unwavering, enthusiastic support of a few of my closest colleagues that carried me through this very trying and difficult period. Fortunately, the tenure decision was reversed and I was able to continue my work. Although my work was never supported by HHMI again, I was extremely fortunate to receive much larger funding from the R. J. Reynolds Company through a program administered by Fred Seitz and Macyln McCarty and shortly thereafter from the Sherman Fairchild Foundation under the direction of Walter Burke. While the vast majority of my funding always came from the NIH, these private sources were crucial in providing funds for the infrastructure which was the thousands of mice and hamsters that were mandatory.  As the data for a protein and the absence of a nucleic acid in the scrapie agent accumulated, I grew more confident that my findings were not artifacts and decided to summarize that work in an article that was eventually published in the spring of 1982. Publication of this manuscript, in which I introduced the term “prion”, set off a firestorm. Virologists were generally incredulous and some investigators working on scrapie and CJD were irate. The term prion derived from protein and infectious provided a challenge to find the nucleic acid of the putative “scrapie virus.” Should such a nucleic acid be found, then the word prion would disappear! Despite the strong convictions of many, no nucleic acid was found; in fact, it is probably fair to state that Detlev Riesner and I looked more vigorously for the nucleic acid than anyone else.  While it is quite reasonable for scientists to be skeptical of new ideas that do not fit within the accepted realm of scientific knowledge, the best science often emerges from situations where results carefully obtained do not fit within the accepted paradigms. At times the press became involved since the media provided the naysayers with a means to vent their frustration at not being able to find the cherished nucleic acid that they were so sure must exist. Since the press was usually unable to understand the scientific arguments and they are usually keen to write about any controversy, the personal attacks of the naysayers at times became very vicious. While such scorn caused Sandy considerable distress, she and my two daughters, Helen and Leah, provided a loving and warm respite from the torrent of criticism that the prion hypothesis engendered. During the winter of 1983, I herniated a disc in my lumbar spine while skiing and this slowed the pace of my work for much of the year. After a laminectomy, I began swimming regularly, which brought relaxation and a much needed quiet time to my life.  Just prior to my back problem, the protein of the prion was found in my laboratory and the following year, a portion of the amino acid sequence was determined by Leroy Hood. With that knowledge, molecular biological studies of the prions ensued and an explosion of new information followed. I collaborated with Charles Weissmann on the molecular cloning of the gene encoding the prion protein (PrP) and with George Carlson and David Kingsbury on linking the PrP gene to the control of scrapie incubation time in mice. About the same time, we succeeded in producing antibodies that provided an extremely valuable tool that allowed us to discover the normal form of PrP. In a very important series of studies, the antibodies were used by Stephen DeArmond to study the pathogenesis of prion disease in transgenic mice. Steve brought the much needed talents of an outstanding neuropathologist to these studies. As more data accumulated, an expanding edifice in support of the prion concept was constructed. Ruth Gabizon dispersed prions into liposomes and purified scrapie infectivity on columns with PrP antibodies. Karen Hsiao discovered a mutation in the PrP gene that caused familial disease and reproduced the disease in transgenic mice while Michael Scott produced transgenic mice abrogating the prion species barrier and later artificial prions from chimeric PrP transgenes. Indeed, no experimental findings that might overturn the prion concept were reported from any laboratory. By the early 1990s, the existence of prions was coming to be accepted in many quarters of the scientific community, but the mechanism by which normal PrP was converted into the disease-causing form was still obscure. When Fred Cohen and I began to collaborate on PrP structural studies, I was again extremely fortunate. Fred brought an extraordinary set of skills in protein chemistry and computational biology to investigations of PrP structures.  As prions gained wider acceptance among scientists, I received many scientific prizes. The first major recognition of my work was accorded by neurologists with many other awards coming soon thereafter. But the most rewarding aspect of my work has been the numerous wonderful friends that I have made during an extensive series of collaborative studies. It has been a special privilege to work with so many talented scientists including numerous postdoctoral fellows and technical associates who have taught me so much. Besides the many collaborators who have contributed their scientific skills to advancing the study of prions, I have had many colleagues who have contributed indirectly to my work by being supportive of the special needs that such a project has demanded. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | 0565 |
| Interview |  |
| Q23 | Welcome to meet the Nobel Laureate in Physiology or Medicine for 1997, Dr Stanley Prusiner, the man who did as very few scientists do, but all of them will get Nobel Prizes I think, they really turn the concept we have upside down, and please tell me Dr Prusiner, what did you really turn upside down? |
|  | I’m not sure I turned anything upside down, it was a discovery that people really didn’t want to accept for a long time because it went against so many preconceived notions. The idea that a protein was infectious and the disease could be both genetic and infectious and then even spontaneous. These were concepts that people had a hard time accepting.  But why was it so controversial?  Stanley B. Prusiner: I think that it was a long time in coming to understand that genes are made of DNA or RNA, primarily DNA. That all infectious agents, the progeny of all infectious agents are encoded by a strand of DNA or RNA and in fact all organisms. So, the idea that there should be something totally different and it should be “alive”, it can replicate in a biological system, just I think was very difficult to accept and I think people were justified in being sceptical because the discovery that DNA is the genetic material of life didn’t occur until the middle of the 20th century. |
| Q23 | So in a way you challenged the central dogma of molecular biology at that time, that all the information was contained, the DNA and the RNA and the proteins were just the templates or the churning out of the … Now you’d proved that proteins in itself, in these cells right could contain information so to say? |
|  | Yes and no. In the beginning it seemed that way, that we were challenging the dogma and as the story emerged, it became very clear that it fit within the dogma of biology, but that one had to make small revisions and these revisions turned out to be groundbreaking in many other areas. The concept that a protein could then exist in two biologically active forms was not well accepted and in fact they were not good examples. |
| Q38 | It took you 10 years to come to this conclusion, to really put forward the proofs for your idea. What kept you going when everyone was suspicious about the ideas? |
|  | Yes, this was a 25 year project, it took me about 10 years to really get into it and lay out what I thought were the real possibilities and then another 10 years to gather the information that made it clear that these ideas were not science fiction but in fact they were real and that people who were sceptical were certainly justified but that there had now came a point where their scepticism no longer was really useful.  But what kept you going, I mean 25 years ago, tell me?  Stanley B. Prusiner: When you make a discovery like prions, you become very passionate about it and you look for other things that are as interesting, where you might not find as much human opposition and when you can’t find something, if you’re not very imaginative, you’re not very bright and you are unable to find another project that’s as exciting, then you say to yourself, well, I’ll just keep going on this and nothing better that I can work on. |
| Q38 | But despite that all the colleagues, well not all but the scientific community around you, really thought you were doing mad things? |
|  | Not everybody, there were enough people who were very supportive and who provided the day to day support as well as being sufficiently convinced that we were doing good work to act as peers in the review of the work, so that it was supported by the National Institutes of Health, because otherwise we would have never been able to survive. In addition we had some private funding that was very important.  That is important.  Stanley B. Prusiner: Yes, the philanthropy was critical. |
| Q6 | It’s seven year now since you came to Stockholm to get the prize and I wonder what has happened since? |
|  | My life has been a little more hectic. In some ways I’ve relaxed a little bit more, although many people would not tell you that was true and the work has continued to move forward. |
| Q3 | Has there been any difficulties, I mean, there were controversies even when you got the prize, in the protein only had part of this work challenged for many respects and as you come up with some even more definite proof that is the protein only theory will hold? |
|  | Yes, this past summer we published two papers, one piece of work we made a synthetic prion with a peptide that we synthesised in the chemical means. This was culminated in four years of work where we’d published the first paper in the year 2000, so that was three years after the prize and then a follow-up paper this past spring. Then in the summer we published another paper in which we made the protein in bacteria and isolated the protein and then refolded it and showed that we’d made a synthetic prion that way. So we’ve done this two different ways where we’ve started with a sequence that either produced an E-coli or produced by chemical means and then changed the confirmation of the protein and turned it into an infectious pathogen.  And you proved that this synthetic infectious prion managed to alter the shape of the proteins, the prions in the infected animal?  Stanley B. Prusiner: If they didn’t do it, then I don’t know what did it.  But you were challenged on this as well, afterwards.  … even after we published these papers, we were challenged by people …  Stanley B. Prusiner: Oh yes, even after we published these papers, we were challenged by people, not a lot, most people think that we have finished the task of convincing the world but I think, you know, there are a few, and that’s normal and they probably will never be convinced. |
| Q33 | When you received your prize, you also gave the banquet speech where you said something like, the Nobel Prize is a celebration of science, yes and culture. |
|  | It’s a celebration of science and culture, well an intellectual achievement in our civilisation and it’s really, I think, unique. There is no other celebration like the Nobel Prize celebration. |
| Q14 | It’s interesting, you mention science and culture together. We just got a new minister in Sweden, in science and culture, the same minister and the same department, Science and Culture, and when he gave a press conference just when he entered his chair, he didn’t get a single question on science from the journalists, just about culture. |
|  | I think that’s not surprising. I think it’s very difficult for people to ask questions about science just off the top of their heads and I think one of the problems I had with the press for so long was that they were so uneducated about science. Now to be fair to the press, they have very little time to write a story or to produce a story and so being thrown into an area where some scientists are telling them the work is excellent and others are telling them that it’s complete fraud and craziness – they don’t know how to judge. I can well imagine, when the Minister of Culture and Science is appointed and the press is asked to come to a press conference, if the press conference materials don’t lay out in detail an agenda for science, so in an understandable lay language, then I can well understand they may not ask any questions.  But maybe you could also wonder whose responsibility is this? If you want to be well known and if you want to communicate with the audience, I mean you can’t alter the journalist, the only thing you can alter is the scientist maybe, yourself.  Stanley B. Prusiner: Right, who are we talking about, the minister or myself?  Who is to blame if the communication doesn’t work, the journalists or the scientists?  … it still is the responsibility of the scientist to try to communicate better with the public …  Stanley B. Prusiner: The scientists. I think that the scientists have to constantly try to translate what they do into language that most people can understand and we are never going to be in a position where everyone is a knowledgeable layman, meaning they have a great scientific background because whatever they learn in a university setting is already obsolete the day they graduate. So the best we can do is hope we can train them in some introductory science courses to give them a little background, but after that, it still is the responsibility of the scientist to try to communicate better with the public and this is very, very hard to do, because each year, science becomes more complicated, there’s more and more specialised vocabulary. One of the things we don’t have as scientists is we don’t have a lot of people around who understand the details of the science intimately who are interested in translating it for the public. |
| Q32 | Because this central idea when we were talking about communication is that we talk about public understanding of science but as you phrase it now, that is not very easy to do, so maybe you should turn the thing around, it’s science understanding a public that is more interesting. |
|  | The science is understanding the public or making the scientists making science more understandable for the public. |
| Q32 | Yes, but also to understand how the public thinks and feels and what their values are, to be able to phrase their science in a framework where people can understand it. |
|  | I think that’s very legitimate, I’m not sure how practical that is in terms of making that happen.  Do you want to try it?  Stanley B. Prusiner: I can try. Whatever you’d like to talk about, I’ll try to …  No, that in a way would be to make science as a part of culture.  Stanley B. Prusiner: I think that’s wonderful but the problem is, where do we start? How do we get this moving and it’s extremely difficult? I mean you would hope that, for instance, the web would be a great place to do this. The Internet is ideal in many respects. The problem with the Internet is there’s so much material on the Internet, it’s uncensored, it’s unreviewed, so for the person who doesn’t have a lot of knowledge, they now Google themselves into some website and all of a sudden they’re confronted with material that they can’t judge whether this material is legitimate, whether it’s reasonable, whether it fits with the scientific data or it’s some wacko person’s ideas about a disease or some physical process. You know, it’s very, very hard for people to judge this.  … you can find all kinds of material, much of which is unsupported by any scientific data …  I’ll give you an example in the field of mad cow disease. You can go into the Internet and look up mad cow disease and you can find all kinds of material, much of which is unsupported by any scientific data. And there are a lot of people out there interested in this because this is a huge economic issue and it’s a huge health issue and yet there’s an enormous amount of information which is available that comes from peer reviewed scientific studies and yet, if you don’t have a reasonable working knowledge, you’ll be confused when you get into this. So it’s very, very hard I think to put science out there for the public and we need to figure out how to do this. It’s not a given, in fact we do it very poorly.  But there’s a big challenge to your colleagues and for the scientific community.  Stanley B. Prusiner: I think the challenge is huge and I must say that I don’t know how to do this. I find it very difficult to identify people who are very interested in doing this. In other words, someone who has a very good working knowledge of science who can really judge and we’re not talking about all science now, we’re saying okay, someone who perhaps is very good in the field of neuroscience and neurological diseases and then finding such a person who wants to devote his or her life to making this available to the public. |
| Q34 | Finally, what would your perspective be for the scientific community or for the society as a whole if you doesn’t succeed in communicating science? |
|  | I think that there are huge problems for society if scientists can’t communicate their science. It’s so important. Number one, funding for scientific research depends upon public support. I think that policymakers, legislators, they need to be informed and they need to be informed in terms that they can understand, not that we want them to understand, that’s number one. Secondly, I think as our planet grows more crowded, people need the information in order to make decisions that benefit others on our planet and third, if we don’t communicate science, we won’t see the science turned into technologic advantages for our civilisation.  So scientists have a huge responsibility, they’re not very good at doing this and at the same time, it’s not fair to put all the burden on them because that’s not what they want to do, that’s not the job they’ve signed up for, they’ve signed up very often to roll back the frontiers of knowledge. So we need people in between, the people gathering the knowledge, the people consuming the knowledge, we need people in between to translate and my guess is that we’re going to need to create such a discipline for our society which our society meaning civilisation on this planet, which each year grows more and more dependent upon high technology.  So, to finish, let’s hope that the audience is googling around on Google to this interview and to share the ideas and the thoughts. Thank you very much for giving us your time.  Stanley B. Prusiner: Thank you. |
| ID | 0566 |
| Biographical | My childhood was spent on the outskirts of the sub-tropical city of Brisbane. I have a younger brother, Ian, and we grew up as part of a traditional, extended family that was very much influenced by the values of our two grandmothers. The one was a devout Methodist, the other a lapsed Quaker who was born in England and embraced the informal Australian life style with great enthusiasm. My parents (Linda and Eric) were first and second generation Australians, the various elements of the family coming from County Louth (in the 1840’s), Lancashire and Essex. Eric Doherty, a clever and entertaining man, trained initially as a telephone mechanic and was an administrator involved in the planning of telephone services. His mother had been left in straitened financial circumstances when my grandfather succumbed to pneumonia during the 1919 influenza epidemic. My father communicated his frustration at not having received an adequate formal education and, with his strong encouragement, the desire to learn and understand became the major focus of my life. Linda Byford was a piano teacher who, with her two brothers, spent much of her youth on the tennis court. After marriage she cared for her family, played Chopin, Debussy, and Beethoven and grew roses. She gave me an appreciation, and emotional need for, classical music, but did not pass on the genes for tennis. The Byfords were devastated by the death of the eldest son, who was captured at the fall of Singapore and lost in a Japanese transport torpedoed by an American submarine. I remember my other Byford uncle shivering with recurrent malaria that he contracted during the fighting in New Guinea. I share Alfred Nobel’s conviction that war is the greatest of all human disasters. Infectious disease runs a good second.  My Irish genetic heritage gave me a very fair skin, making me totally unsuited for life in a city that is known as the melanoma capital of the world. This limited my participation in the outdoor-oriented Australian way of life, and caused me to spend a great deal of time reading anything and everything. Even so, the Australian landscape was at our back door, there were adventures with home made canoes, I played tennis and Australian Rules football, and the extended family went to the beach for at least three weeks each year. The two things that I miss most when living out of Australia are the bush and the Pacific coast, especially fishing in the surf at night! My father had a workshop and I learned to be a carpenter, a skill that has resulted in the manufacture of some very substantial coffee tables and a fair amount of time working on houses. My most ambitious project as a teenager was the construction of a photographic enlarger and darkroom, but all the photographs that I took at that time seem to have been lost after my father’s early death (in 1961) and the selling of the family house.  I went to the local public schools and Methodist church. The commute to the high school involved daily trips on a steam train. I played basketball, and was a sergeant in the army cadet corps. Physics and chemistry came easily, but my natural inclinations were towards literature and history. Growing up without much money, however, also left me with the conviction that I needed to get some sort of reasonable job. An older cousin, Ralph Doherty was a brilliant scholar who was in the process of establishing himself as a leading viral epidemiologist. What he was doing seemed fascinating, but my contacts with the local general practitioners left me with no great enthusiasm for the idea of following his path to medical school. A visit to an “open day” at the University Veterinary School was my first real contact with biology in the formal sense: the subject could only be studied by girls in the Queensland public schools of that era. Another major influence at the time of my matriculation, was that I was reading Aldous Huxley, [Jean Paul Sartre](https://www.nobelprize.org/nobel_prizes/literature/laureates/1964/index.html) and [Ernest Hemingway](https://www.nobelprize.org/nobel_prizes/literature/laureates/1954/index.html) simultaneously. I decided to be the man of action rather than the philosopher, and resolved to graduate in veterinary science and pursue a research career. At this stage I was just 17 years old, and would probably have made a very different decision if I had been more mature.  The then vice-chancellor of the University of Queensland pursued a policy of open admission, from the conviction that matriculation results bore little relationship to later academic performance. As a consequence, the veterinary school had a number of mature students who had worked in the bush, while more than 50% (mostly school leavers) did not make it past the examinations at the end of the first year. This was one of two veterinary schools in Australia, and the survivors were joined by a spectrum of students from other states, New Zealand and south-east Asia (under the Colombo plan) at the beginning of year two of the five year program. Being exposed in this milieu, together with spending the long vacations employed on sheep and cattle properties and seeing practice with rural veterinarians, caused me to grow up quickly. I soon discovered that I had little interest in small animal medicine or surgery, but retain a sense of nostalgia for the satisfaction and physical challenge of working with large domestic animals.  The veterinary school was staffed by a fairly young group of teachers, many of whom had strong research backgrounds. Courses in the physical sciences, zoology, botany and biochemistry were taught from the science faculty, and physiology in the medical school. I was introduced to the principles of ecology in first year zoology, with the commitment of my professor to marine biology almost causing me to switch to that discipline. Infectious disease was taught by John Francis, who communicated great enthusiasm for research, and immunology by the parasitologist, J. F. A. Sprent. Another course that influenced me strongly was population genetics given by Glenorchy MacBride. I also read F. M. Burnet and R. M. Stanley’s books on viruses, some of Burnet’s writings on immunology and cancer and wrote a final year thesis on the UV-induced squamous cell carcinoma (cancer eye) of Hereford cattle. Burnet’s teleological Darwinism, the idea that the body is a set of ecosystems and the realisation that good science involves quantitation have stayed with me from those early days.  When I graduated, I was contracted (under the terms of a “bonded” scholarship) to work for several years in the Queensland Department of Agriculture and Stock. I expressed enthusiasm for laboratory-based research, so the Department immediately sent me to the country as a rural veterinary officer. I spent some months driving large distances to post-mortem cattle and pigs that had died of unknown causes, and to survey cattle for various venereal diseases. This resulted in the diagnosis of Trichomoniasis in an area where it was thought that complete eradication had been achieved. Realizing that I was a danger to their regulatory effort, the Department quickly brought me back to the state veterinary laboratory, the Animal Research Institute (ARI), Yeerongpilly. My task was to conduct a large-scale, externally-funded experiment on the epidemiology of bovine leptospirosis. This project involved injecting several cows with *Leptospira pomona,* then watching the spread of the disease throughout the herd. I became adept at dark-field microscopic analysis of urine for spirochetes, the histology of the bovine kidney and the serological test for the organism. This work was submitted for a master’s thesis and published in local journals. I was also involved in the diagnostic veterinary pathology service.  The ARI was in the process of establishing a facility for diagnostic virology, and had employed a very attractive young microbiology graduate, Penny Stephens, to develop the laboratory. We married in 1965. Knowing of my interest in virology the ARI Director, Les Newton, sent me to Melbourne for six weeks to learn basic techniques. I worked with Toby St. George in the Commonwealth Scientific and Industrial Research Organization (CSIRO) laboratory of Dr. E. L. French, spent time in the virology group at the Commonwealth Serum Laboratories and (en route) visited F. J. Fenner’s Department of Microbiology at the John Curtin School of Medical Research (JCSMR), Canberra The latter was motivated by the desire to meet C. A. Mims, whose work on viral pathogenesis had considerably influenced my thinking about disease processes. On returning to Brisbane, I realised fairly quickly that I am an experimentalist at heart. A career as a diagnostic virologist was not for me!  I tried for a Ph.D. scholarship to work with Cedric Mims, but was told to apply again later because he already had a “scholar” and would take only one student at a time. At about the same time I got to know J. A. Roberts, who had done an excellent series of experiments with Mims on the ectromelia model and had recently returned from Cornell to a position as a research parasitologist in the CSIRO laboratories on the Yeerongpilly site. John Roberts told me that he had been very impressed by a visit that he had made to the Moredun Research Institute in Edinburgh, where there was a major research effort on scrapie, the then enigmatic “slow virus” disease. The Moredun also trained graduate students, who were affiliated with the University of Edinburgh. The following week a job in the Department of Experimental Pathology at the Moredun was advertized in *Nature.* We sailed for Britain in early 1967, on a very slow and cheap ship.  The experimental pathology position at the Moredun required that I do research and help to run the diagnostic neuropathology program that the institute operated for the Scottish Veterinary Investigation Service. I learned neuropathology from the head of the department, R. M. Barlow, and from Hugh Fraser who was doing seminal studies with Alan Dickinson defining the genetics of the scrapie mouse model. Dick Barlow also taught me to write clear, concise English. My initial intention was to work on sheep scrapie, but I quickly realised that this was not a good project area for an experimentalist. My abiding interest in infectious disease caused me to focus on the tickborne flavivirus, louping-ill virus, which was then regarded as problematic because of concerns about the safety of the vaccine, first developed at the Moredun many years previously. I enroled as a part-time graduate student at the University of Edinburgh medical school and, after I had been working with the virus for some time, developed a collaboration with another young veterinary graduate, H.W. Reid. Hugh Reid did the virology and serology aspects of the ensuing sheep experiments, while I concentrated on light and ultrastructural pathology. Part of Hugh’s role was to test my blood for the presence of virus and antibody when I injected myself in the finger, an inadvertent human experiment that I later wrote up for the *Lancet.*  We greatly enjoyed living in Edinburgh. Penny worked with E. C. R. Reeve at the Institute for Animal Genetics until the birth of our two sons, James and Michael. The Edinburgh Festival and the Traverse Theatre were high points and, for the first time in my life, I could spend the whole day outside without the penalty of sunburn. Our long vacations were used for camping holidays in Europe, including our first trip to Scandinavia and Stockholm with a young child in the back of a Volkswagen van. I went to veterinary research and neuropathology meetings, and we came very close to staying permanently in Britain.  Eric French visited the Moredun, and raised the possibility of a permanent appointment in the veterinary virology group at the CSIRO laboratories in Melbourne. At about this time I heard a seminar by Mel Greaves at the Metchnikoff Club, an Edinburgh group organized by Spedding Micklem and Angus Stewart, that convinced me I had no real understanding of contemporary immunology. Cedric Mims also came through and talked about the work that he and R.V. Blanden had been doing on T cell responses in virus infections. Shortly afterwards a junior academic appointment was advertised in the Department of Microbiology at the JCSMR, with a job description that seemed to fit me reasonably well. Fenner’s successor as head of the department, G. L. Ada, had actually written it for Bob Blanden, but offered me the only other position that he had available, a postdoctoral fellowship to work with Cedric Mims. I left my permanent research position, and turned down the offer of another, to take this opportunity to learn basic immunology. My long-term intention was to return to veterinary research. My only formal involvement in the veterinary world since then has been to serve (1987-1992) on the board of the International Laboratory for Research In Animal Diseases, Nairobi, Kenya. This was an enormously broadening experience, and I learned a great deal from (in particular) my African colleagues.  We moved from Edinburgh to Canberra in December 1971. Cedric Mims had by then decided to take the Chair in Microbiology at Guy’s Hospital Medical School so, though we overlapped by six months or so, we did not ever formally work together. At first I studied the pathogenesis of Semliki Forest virus infection in the mouse, then switched to the lymphocytic choriomeningitis virus (LCMV) model which was a much more powerful tool for immunological analysis. I first met [Rolf Zinkernagel](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1996/index.html) when he arrived to work with Bob Blanden in 1973, and Gordon Ada (for space reasons) moved him into the laboratory with me. We also lived in the same university housing complex, and shared rides to the JCSMR with a physicist from Trondheim, a Japanese pharmacologist, and a biochemist (Bob Gerdes) who is now working at the Karolinska Institute. The story of our scientific interaction through that time is told in the accompanying articles, and in an account that we wrote jointly some time back that is yet to appear in “Immunology Today”. We were then (and have remained) good friends, though we don’t always agree on everything.  The basis of the “single T cell receptor altered self” hypothesis was fairly much worked out by the time of the Second International Immunology Meeting in Brighton, England. I traveled through the United States and gave the same talk in about 20 institutions. Among my hosts were Alan Rosenthal at NIH, Bethesda, and David Katz at Harvard. I also met Gene Shearer, who had results comparable to ours with haptenated cells. This was probably the first time that the immunology establishment became fully aware of what we were saying. Our ideas both contradicted the accepted North American model for the role of immune response genes, and turned the perception of the transplantation system on its head. Many people have told me years later that they heard this seminar, came away with the sense that the findings were significant, but did not fully grasp the import. Evidently some were also infuriated by what we were saying. Rolf traveled more extensively through Europe, and I also visited a number of institutions in England and traveled to Stockholm to speak to Göran and Erna Möller’s group at the Wallenberg Laboratory in Lilla Frescati.  Despite the fact that we had made a major breakthrough, the rigidities imposed by the excessive use of tenured contracts through the earlier years at the JCSMR had made any prospects of long-term appointments there fairly remote. Rolf accepted a faculty position at the Scripps Institute, and Hilary Koprowski called on my 34th birthday to offer me an Associate Professorship at the Wistar Institute. I had visited Hilary, who was a good friend of Cedric Mims, during my publicity tour en route to Brighton earlier that year. We moved to Philadelphia in 1975, and I quickly became involved with the outstanding Immunology Graduate Group headed by Darcy Wilson and Norman Klinman at the University of Pennsylvania. The Wistar/Penn axis was a highly interactive, and very open, intellectual environment. I collaborated extensively with Walter Gerhard on the influenza model, did some experiments with the late Tad Wiktor in Hilary Koprowski’s rabies program and was part of a large, campus-wide multiple sclerosis research effort. I talked a lot with John Sprent, the son of my parasitology professor in Brisbane, who taught me how to do lymph duct cannulation in mice. Penny went back to school, and developed a new career in the area of drug information. I wrote grants, was a member of the immunology circuit, worked with outstanding graduate students and became an established scientist and academic.  My self confidence was such that I made the major mistake of accepting an offer to return to the JCSMR as Head of the Department of Experimental Pathology, intending to build a vital program comparable to that Gordon Ada had been able to create in the early 1970’s. However, the era that this was possible had passed, and my decision was made on emotional grounds rather than on the basis of what was actually being offered. The less said about this time (1982-1988) the better, as I am still trying to get the overall experience in perspective. The most positive aspect was my interactions with some excellent colleagues, particularly Jane Allan and Rhodri Ceredig. With the passage of the years, the retirement of many of the tenured staff, the adoption of a more flexible appointment structure, and the return from Denver of Kevin Lafferty as Director, things at the JCSMR are now greatly improved. At the stage that I was there the situation looked hopeless. I decided to move back to a scientific world that I knew I could handle.  The opportunity to rebuild my research career came with the resources offered to me by J. V. Simone, then the Director of St. Jude Children’s Research Hospital (SJCRH). I had first visited SJCRH during my swing through the USA in 1974. At that stage it was still a small institution, with a strong virology department headed by Alan Granoff. My contact was via Rob Webster, who had trained with Stephen Fazekas de St. Groth in Frank Fenner’s program at the JCSMR and remains a close colleague of the JCSMR virologist, Graeme Laver. Alan and Rob engineered my move to Memphis, and Rob has been an outstanding friend and collaborator. This is a superb, open, research environment, that is extremely well funded. The two problems are that there is too much sunshine, and that we are too far from the Pacific Ocean. Such is life!  My characteristics as a scientist stem from a non-conformist upbringing, a sense of being something of an outsider, and looking for different perceptions in everything from novels, to art to experimental results. I like complexity, and am delighted by the unexpected. Ideas interest me. I was influened early on by reading Arthur Koestler and Edward de Bono, and more recently by the writings of Karl Popper and Thomas Kuhn. My research career has been highly unconventional, and I have not been a full-time student in the academic sense since I was 22 years old. I have never had a powerful mentor who saw me as the product (or continuation) of his program, a situation that probably helped to determine the outcome of my two attempts to return to Australia. Intellectually, I march to the beat of my own drum and have little interest in competing in “races”. There are too few people working in the area of viral pathogenesis and immunity, too little funding, too many problems and too little time. |
| Autobiographical |  |
| Podcast | “This is the first time we have had a completely novel virus infection and we are trying to vaccinate our way out of it” In this conversation, conducted in January 2021, immunologist Peter Doherty speaks about how we should learn from the current corona pandemic to be better prepared for and preferably prevent future pandemics.  The host of this podcast is nobelprize.org’s Adam Smith. |
| Telephone  interview | 0566 |
| Interview |  |
| ID | **0567** |
| Biographical | I was born in 1944 in Riehen, a village near Basel, and spent almost all of my first twenty-five years with my family in the same house. My grandfather on my father’s side had bought this house in 1918 after moving with his family from Tübingen to Basel to become Professor of German Literature at the University of Basel. My father grew up in Basel, went through the schools there, and studied biology, finishing with a thesis under the guidance of Prof. A. Portmann. Portmann was an outstanding zoologist-palaeontologist, with a very broad perspective on human development seen in an evolutionary context, not only anatomically, but also psychologically. With this training my father became the first PhD to be employed by the JR Geigy AG – one of the former four big pharmaceutical companies in Basel – not as a chemist, but as a biologist. This in a way heralded a new era of biologically oriented pharmaceutical research and development.  My mother grew up in La Chaux-de-Fonds, in the French-speaking Jura mountains, raised by parents whose family was in the watch-making business and in banking. After moving to Basel, my mother became a lab technician and met my father at work. I was the middle child of three, my brother Peter, born in 1942, became an architect and my younger sister Anne-Marie, born in 1945, became a lab technician.  I went through public school in Riehen, then in Basel, to the Mathematisch-Naturwissenschaftliches Gymnasium, the same school attended by both my father and father-in-law. Since this school didn’t teach Latin as a compulsory subject, which was at the time still necessary for several disciplines, such as medicine or law, I took four years of voluntary Latin as well as the school’s more mathematically and science-oriented subjects. During that time I had a great number of hobbies: I was introduced by a chemist and collaborator of my father’s – who is also a gifted painter – to the prehistory of the Basel region. This was extremely interesting, because during the last glacial period this area was not covered with ice, so that many sites of the previous inter-glacial period have survived. At the same time I also attended several handicraft courses, learning cabinet-making and smithing, as well as enjoying dancing and going to the mountains with the Swiss Alpine Club. My father sent my brother and me on a holiday exchange program to England to learn English. I read a lot and was allowed to do a fair amount of travelling through England, France and the Scandinavian countries, between the ages of twelve to sixteen. When I obtained my matura in 1962, I was uncertain as to what to study. The two areas I favoured were either medicine or chemistry and, because of the greater range of choices the medical profession could offer, i.e. research, clinical activity, or private practice in the mountains, medicine was my target for the next 6 years. I first had to acquire my matura in Latin, however, and in parallel with the medical studies I also had to do my military service. I somehow managed all this by working hard during the first two or three years of medical school. During that time I met my wife, Kathrin, who was studying in the same class, also at the university of Basel. We took our final exams together, which we had prepared with a very nice group of four medical students. In November of 1968, two weeks after the final board exams, we got married. We had originally wanted to go to Africa, where I would have liked to work and learn about leprosy. We applied to the WHO in Geneva and other international organisations, but we were not accepted because of our lack of experience. On the first of January 1969 I began to work at the surgery department at one of the hospitals in Basel, and Kathrin started at the University of Basel Eye Clinic. However, within that first year I somehow became aware that surgery might not be the career l should pursue for the rest of my life and I started to look around for alternatives. After many discussions about my career with several researchers (including A. Pletscher, J. Lindenman and many others), to find another goal, I applied to the postgraduate course in Experimental Medicine at the University of Zurich. To fill in the time between surgery and this course, I did some studies on capillary growth in the epiphysis of the long bones in the Institute of Anatomy at the University of Basel, under the direction of R. Schenk and U. Riede. The course in Zurich is a unique institution that is financed by the Swiss National Science Foundation and the state of Zurich, it gave some ten medical students from all over Switzerland the opportunity to learn more about modern science, in particular molecular biology, biochemistry, genetics, neurobiology and immunology, and to catch up with what had been missed during medical school. Starting in October 1970, I spent two years in the Department of Biochemistry at the University of Lausanne, under the direction of H. Isliker, learning about immunology, immuno-chemistry and the frustrations of experimental lab work. In Lausanne, I was asked to apply to bacteria a technique that had been made popular by T. Brunner and then by J. C. Cerottini, the 51Cr release assay to monitor the destruction of the immunological effector functions of host cells. This test involved the labelling of cells with a radioactive isotope, to monitor the immune mechanism destruction of host cells. The process was measured by determining the relative amount of radioactivity released from the dying cells. This project proved very difficult and did not produce any conclusive result: The chromium was not properly absorbed by the bacteria and this release assay was therefore not easily feasible. Nevertheless some work was accomplished on the role of IgA, which was obtained from hyperimmunised cows that release a significant amount of IgA into the colostral milk. I was evaluating whether such hyperimmune milk products were able to protect in an ileal loop model against the entrotoxin-releasing entropathogenic *E. coli.* This confrontation with an infectious disease and the potential of immune responses to protect against it, motivated me to look for a second postdoc position in the same field. Together, Kathrin and I sent about fifty applications to various labs throughout the world, including ones in the UK, the USA, and in Australia, but we either got no answer back or only negative ones. At that time we already had two children and my wife was also trying to find a position to pursue her own career as an eye doctor.  In 1972, while I was looking around for positions, H. Isliker discussed my plans with Professor G. Ada, Head of Department of Microbiology of the John Curtin School of Medical Research in Canberra at the Australian National University, and with Robert Blanden, a professorial fellow at the same institution. G. Ada and H. Isliker were working together at the International Union Against Cancer in Lyon, and R. Blanden came by to teach at the WHO course on immunology at our institution, which was hosting the WHO training lab in Lausanne. This juxtaposition opened up the possibility that I could join the Department of Microbiology in Canberra with the condition that I brought my own salary. The post-doctoral fellowship from the Swiss Foundation for Biomedical Fellowships granted me 32’000 SFr. per year for two years to go to Australia. Fortunately Kathrin did not object to such a drastic move with our two small children Christine, 2 1/2 years, and Annelies 11 months old. We flew to Canberra in January of 1973. My plan was to work with R. Blanden on cell-mediated immunity against Salmonella and Listeria to learn more about the role of cell-mediated versus antibody-dependent immune effector mechanisms in these infectious disease models. When we arrived in Canberra we were very lucky and happy to find a generous infrastructure offered by the Australian National University, which provided us with a detached four-room family house within a group of some thirty houses lovingly called the “University ghetto”, in Hughes. It provided an extremely nice and congenial environment for students, young and middle-aged post-doctoral, pre-doctoral and professorial visitors from all over the world. Kathrin soon found a position as a part-time physician at the emergency room of the Woden Valley Hospital, the kids found access to play-groups and kindergarten, I spent all day in the lab studying immunity to infectious diseases and we made many friends amongst the Hughes community.  Within the department, the only empty space in the small labs at the John Curtin School, was in the lab occupied by [Peter Doherty](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1996/index.html). He had arrived as a post-doc from Edinburgh at the end of 1971, his interests being mostly in inflammatory processes in the brain, particularly in mice with the Semliki Forest virus or with lymphocytic choriomeningitis virus (LCMV). We started to cooperate on immune responses against the LCMV virus; he was tapping the cerebral spine fluid and doing the inflammatory and immunopathological analyses in the brains, while I was doing the cytotoxicity assays, since I had become familiar with them in Lausanne. This collaboration resulted not only in the discovery of the MHC restriction, as will be detailed in our lectures, but also encouraged me to eventually enrol at the age of 28 as a PhD student at ANU. I had two reasons: one, obviously, was to add a PhD to the doctorate that I had earned with a thesis on the clinical problems of neuritis of the plexus brachialis at the University of Basel. The second motivation was that the exchange rate of 5.2 Swiss Francs for 1 Australian dollar made life rather difficult at the time. The PhD scholarship added a welcome 2000 Australian dollars to our budget.  The two-and-a-half years in Canberra were particularly successful because the group of people that had come together in G. Ada’s department (including R. Blanden, K. Lafferty, A. Cunningham, P. Pletscher, P. McCullagh and many others), was just the right mix of investigative, critical if not aggressive, intelligent if not inquisitive, humorous if not bitter, and enjoyable minds working together and making sure that one’s feeling of being right was constantly questioned and challenged. Of course, the fact that all these people – or at least most – worked with biological model situations, either involving infectious diseases or the transplantation of organs, made all of us very aware that immunology really had to deal with defence in vivo and not with artificial antigens in an in vitro setting.  As soon as our first papers were published in *Nature* I had to look around for the next post-doctoral or professional situation and was contacted by F. Dixon of the Scripps clinic in La Jolla, who was looking for an assistant professor to join Scripps to work on cell-mediated immunity of auto-immune mice; he had heard from J.C. Cerottini in Lausanne about our work in Canberra. I had also approached [B. Benacerraf](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1980/index.html) at Harvard to find out whether there would be any chance of working in his Department of Pathology to continue studying infectious disease immunology. At the second International Congress of Immunology in Brighton in 1974 P. Doherty and I had various opportunities to report on our findings of MHC restriction. I met with F. Dixon and B. Benacerraf. After several discussions and because I could no longer continue to work with the virus in the Boston lab, but also because California, the sea and sun seemed attractive, the decision to join the lab of F. Dixon in La Jolla was easy.  Our two children were very happy in Canberra and they both spoke the most beautiful Australian English. Our second daughter, Annelies, however, went through repeated colds and middle ear infections, one of them causing a near-lethal Haemophilus influenza meningitis, signalling a selected IgA defect (that turned out to be transient). On December 9th, 1974 Kathrin gave birth to our Australian son, Martin, at Woden Valley Hospital, while I was summarising our experiments on MHC-restricted T cell recognition during the annual meeting of the Australian Society for Immunology assembled in Canberra.  Kathrin moved back to Switzerland in early January 1975 to spend a few months with our parents and to get another 6 month’s training in ophthalmology, while I had to write up my PhD thesis and Peter Doherty was sweating to correct my offences to the English language. So for another 3 months I finished up several studies in the lab in Canberra and then travelled through Australia by train and bus. The two following months in Switzerland were spent by renovating a 16th century house in the Jura mountains with my brother Peter. In early July 1975, we all moved to La Jolla with a green card, i.e. as US-immigrants, to join the Scripps Clinic of Medical Research. The decision to apply for a green card was suggested by F. Dixon not only to avoid time restrictions during my stay in the USA but also because the prospects for finding an interesting job in Switzerland were virtually nil. Work at Scripps started well, not least because Alana Althage, one of F. Dixon’s technicians, was assigned to me. She has been helping me ever since by preparing much of the experimental work and by keeping the lab running for the past 20 years. I continued studying cell-mediated immunity and LCMV. This virus had also been studied for several years at Scripps by M.B.A. Oldstone and F. Dixon. We were using experimental surgical techniques to evaluate whether or not the MHC of the thymus played a role or not in the selection and expression of the T cell specificity for self. A series of similar data was obtained by experiments done in parallel by M. Bevan at the MIT. They resulted in the discovery that the MHC-molecules of the thymus dictated the restriction specificity of T cells for self-MHC. These results caused major excitement in the immunological community because they fitted in nicely with what one knew about the role of thymus in T cell maturation as originally described by J.F.A.P. Miller in England and in Australia.  My wife worked as a voluntary collaborator at the ophthalmology clinic at Scripps for about 10 to 20% of her time; she kept her medical skills alive, particularly in 1978, when she decided to study for – and successfully passed – the US-medical board exams.  The University of Zurich had approached me in 1976 to look into the possibility of taking over a position that had been freed in 1975 by Professor G. Zbinden, Head of Toxicology of the University and the ETH. This division of Experimental Pathology within the Department of Pathology was an attractive chance to go back to Switzerland and to start a larger group. Although the Medical Faculty of the University of Zurich had voted on a finalist for this position sometime in 1977 and had put me in first position, it took another two years of tough negotiations with the government before we could move in the fall of 1979. This required a lot of patience from Kathrin, F. Dixon and all of us; the signed contract only arrived about 10 days before the planned starting date in Zurich!  For the past 17 years we have lived near Zurich, first in Zollikon, and now in Zumikon, in a cosy old house with huge woodstoves, a beautiful flower garden and a handy vegetable plot, chickens, and an Appenzeller dog. Kathrin finished her ophthalmology specialisation in the first few years, then started up her own practice. The children adapted reasonably well to schools here and are just about to finish medical school.  Work in the lab was difficult at first because we had to organise all installations, equipment and animal quarters for infectious experiments. This was made much easier when Hans Hengartner, a molecular biologist from the ETH, joined the lab; he had spent 4 years at the Basel Institute of Immunology. In 1978, he approached me to plan a possible move together to Zurich. This was another lucky event in my life, comparable to the moves to Australia and to Scripps; the collaboration with Hans, first in the division of Experimental Pathology and subsequently in our Institute of Experimental Immunology, as associate – and eventually as full professor of both the University and the ETH – has been extremely productive, exciting, stimulating, straightforward and mutually complementary. Joining our molecular, immunological and physiological capabilities and expertise has helped to achieve far more than either of us could have done alone. Together, we continue to follow viruses in infected hosts to find out more about how the host immune system functions and how viruses and immune system have co-evolved. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0567** |
| Interview |  |
| Q25 | Rolf Zinkernagel, welcome to this interview. You were the co-recipient of the 1996 Nobel Prize in Physiology or Medicine with Peter Doherty. I’d like to start by exploring a few general themes. If I say the word mentorship, what does that conjure up for you? |
|  | I get the whole process of being taught and educated in whatever field. For me it’s medicine and biology. And as always is the case, you have a few key figures on your way into a certain area and I think that applies to everybody. In my case, teachers in Switzerland like Jean Lindenmann who discovered Interferon, together with [Alick] Isaacs, a long time ago, 50 years in fact this year. Then Henry Isliker, a complement researcher in Lausanne, played a major role. Then in Canberra, I’d say Bob Blanden, Gordon Ada, Frank Fenner would be amongst them. And in the US, Frank Dixon would be one of these persons. |
| Q25 | And is there anything that you particularly carry over from them in your mentorship of people? |
|  | Yes, for example we always used what we call the Bible Allah in our teaching for post docs and doctoral students in Zurich. And this is an idea I took over from two persons, one at the Basel University where I grew up, his name is Adolph Portmann, he is a human physiologist in the broader sense. And he had a course which I attended during medical school which was called Classical papers in zoology and biology. We read classical papers of Lamarque or Darwin and so on, and he put that into connection of time. And Gordon Ada had a similar project where we went through certain papers in immunology, and I sort of combined this and taught a class every two or three years about very important papers over the first 100 or 120 years of immunology.  Incredibly useful but quite a rare thing to do now I imagine.  Rolf Zinkernagel: I guess so because *Medline* stops I think at, for most things now, at about 1970 or 1965. And many of these older types of studies have been incredibly ingenious.  So that’s primarily what you’re teaching. You’re teaching ingenuity through …  Rolf Zinkernagel: Through that course, yes absolutely. And just for youngsters getting a perspective of that immunology didn’t start in 1997; it started much, much earlier. And I think this is true for most areas of medicine and biology. And I think it’s good to get a sort of perspective of both history, but also to make us all more humble because other people have been probably much more clever than we have. |
| Q26 | When you choose students to come and work with you, what do you look for in the student? |
|  | We look mostly for performance, are they good? And the second is we always have them visit at least twice the lab to talk with people. And thirdly, we ask their mentors or whoever knows about them personally.  So having them visit the lab is a way of finding out whether they’ll fit in.  Rolf Zinkernagel: Correct. And I think particularly in a relatively small lab like ours, I think the personalities and characters are usually the limiting factors. It’s not the brains. |
| Q26 | That leads me onto the next question I was going to ask you, what sort of lab environment do you like to create? |
|  | What we have done over the past 30 years, and this is also largely influenced by my experience in Lausanne at the Biochemistry and Henry Isliker’s lab, but also in Canberra. There you have a very open, flat hierarchical type of structure, where the only thing that really counts is what your competence is and how good you are, and how intelligent in combining things together, advising people, and have them accept you as a character. |
|  | Is that easy to do? Because I imagine that hierarchies are sort of inbuilt for students.  Rolf Zinkernagel: Yes, but I think as long as the hierarchy is linked to knowledge or expertise, it’s easy. Because I think you cannot fool yourself nor the others very easily.  That’s true. But you need to bring students’ confidence up to a level where they’ll start to …  Rolf Zinkernagel: Yes, but I think if you are confident in the students, they are usually confident in you as a teacher. And I think if you basically behave like a decent person towards them, they will also in very general terms be a decent counterpart. So, I think it’s easy. |
| Q43 | As well as having an open communication, do you also have an open lab structure? Do you have people working together next door to each other, bumping into each other? |
|  | Absolutely. We have this in Zurich, but this basically has been my experience in all other places I’ve been. You’re very much limited in space. People cannot avoid bumping into each other. I think that also makes the priority clear that they have to fit somehow, otherwise this is not possible to be living together on the very small amount of space.  I’ve sometimes wondered whether some of the problems of the drug industry might be put down to the fact they have too much money when they build their labs and they create too much space between people.  Rolf Zinkernagel: I don’t think this is the problem really. I think their problem is more that they are under a certain pressure to deliver. I think that’s one problem. The other problem is that, and this is a positive problem, what you say, you have more money available once you are on the subject of interest to the company. But the disadvantage, nothing is black and white, so I think the cost point is that if the company or the firm decides after three years that’s not going to gel out and you have to change your subject, that’s very difficult because you have invested a lot of time in developing your baby. And then suddenly you have to jump from x to y. And I think you can do that once, maybe twice, but the third time it already gets at your very innermost desires. And I think that is, with time, a huge problem. |
| Q38 | You say that the pressure to deliver is a problem in the industry. Why do you think that that pressure to produce is …? |
|  | It’s very simple. If the industry or the company cannot develop products that deliver the goods, that are active and relieve certain symptoms or disease, improve certain disease states, then the company’s out. This is very much Darwinian type of evolution. |
| Q38 | But the pressure to deliver could have a positive effect on the people who are actually doing it? |
|  | It always has. But it’s just more drastic. In academia, if you don’t deliver next year, you are usually given a chance to come up with the goods two or three years later, because you’re granting period is usually 3-5 years. Or the university backs you up for a certain period. I think that’s a big difference to industry. |
| Q1 | Turning to your own development, you took some time to decide what you wanted to be when you were young, I gather from your autobiography. And eventually settled on medicine initially, how did that path come about? |
|  | My choices were pre-history, ethnology, chemistry, organic chemistry or medicine. It’s difficult really to rationalise why, but I just had to make up my mind at some time. And I think this is probably true for everybody and is also true for a scientist’s life because every day you have many more questions than you can attack or solve. So you have to reduce your choices. I think that’s what I did.  But a lot of people say that it’s important to capture scientists when they’re in their early teens, you have to get them young and there needs to be a huge focus on education at that point. But for you, there were lots of things going on.  Rolf Zinkernagel: That’s right, maybe too many. Then to make choices is more difficult. But I have no regrets. I think the choices were ok. |
| Q56 | It seems that quite an important event was attending the experimental medicine course in Zurich, which was 40 years ago or so almost, and that seems to be quite precocious in a way because now experimental medicine is much talked of and people are really investing in it. For Zurich to have a department of experimental medicine at that point seems to be ahead of its time. |
|  | It was quite unique actually and what happened at the time, during the 1960s, was that a reasonable number of young Swiss spent their post-doc time in the US or in England or somewhere else. And came back home developing new departments. That was the time when science and science endeavours had only upsides and everything went up. And at that time, it became apparent that, and this is a general trend I think it applies to the US and the UK, that the number of MDs, of doctors actually choosing to do clinical research or basic research dwindled. And this had of course many reasons, amongst them I guess the bread baskets hanging lower or higher. That there was perhaps not quite the open culture in clinical medicine as let’s say in the Anglo-Saxon countries. So that was basically what a group of physicians tried to change and they created the course. I think the first course was about in 1967 or so. And a number of very good people actually, because it was highly selective from all of Switzerland only 10 people could attend the course per year. You got a reasonable bunch of youngsters and it was very good. |
| Q59 | Would it be fair to say that it turned you towards basic research from medicine or were you already heading that way which is why you joined the course? |
|  | I was still seeking or looking for something because initially I wanted to become a surgeon, which I thought was the most honest way to practice medicine. But somehow this didn’t really preoccupy my mind, so I was looking around, then just got onto that course and from there things went in a bended way, but still relatively straight forward for the next 40 years. |
| Q3 | What focused you on immunology? You quite quickly found that was your path. |
|  | Infectious disease is still I think the biggest problem in medicine. To relate infectious disease, to understand host/infectious agent relationships and so on, was in a way logical for an MD. |
| Q11 | And your second post-doc was in Canberra where you found yourself at the Australian National University. And working with Peter Doherty you had very rapid results and came up with MHC restriction as an idea within a year of joining together. |
|  | Even less. This I think is a good example how chance really operates because the original plan was not to work with Peter but to work with Bob Blanden on the faculties of intracellular bacteria, such as listeria or salmonella or TB. And then the lab sizes at the ANU in micro are very small. In each so-called lab there actually were two heads and one pair of hands. And the heads could be PhD students or post-docs or a professor and the technician basically. And the only open space in the whole floor was actually in Peter Doherty’s lab. So I started doing some experiments with Bob Blanden, but by co-infiltration and co-adaptation, we started to simply work on a problem he was interested in, which was at the time information in the brain. And I came from an institution where so-called cytotoxicity, I say is namely that T-lymphocytes or cell mediated immune effected cells were measured by their capacity to liaise or destroy in-vitro cultured cells with some abnormalities or additions. And since I had learned that test in Lausanne that fitted nicely to the problem of information in the brain. And then we started to combine our expertise and that was the beginning of the end. |
| Q20 | In your banquet speech at the Nobel ceremony you talked about the combination of Peter the mystic and Rolf the collector. It was obviously a great combination of talents and complementarity, what was special about that relationship? |
|  | I think that the most important part is really that Peter and I had a very similar sense of humour which was very good. And in terms of character, him being a vet, myself being an MD, I think we had complementary types of views on certain things and doing certain things and thinking about things. You cannot plan these things they just happen or don’t happen. We got along extremely well. And I think very important if you work in two’s or three’s, I think we both had an extremely open discussional relationship which meant at the end none of us were afraid of the other. In contrast we really had a very easy relationship.  Open and giving – no secrets.  Rolf Zinkernagel: Yes. |
| 59 | The work you did basically appeared in two nature papers and as very often happens, the Nobel Prize was awarded sometime after that, it was actually about 22 years gap. Did it take that long for the importance of the work to be recognised do you think? |
|  | I think in our case it’s a combination of several factors. I think the repetition and the confirmation of the work happened fairly quickly, within two years or so. But then what remained unclear is how? How does it? Why? How does it happen? This then took a fair amount of time. So that’s my interpretation, that perhaps Stockholm waited for a certain molecular explanation of the initial observation. Which then came along, there’s a number of people involved, Emily /- – -/ who described how antigens, foreign stuff taken up by macrophages or similar cells and then being digested and re-presented on the surface in the connection of these major transmutation antigens of the class 2 type came about. And there were several people around that. Then Alan Townsend, who did the same for the MAC class 1, which was a big splash at the time because it simply wasn’t understood how this combination of this presenting molecule and the virus antigens, how this should happen. And then I think the second general finding was the crystal structure of the major transmutation molecules, of class 1 and class 2. That put the corner stone into the pot. And I think that happened roughly 1996 or -97. And then came the T-cell receptor, also 1984-87, the crystal structure was done. And this then convinced everybody that maybe the original observation triggered all this evolution of science and we probably were very lucky that we got the prize and not the others. That’s how it is. |
| Q41 | As the mechanism was worked out did the applicability of the discovery become much broader as well? Was it realised that it could be of much more benefit if you like? |
|  | Yes and no, like always. I think the detailed understanding is very satisfying because if you understand something, but the practicability, the hope was that once we understood everything, we could just take peptides, which are sort of localised in this presenting molecule and immunise easily and tumours and all sorts of things, and that hasn’t happened. It’s the biology at the end of the day that shows where the limitations are and in a way I find this very satisfying being an MD, a physiologist basically, that physiology counts. That understanding counts as well of course, it’s very important and satisfying. But to have function and improve disease states or prevent death is usually much more complicated than see the molecule.  You need to see the basic mechanism operating within the system.  Rolf M. Zinkernagel: You need both. |
| Q4 | We’re here at the Lindau meeting where Nobel Laureates mix with a large number of students and your lecture here was entitled ‘Why don’t we yet have a vaccine against TB or HIV?’ So we seem to have found our way into that question. What answer did you provide to the students |
|  | Despite the fact that we know all these details, where T-cells recognise how cell mediating immunity functions, how it’s getting triggered, theoretically you would have thought, put things together, express things, make the molecules, should go. It doesn’t. And I think what I try to do is to show some commonalities between the problems we have solved like the acute childhood infections, what they have in common, versus all the infections where we haven’t succeeded in making a vaccine. What are their commonalities? And to put it in very simple terms, the commonality is that for the acute /- – -/ killing types of infections, the only thing you need is a high enough antibody level, because in a way evolution has chosen that pathway as a successful pathway because the mother can give these antibodies to you when you are born. Whereas the other group of infections, including malaria, schistosomiasis, TB, leprosy, HIV and …  Which come later in life, yes?  Rolf Zinkernagel: No they don’t come in fact, they also come very early. But in most of these cases it’s not sufficient to have just maternal antibodies. You need an excellent immune response that actually keeps on being driven by low level infection that you cannot get rid of. And I think that part, namely to have a vaccine that imitates, starts a very low level of infection, to actually maintain and boost the immune response all the time. That is what we haven’t succeeded. Take TB, there is a so-called vaccine against TB, it’s called BCG, the bug that has been selected and developed at Pasteur in the 1920’s. Now interestingly, BCG can reduce the chances of very small kids, between 0-2 years, to catch what is called an overwhelming type of TB infection. But it cannot change TB disease after that period of time. And this correlates virtually to the month with the persistence of the BCG bug in the small kid, because the BCG is so much attenuated that after one or maximum of two years, the bacterium has been eliminated from the host. And once that has happened protection decays, is finished. And I use this example to explain that in my view, and this is not a popular view, that what we call memory, immunological memory, that is having seen an antigen or infection once, protects you for the rest of life, is not true. It’s an academic idea which is nice and interesting but doesn’t correlate with the experience we have in clinical medicine.  Although it’s the basis for all vaccination programmes, is it not?  Rolf Zinkernagel: Yes, but you see the key point is that for all the cases where the classical vaccines protect and work, the only thing you need to have is a high enough antibody level. If that is fulfilled, and there are many ways to fulfil that, then you are ok. But in all other cases where you apparently cannot inject something and then be protected for the next 40 years of your life, there is no reasonable explanation.  So what’s the approach?  Rolf Zinkernagel: It’s in a way to create infectious agents that fulfil the requirement of persistence without causing disease.  So sufficiently stimulating throughout.  Rolf Zinkernagel: Correct. For many, many years. But the experience just shows that evolution or co-evolution between let’s say TB or leprosy or malaria, has done an excellent job. Because over many, many years, millions probably, the adaptation has reached such an elegance and minimal entropy level that you virtually cannot improve. Or you have to be extremely optimistic to think you can do better. But it’s not impossible. But it’s just very difficult.  As well as theorising about it are you working on this precise problem?  Rolf Zinkernagel: Yes, we try. We follow certain possibilities, for example, in the virus we use which is called lymphocytic choriomeningitis virus, LCMV, in mice, it has exactly those characteristics. Usually, it’s controlled very well in mice, but then persists at a very low level and keeps up the immune response. We’ve found an unexpected way how virus actually seem, this is an RNA virus, but isn’t a so-called rhetoral virus. It’s not like HIV, nevertheless we find in mice footprints of this virus, but not in RNA form. We also found RNA’s of the virus. But in some cases we find a DNA form of certain viral antigens, which is completely unexpected. So we now try to understand what is going on. And the interesting part of that is that LCMV is highly adapted, like in a way HIV to higher primates is highly adapted to the mouse. HIV in the mouse is completely different from HIV in a rat. And rats and mice are fairly close. And in rats this does not happen. In rats the virus cannot create DNA, in mice it can. It must be highly species specific.  So the problem you’re really battling is co-evolution of …  Rolf Zinkernagel: Yes, in a way. Because at the end of the day both have to survive. And the virus is not interested in killing the host.  You returned to the ETH …  Rolf Zinkernagel: I am actually at the university. |
| Q34 | You returned to the university in 1979 and have been there ever since. It obviously provides an environment that suits you well. Is there anything special about it? |
|  | I guess it’s a combination of many factors. Both my wife and myself come from Basel, which is about 50 miles away from Zurich. Our kids basically grew up in Canberra, in La Jolla for five years and have now grown up in Zurich, we feel very comfortable. It’s a very interesting, culturally rich university life, small city, it only has about 400,000 inhabitants. But you have two excellent universities. So if you can’t solve or attack a problem, you find somebody to do it with you or for you. So it’s a very good environment. But I think La Jolla was an excellent environment, Canberra …  Wherever you can do good work.  Rolf Zinkernagel: Yes, in a way. |
| Q59 | In parallel to your research work you’ve become, especially in recent years, quite a spokesperson for the animal experimentation movement. And also, you’ve spoken out in favour of gene technology. What do you think needs to be done from the research community’s point of view for those causes? |
|  | I think there are two major aspects. One is the media, the public opinion side and the other is the research side. I think researchers have to make all reasonable efforts to report and talk about what they do and how they do it. I think some people do that fairly well and others have an intellectual arrogance that is not very conducing to these efforts. So, on the other side you have the media and it’s not a secret, I think this is a worldwide phenomenon that the of course media in very general terms, there are exceptions, but are leaning towards a red/green type of tingeing of their glasses. So basically because of the atom bomb, physics and chemistry is very bad for you because of infections. Science is bad because of …  Chemicals can’t be good etc.  Rolf Zinkernagel: But this of course is over simplified and is not correct in this, but it’s a brave form of formulating the concerns. So, I think that’s one part, and the other part is to report on scandals in science is very attractive to the media, because I think that’s the major justification for media. And the second part is that to report that science is very hard work, very difficult, requires an enormous dedication because in fact 99% of the experiments go down the drain and are unsuccessful. The media are not interested in all that part. They simply pick the few raisons or cherries out of the cake that are enormous. And some of these picked cherries turn out to be rotten cherries. This gives a very strange atmosphere. But I think the sports is the same. As long as somebody jumps eight metres he’s ok, but if he’s doping, of course he is not ok. So I think the same happens with science. And this makes the business very difficult because the third aspect is I think as scientists we must not create hopes that are unjustified. Because that is very dangerous. And I think that happens too often.  Yes, there’s a lot of claim of potential cure.  Rolf Zinkernagel: And this has happened with HIV vaccines for example for many years. And I think we should be much more careful. But then I think we need the honest cooperation of the media because I think it’s, in a way, as much in the interests of the media to make a big splash about some hope. We need some co-evolution I’d guess. |
| ID | **0568** |
| Biographical | Dr. Lewis received the B.A. degree from the University of Minnesota in 1939 and the Ph.D. from the California Institute of Technology in 1942. He served to the rank of captain in the United States Army Air Force from 1942-1945 as a meteorologist and oceanographer in the Pacific Theater. He joined the Caltech faculty in 1946 as an instructor. In 1956 he was appointed Professor of Biology and in 1966 [Thomas Hunt Morgan](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1933/index.html) Professor of Biology. He was a Rockefeller Foundation Fellow at Cambridge University, England (1947-48) and Guest Professor at the Institute of Genetics, University of Copenhagen, Denmark (1975-76).  He is a member of the National Academy of Sciences, the Genetics Society of America, the American Philosophical Society, and the American Academy of Arts and Sciences. He is a foreign member of the Royal Society (London) and an honorary member of the Genetical Society of Great Britain. He is a recipient of the Thomas Hunt Morgan Medal (1983), the Gairdner Foundation International award (1987), the Wolf Foundation prize in medicine (1989), the Rosenstiel award (1990), the National Medal of Science (1990), the Albert Lasker Basic Medical Research Award (1991), and the Louisa Gross Horwitz prize (1992). He holds honorary degrees from the University of Umeå, Umeå, Sweden (1981) and the University of Minnesota (1993).  Dr. Lewis and his wife, Pamela, an artist, have three children: Hugh, an attorney who lives in Bellingham, Washington, Glenn (deceased) and Keith, a biology research assistant who lives in Berkeley, California.   |  |  | | --- | --- | | Principal works of Edward B. Lewis | | | 1950 | Lewis, E. B. The phenomenon of position effect. Advances in Genetics 3: 73-115. | | 1951 | Lewis, E. B. Pseudoallelism and gene evolution. 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| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| ID | **0569** |
| Biographical | I was born during the war, on October 20, 1942, as the second of five children. My father, Rolf Volhard, was an architect. He was the eighth of ten children of Franz Volhard, a professor of medicine in Frankfurt, and specialist for heart and kidney. My mother’s mother, Lies Haas-Möllmann, was a painter but had given up her career for her family. I remember her well, because I visited her frequently during Easter vacation in her apartment in Heidelberg. She was a remarkable woman of strong discipline and character, who interested me very much. Her paintings and drawings are very beautiful, impressionist style, and show a great eye. I do not remember my other grandparents. Both my father and mother were from families with many children, and I once counted and found that I have 33 cousins! Most of my relatives lived rather close to us in Frankfurt, or Heidelberg, so I know most of them reasonably well, with some I am good friends.  We lived in a flat in the south of Frankfurt, with a rather large garden, close to the forest. I had a happy childhood, with many stimulations and support from my parents who, in postwar times, when it was difficult to buy things, made children’s books and toys for us. We had much freedom and were encouraged by our parents to do interesting things. I remember that my father showed much interest in what we did, and thereby had a great influence in our performances, without being particularly ambitious (although good grades at school were more or less a matter of course). I tried to explain to him what we did in mathematics, and we discussed Goethe’s scientific papers. My mother had great social talents and a very good way of taking care of children, and other people who needed help, in an unassuming and practical way. Both my parents were good musicians, and painted, so we kids did that too, with much pleasure and support. I learned to play the flute, but, although I tried hard, I never drew as well as my sisters and my brother. When we grew up we did not have much money, so we learned to sew our own dresses, and generally were educated to make things we could make ourselves, rather than buying them, or finding other people to make them for us. One sister and my brother are architects, another sister studied music, and the youngest sister studied to be an arts teacher. We have been and are still very close.  I remember that already as a child I was often intensely interested in things, obsessed by ideas and projects in many areas, and in these topics I learned much on my own, reading books. Early on I was interested in plants and animals, I think I knew at the age of twelve at the latest that I wanted to be a biologist. As a small child I had spent several vacations on a farm in a little village, the refuge of my grandparents in the last year of the war. I have very fond memories of these visits, the people were very kind and allowed me to help with the animals and with harvesting, and the food was wonderful. I loved our garden and kept some pets, but I missed having someone knowledgeable in plants and animals, who could explain things to me, so I tried to find out much by myself, and from books. Within my family I was the only one with lasting interests in sciences. This was supported by my parents by giving me the right books, and by my brother and sisters by listening to my tales and theories.  I enjoyed high school where I learned a lot from excellent teachers. As I was lazy and rarely did my homework, I finished high school with a rather mediocre exam. I almost did not pass in English language. Recently, my previous teachers allowed me to see their report on my high school performances, which included the following statements: *Despite the fact that her talents are rather equally spread among many areas of knowledge, her performances are rather different depending on the distribution of her interests. Thus, with her strong display of self will she can be decidedly lazy in some topics over years, while in her areas of interests she performs to a degree far extending that required for normal school purposes. Thereby she gets into increasing difficulties and a certain nervosity, because she simply cannot cope with everything she would and should like to perform, and then loses stamina.* On the other hand, the statement also acknowledges that *she is gifted above average, has a critical and qualified judgement, and the talent for independent scientific work.* Luckily, school education was good and interesting, particularly German literature, mathematics and biology. We had very engaged teachers, mostly women. In the final class our biology teacher discussed many modern topics with us such as genetics, evolution, and animal behavior. I remember that I tried to develop a new theory about evolution, when we discussed Darwin at school. For the celebration of our Abitur, at the end of high school, I gave a speech “On language of animals” (Sprache bei Tieren). This speech was the result of reading of [Konrad Lorenz](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/index.html) and other German biologists on animal behavior that interested and still interests me much.  My father died suddenly on the day of my high school exam, 26th of February, 1962. At the time I finished high school, I was determined to study biology, deeply convinced to eventually be a researcher. I had briefly considered studying medicine, because of its relevance to mankind. To find out whether I could be attracted to studying medicine, I did a one month course as a nurse in a hospital. This experience greatly supported my conviction not to become a doctor.  Initially I was disappointed by the university and missed school, and my friends at school. I also was rather shy and found it quite difficult to design my curriculum on my own and get to know fellow students. The courses in biology in Frankfurt University were quite dull at the time, it seemed that I knew the more exciting things already, and what was new was boring, although there was one course in botany which I enjoyed. Soon I discovered physics, by an excellent series of lectures by Martienssen, a professor of experimental physics in Frankfurt. I also did courses in mathematics and theoretical mechanics which fascinated me for a year, until I found these topics too difficult. Via the class in chemistry I got reminded of my true interests in biology. At that time (Summer 1964) a new curriculum for biochemistry, the only one of its kind in Germany, was started in Tübingen, and I made up my mind quickly, and went there to study biochemistry, leaving family and friends behind. Being a student in Tübingen, a very lovely old town, was fun. I lived close to the market place, right across from the best movie theater. Rather primitive, but pretty, no shower, cold water, no central heating, but everybody I knew lived like that and it was quite romantic. My friends were largely language students, studying Latin, and Rumanian, and English language. I did not like the biochemistry curriculum very much, too much organic chemistry, too little biology. But on the whole it was a good thing to do, because it provided a very solid training in many basic courses, such as physical chemistry with thermodynamics, and stereochemistry, which I liked. In the final year two new professors taught microbiology and genetics, which I liked very much, and I also had a chance to attend seminars and lectures from scientists of the Max-Planck-Institut für Virusforschung, Gerhard Schramm, Alfred Gierer, Friedrich Bonhoeffer, Heinz Schaller, and others. They were teaching very modern things such as protein biosynthesis and DNA replication. This excited me much although I hardly understood the lectures at the time. I did my exams for the Diploma in biochemistry in 1969, as usual for me, with rather mediocre grades because I had not always paid attention, and often had lost interest.  From Heinz Schaller with whom I did my Diploma work I got my first real training in a laboratory. I was his first graduate student and very keen. Heinz is a chemist, and taught me to think in quantitative terms, yields, completeness of reactions, he is an excellent experimenter. My first thesis project on the comparison of DNA sequences of small phages by RNA-DNA hybridisation was given up, after the realization that it would involve predominantly the refinement of techniques, with uncertain success. I finally developed a new method for large scale purification of very clean RNA polymerase, and, in collaboration with another graduate student and friend, Bertold Heyden, isolated RNA polymerase binding sites from fd Phage in order to understand the structure of a promoter. We determined the composition of the strongest binding site and found it to be rather different from that of other sites such as the strongest of ØX 174 and the second strongest from fd. At the time DNA sequencing was not easily possible, so we characterized the sequences by their oligopyrimidine pattern, for which we had developed a new and simple method. It was a quite interesting story which got published as a letter to NATURE.  Although I was an experienced molecular biologist, I got bored with my projects at the end of my thesis (1973). The prospect of continuing the study of transcriptional control via the structure of promoter regions meant developing new methods for DNA sequencing. The field of recombinant DNA technology was growing and a fellow student and good friend, Peter Seeburg, argued strongly for it. I was sceptical, and at that early time, like most other people in Tübingen, did not foresee its powers. At that time, the Max-Planck-Institutes in Tübingen were interesting places. Wolfgang Beermann and Alfred Gierer taught courses in cell and molecular biology. The Friedrich-Miescher-Laboratory was founded, with Friedrich Bonhoeffer, Günther Gerisch and Rolf Knippers as first group leaders. In the laboratory of Alfred Gierer, people were studying regeneration processes in Hydra. Gierer and Hans Meinhardt, a theoretician, developed their gradient model explaining self organisation of polarity from initial fluctuations by lateral inhibition. Although I was far from understanding the model, I realized how interesting the problem of pattern formation was. I looked around and sought advise from two of the hydra people, the American postdocs Hans Bode and Charles David. I also started reading textbooks such as the lectures on developmental biology by Alfred Kühn. Another strong influence came from the work of Friedrich Bonhoeffer in molecular genetics. Friedrich studied DNA replication in *E.coli* at the time. He performed a genetic screen for mutations affecting replication, using quite sophisticated and elegant methods to make it work with large numbers and high efficiency. His work, which resulted in the identification of the gene encoding the replicating DNA polymerase and a number of other novel genes, convinced me of the powers of genetics in analysing complex processes. I looked around for an organism in which genetics could be applied to developmental problems, and found the descriptions of the early *Drosophila* mutants, including *bicaudal,* in a review by Ted Wright (1971). Further, the description of the first rescue experiments of a maternal mutant was published by Garen and Gehring in 1972.  I read and thought and discussed, and finally decided as a postdoctoral project to score for mutations affecting the informational content of the egg cell, with the aim of using them to isolate and identify morphogens in injection assays, in which the rescue of a mutant phenotype was indicative of the presence of an activity lacking in the mutant embryo, possibly the gene product. The only interesting maternal mutant known at that time was *bicaudal,* which had been discovered by Alice Bull, and described in 1966. Mutant embryos display mirror image duplications of the abdomen, a spectacular and very puzzling phenomenon, which however showed little penetrance. I met Walter Gehring at a meeting in 1973 in Freiburg, and had the courage to ask him about *bicaudal,* and whether he would let me work in his laboratory in Basel. I went there at the beginning of 1975, supported by a long term EMBO fellowship.  I immediately loved working with flies. They fascinated me, and followed me around in my dreams. Basel and the Biozentrum was a very good place to spend ones postdoctoral times. I met [Eric Wieschaus](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1995/index.html) who just had finished his thesis in Walter Gehring’s lab. His thesis project on the origin of imaginal disc cells in the blastoderm interested me very much. I learned a great deal about the use of genetics to study development in discussions with Eric. I also learned to have conversations with my fellow postdocs in English, and enjoyed the Swiss language and the lovely old town. It was difficult to be a beginner in everything, after having been an expert in almost everything in the previous lab. Soon after I started as a postdoc, most people in the Gehring lab began to work on recombinant DNA and molecular biology with the aim to clone developmentally interesting genes. Spyros Artavanis, Paul Schedl and David Ish Horowicz were postdocs at the same time. Eric, soon after I came, left for Zurich to do a postdoc in the lab of Rolf Nöthiger, but continued his collaboration with two postdocs in the lab on the transplantation of pole cells in order to investigate the female germline in chimeras. Jeanette Holden, an excellent geneticist who had done her thesis with David Suzuki on dominant temperature sensitive mutations taught me genetics of *Drosophila.* The problem of studying embryonic mutants at the time was that the methods for collecting eggs and inspecting embryos were both tedious and unsatisfactory. It was hard to see structures, segments, and their polarity in the living embryo, and fixation and clearing methods were not available. With the help and support of Jeanette Holden and David Ish Horowicz, we developed some tricks which proved helpful in scoring mutant embryos from many lines. The most important of them, the block system for egg collection and replica plating in flies is my first *Drosophila* publication, in *Drosophila* Information Service, 1977. With Jitse van der Meer, we developed a fixation and clearing technique which enabled the scoring of the larval cuticle in great detail. Using these techniques, I recovered and investigated the original *bicaudal* mutant. I also did a small screen for maternal mutants which was successful in that it taught me how difficult such a screen was to do on a large scale. In this screen of 100 chromosomes, a maternal mutant which later was found to be immensely interesting, C79, later called *dorsal*, was isolated. I did a detailed study of *bicaudal*, the most difficult mutant I ever studied, with unbelievable patience and in retrospect little reward. I published a paper on *bicaudal*, but I did not easily find a job.  With a fellowship from the DFG I went for a year (1977) to work in Freiburg in the lab of the famous insect embryologist Klaus Sander. Klaus Sander had been the first to describe gradients in the insect egg. He had done elegant experiments in which he translocated a symbiont ball localized to the posterior pole in a leaf hopper embryo and thereby changed the polarity and pattern over large distances of the egg. In Freiburg, with Margit Schardin, we did a fate map for the larval cuticle using laser ablations of *Drosophila* blastoderm cells. This experiment was important in showing that the primordia of individual segments in the blastoderm stage were no more than three cells wide. It also led to a very detailed examination and description of the segmental pattern of the *Drosophila* larva which we later used in our screens. I continued the work on *dorsal*, discovered the recessive phenotype and interpreted the phenotype postulating a gradient determining the dorsoventral axis. At that time, gradients were not widely accepted as mechanisms, in particular biochemists were highly sceptical, however the Tübingen influence made such models attractive to me. I presented this and the *bicaudal* work at the annual symposium of the American Society of Developmental Biology in Madison in 1978, my first trip to the US. Pedro Santamaria, a postdoc with whom I shared the lab in Freiburg, was a skillful transplantation person, he did some attempts to rescue the *dorsal* phenotype by transplantation of wildtype cytoplasm. We could not see much of an effect, but later in Heidelberg I looked at the preps again with a better microscope and found that there was some rescue! Unfortunately by that time Pedro was back in Paris and I had lots of other things to do – so this story had to wait – it finally got published 5 years later.  Both Eric and I got a job offer from [John Kendrew](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1962/index.html), the director general of the European Molecular Biology Laboratory in Heidelberg, that was newly founded and recruiting in many areas. We both accepted and worked there for three years, 1978-1980. I had applied to the EMBL earlier, but at that time they did not think I could establish a fly group alone. When our joint offer came, we were very pleased, because we could imagine that it would be fun to share a lab, and at least I did not have another option. Eric and I always had kept in touch, while I was in Basel and Freiburg and he in Zurich, and we used to discuss our experiments together. I felt at the time that Eric was much more successful than I, he was extremely productive during his time in Zurich, and worked on many very original projects, germ line, cell lineage, sex determination, where not many people could follow him. I also had the impression that I was dependent on him because he had more fly experience and without him I would not have gotten the job. This made our start in Heidelberg a little difficult, until we sorted things out, and from then on we thoroughly enjoyed working in the same lab. It was tiny – we, although both group leaders, shared a technician, Hildegard Kluding, and a stock keeper who also did cuticle preps for us. Initially we both had our own projects which we tried to pursue independently (while discussing them all the time). Soon we realised that the problems of close proximity and in sharing a technician would be eased if we let Hildegard do projects that interested us both. One of our first joint projects was the analysis of *Krüppel*, a segmentation mutant which we found published in a textbook by Alfred Kühn. It had originally been described in 1950 by Hans Gloor, who, in Geneva, still kept the stock and sent it to us. We let Hildegard do most of the *Krüppel* experiments. Our collection of mutants affecting segment number increased, tempting us to do a “shelf” screen. In the cuticle preps of embryos produced by our stock collection (we took from the shelf) we found a number of interesting and novel phenotypes. Gary Struhl, then a graduate student with Peter Lawrence in Cambridge, showed us homozygous *Antennapedia*, and *wingless* embryo preparations, which were very exciting. We realized that the screening for embryonic mutants would be very rewarding, and that we were the only people in the world who could do it. In contrast, the screen for maternals, which I was trying to work out at that time, was much more difficult, because it requires an additional generation and selection system. We invented some more tricks such as the little nets to fix and clear embryos from 7 mutants at the same time, and did the first screen, for zygotic mutants on the second chromosome, just Eric and I, supported by Hildegard and a second technician. The screen of 4200 second chromosomes took no more than three months (autumn 1979). It was extremely exciting – no major disasters, hard work, and great fun. Early on it was already evident that the screen was a success, and early on we realized the pair rule, the strange skipping of portions from every other segment (“2-4-6-8-type”). We had seen the mirror images displayed by the segment polarity mutants (“gooseberry type”) before, also the “notch type” – the neuralized mutants. As a side project we grew up the homozygous flies from the 1000 or so non lethal lines and tested their fertility, and the fertility of their daughters (to screen for grandchildless mutants). We recovered *torso, gurken* and *tudor,* three very valuable maternal mutants in this screen. We also, by chance, found the first *Toll*, *BicD* and *easter* allele. At the end of the screen Gary Struhl, and somewhat later Gerd Jürgens joined us, very stimulating, critical and knowledgeable discussants. We sorted things out, owing to the very competent help of Hildegard and the stock keepers, in a very short time, and decided, after some debates whether to wait until the screens of the other two chromosomes had been done as well, to try to publish the essential conclusions on the segmentation genes in an article in Nature. Although there were not many people working close enough to be competing with us, people started to get interested in this type of mutants, and although we certainly had the most complete collection, reports on individual mutants where probably able to spoil much of the fun for us. The paper was published in October 1980, with a very pretty cover picture, in NATURE.  We continued with the screens of the two other chromosomes, with Gerd Jürgens who, as a very skillful and experienced geneticist, organized the third chromosomal screen. We even got a little bit more space and an extra “Denkzimmer” (office space), but on the whole the EMBL of that time, with its strong emphasis on expensive high tech experimental set ups, was not the best place for us, and sometimes it struck us how strange it was to discover very exciting things and know at the same time that there was not a single person in the entire institute outside of our lab who would appreciate it. There was one other laboratory working with *Drosophila,* they tried to develop cloning techniques and finally cloned an eye colour gene, *white.* Admittedly, we also did not have great interest in what other people were doing at the EMBL, it was so far from our work and we had so little time, but we enjoyed the international atmosphere and were good citizens of the place. We had very good working conditions, as people at the EMBL had them, and we used our great chance – we could not have been more successful – but the people who had given us this chance were unable to realize this. Eric even before finishing the first screen started to apply for jobs in the US, and got an offer in Princeton for work he had done before the screen. I got an extension to my contract for another three years, but felt uncomfortable to stay at the EMBL without Eric. Luckily I got an offer for a junior position at the Friedrich-Miescher-Laboratory of the Max-Planck-Society in Tübingen and moved there in spring 1981.  The FML consists of four groups, the groupleaders stay for not longer than six years, and are entirely free in their research topics. They have a generous budget, enough space and no teaching obligations. Great conditions and a great challenge. At the time I was there, I much enjoyed the interactions with the groups of Rolf Kemler and Walter Birchmeier, and, in the last year, Peter Ekblom. I was lucky because Gerd Jürgens came along and soon we were joined by Kathryn Anderson as a postdoc. Kathryn wanted to work on *dorsal* and pursue the rescue experiments. Both Gerd and Kathryn are excellent geneticists with whom it was an intellectual challenge and pleasure to collaborate. In 1982 we did the large scale screen for maternal mutants on the third chromosome in which many of the genes involved in axis determination, including *bicoid,* and *oskar* and most of the *dorsal*-group genes were identified. Gerd, whose interest was to look for maternal homeotic mutations, prepared the screen that involved an elegant crossing scheme proposed by Gary Struhl. As students, Hans Georg Frohnhöfer and Ruth Lehmann started during the first year. Hans Georg initially did pole cell transplantations to investigate the maternal contribution of several zygotic mutants, he later worked on *bicoid.* Ruth had worked with Campos Ortega before on the neurogenic genes, she already had much knowledge on fly embryology. All were very enthusiastic and made a great team. However, the technicians in Tübingen enjoyed the fly work decidedly less than those in Heidelberg, and we had some difficult times getting food and keeping the stocks, owing to that. But soon we got efficient help from undergraduate students, some of whom came to us via lab courses we taught during the university vacations.  The maternal screen was much harder than the screens we had done before. It was also a difficult task to divide up the work between the people, as the importance of the individual mutants only became clear following rather detailed studies. The obvious groups of phenotypes were readily analyzed, what was more difficult was to take care of all the other mutants (more than 300 total) we had collected. After several attempts to sort those out, we decided to concentrate on the maternal mutants involved in axis determination, and not complete the genetical and phenotypical characterisation of the entire collection. Gerd and I still had to finish some of the projects on segmentation mutants, including the papers on the zygotic screens done in Heidelberg, which finally got published in three papers in Roux archives in 1984.  For the phenotypical and genetical analysis, the maternal mutants, soon including the ones on the second chromosome Trudi Schüpbach and Eric Wieschaus had isolated, were divided into phenotypic groups, which roughly corresponded to the four systems of axis determination defined later. Kathryn Anderson, later Siegfried Roth and Dave Stein, studied the *dorsal* group genes including *cactus,* Ruth Lehmann concentrated on the posterior group, and Hans Georg Frohnhöfer on the anterior mutants. Initially he also worked on the genes *torso* and *torsolike,* which he recognized as acting independently of the anterior group of genes. Martin Klingler concentrated, later, on this terminal group. An important method to analyse the function of the genes we used in my laboratory was cytoplasmic transplantation. These experiments were very successful. Kathryn Anderson showed that among the *dorsal*-group genes in many cases the RNA was the rescuing principle. Hans Georg and Ruth discovered localisation of activities with long range effects at the anterior and posterior pole of the egg. These studies were started with the mutants *bicoid* and *oskar,* but also extended to wildtype embryos. A first model describing the three independent systems involved in establishing the anteroposterior axis was presented in an article in SCIENCE, with Frohnhöfer and Lehmann, in 1987. At the time the first *Drosophila* segmentation genes had been cloned and found to encode transcription factors. The first gap gene, *Krüppel*, was cloned in the group of Herbert Jäckle, who had a small independent research group in the neighboring Max-Planck-Institut für Entwicklungsbiologie (formerly Virusforschung, the institute in which I had done my PhD). In my lab, molecular analysis was begun rather late, as we felt it important to investigate the properties of the individual genes as carefully as possible before embarking in tedious molecular cloning, that was not easy at the time.  In the meantime, I was appointed as director of an independent division at the Max-Planck-Institut für Entwicklungsbiologie, the position I am still holding. We moved across the yard in 1986. The institute has four more directors, working on cell biology, with frog (Peter Hausen) and neuroembryology, with chick embryos (Alfred Gierer, Friedrich Bonhoeffer and Uli Schwarz). My group got larger, and we started doing molecular work, with the analysis of the localization of the RNA of *bicoid* (cloned in the lab of Marcus Noll in Basel). Wolfgang Driever as a graduate student made an antibody against the bicoid protein and discovered the bicoid protein gradient that determines, in a concentration dependent manner, the expression pattern of other segmentation genes. Wolfgang established many molecular methods in my lab, and subsequently Frank Sprenger and Leslie Stevens cloned *torso,* followed by Daniel St Johnston with the cloning of *staufen,* and Robert Geisler’s cloning of *cactus.* The improvements in the techniques of visualisation of the gene products by *in situ* hybridisation and antibody stainings complemented the transplantation studies done earlier, resulting in several exciting discoveries concerning the establishment of gradients in the extracellular space and by nuclear localisation by Dave Stein and Siegfried Roth. These investigations gradually lead to a more comprehensive understanding of the principles of axis determination in the embryo, presented first in a review in DEVELOPMENT in 1990.  Already in 1984 or so – I got excited about the 1982 paper of George Streisinger on Zebrafish, and at the side explored whether zebrafish could eventually be established as a system for the genetic analysis of vertebrate development. The basis for this interest was the problem of generalisation, the question to what extent our results could be applied to an understanding of vertebrates including man. These early intentions to investigate zebrafish were retarded significantly by the subsequent demanding molecular studies on *Drosophila,* with the success that I had not expected when, as early as 1986, I brought the first fish tanks into the lab. Two graduate students, Stefan Schulte-Merker, who started in 1988 and Matthias Hammerschmidt, were the first fish people in the lab, and Nancy Hopkins from MIT spent a sabbatical year with our fish and us. They and others who joined later were very helpful in developing the tools for breeding and keeping many stocks of fish with safety and efficiency. These efforts resulted in the building of a fish house, with 7000 aquaria of our design, inaugurated in September 1992. Almost to the day three years later we submitted for publication the manuscripts describing 1200 zebrafish mutants, which a group of twelve scientists, with a number of technicians and students, had isolated in a large scale screen.  In my lab, we will continue working on the investigation of the molecular mechanisms involved in the establishment of polarity in the *Drosophila* embryo, as well as continue the exploration of the zebrafish as a model for the study of vertebrate specific features. We believe that the combination of several approaches and systems in one laboratory provides a powerful basis for further understanding of the development of complexity in the life of an animal.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1995*, Editor Tore Frängsmyr, [Nobel Foundation], Stockholm, 1996  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1995 Addendum, January 2018 From 1985 until 2014 Christiane Nüsslein-Volhard was a director at the Max Planck Institute of Developmental Biology at Tübingen.  As an Emeritus Professor she is still leading a research group at the Institute focusing on pattern formation, growth and cell migration in the zebrafish, a new vertebrate model organism.  For the discovery of genes that control development in animals and humans, and the demonstration of morphogen gradients in the fly embryo, she received a number of awards and honours, among others the Albert Lasker Medical Research Award (New York/USA) and in 1995 the Nobel Prize in Physiology or Medicine together with Eric Wieschaus and Edward Lewis.  She was secretary general of the EMBO, which promotes excellence in the life sciences, until 2009 and a member of many scientific councils ( GDNÄ, National Ethics Council of Germany, ECR).  She has been chancellor of the order *Pour le Mérite* since 2013.  In order to support women with children in science she founded the Christiane-Nüsslein-Volhard-Stiftung in 2004. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0569** |
| Interview |  |
| Q85 | Professor Nüsslein-Volhard, it’s so nice to have you here in Lindau. What you said today, that scientists have to be humble, could you explain that a little bit more? |
|  | Yes. The importance of genes was of course recognised very early on and I think the term gene was coined about 100 years ago and I knew they were sort of carrying the information from which determining living organisms. Then people set out with the human genome project to decipher all the genes in humans and they had the vision, I think, that when they had deciphered them, they would know a lot more about humans than they knew before and the written out genome would tell them everything about humans.  This is a pretty naïve view and there are rather a large number of surprises which came out after the whole genome project was done and one was, for example, that the number of genes was much smaller than the number of say phenotypes or traits which you can see features of an organism of a human being, if a lot of features you can write out, I mean enormously large numbers of features and it’s impossible that for each feature you have a specific gene. Actually this is a notion that you don’t have a one to one correlation between affinity, big feature and a gene, that is a notion also geneticists know and geneticists have phrase for example, [Thomas Hunt Morgan](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1933/morgan-facts.html), Nobel Laureate I think 1930 or so, he did sort of say that in his lecture and for fly geneticists it’s obviously that there are many more than one gene determining the eye colour for example of a fly and if you look at a wing, there are many genes which determine the wing.  … analysing a gene or diagnosing a particular gene doesn’t really tell you everything …  On the other hand, what we also observe in studying genetics or developmental genetics in flies or fishes also, when you have one particular gene and you hit it, then you have effects on many more than one trait and in the display of the human genome, it’s very clear that the 35,000 genes or so can also only function this way, namely that you have a complex interaction, a complex relationship between features and gene and this means also that in analysing a gene or diagnosing a particular gene doesn’t really tell you everything about what the human being would look like and this is something people had expected, that they would be able to predict and then they thought, I know the gene, I can take it in or out and this is what I mean with more humble. |
| Q16 | What does it actually mean for example to the general public? There has been a lot of talks about gene testing and by doing that we could prevent people from getting sick and so on, but it seems like that is not actually applicable? |
|  | In some cases yes, I mean there are some various genes with simple causes, namely just one mutation and these are rare cases but these are the inherited diseases, monogenic inherited diseases, and this is actually true when you diagnose it. You know that this person, if the gene is defective in both copies, then you know you can predict with 100% certainty this child will be ill, and this type of diagnosis is of course valuable when it’s done, but the other type of predictions do not hold true because, as I said, traits depend on many genes and a gene has different effects on. So there are many diseases which are probably where you have a predisposition with a particular genetic background that you might get it more frequently than other people might get some diseases but it’s never totally predictable and this is why the diagnosis doesn’t really help you much.  I mean it doesn’t really help you to be told by your diagnosis that you have a 5% higher chance to develop a certain type of cancer, this you don’t need to know that and it’s like, if you eat Birchermüesli every breakfast, you might acquire some strange disease with 5% more frequency than something else, I mean so your daily habits are as or more important than your … well it’s tough, it’s really something which is sort of difficult to say with uncertainty, but in many respects, the daily habits are more influential of your disease pattern than your genes, your genetic background. |
| Q55 | So the risks, we’re not talking about one in certain groups of people are talking about, you can’t see when it’s going to be misused in a certain way? |
|  | I don’t think it’s misused yet, people are afraid of it might be misused but on the other hand, there is also value in finding out about the relation between several particular predispositions. You might be more careful if you are told that your genetic background is such that you shouldn’t eat fat in large amounts or so, it does help you change your life a little bit and so it’s not so bad, but it’s hard to find out which genetic background is causing these things.  And this is why we have now these genomic projects where populations are tested, the genome is analysed, a pattern of variants is sort of recorded and then their habits and their way of life is recorded, and then also their disease pattern is recorded. And then you might find a correlation between some diseases and a genetic predisposition and this is a little bit the hope now that you might find which dispositions are particularly prone for certain irregularities and this might to help people change your diet or run longer every morning or don’t run at all or something like that. But it will not have a big effect, it will not have a big effect and it will be so uncertain that it might not be widely used perhaps. |
| Q13 | With your scientific work, I think there are a lot of students who need role models and I would say a lot of female students need role models as well, we don’t see as many female students, I mean scientists, yet. Do you think there is a way to encourage more female scientists? |
|  | In Germany it’s very clear what you could do and the thing is you have to have better schools, you have to have day schools and you have to educate the people, having someone else educate your child is often better for the child than you do it yourself, but this is not generally accepted in Germany. So many women just are sort of torn between the two things, they want to do the best for their children and they want to do a good job, but I think there is still a distrust that if you let your child be brought up by a day Mother or in a day care, that it might not be as good for the child as you wish and this is also perhaps in many cases true, because there is not a large culture of day cares in Germany, in contrast to the Scandinavian countries I think. There it is clear from looking at the results now that for the children it’s as good or even better if they are with other children and they are educated by a professional. For women in Germany, the big problem is they usually tend to interrupt and they are slowed down in their progress and they can’t compete as much as they should with men who don’t have to do that. |
| Q13 | If you look for example at a female athlete or sports people, I mean they are more celebrated and honoured and they get funding from companies and so on. Will there be such a way to sort of move forward and make science a little bit more popular? |
|  | Yes, this is another thing. It was this morning, the speeches by the politicians were quite telling. I mean if children are mocked because they’re good at school, you can see why female scientists especially who are successful, do not have a better standing. On the other hand, I mean, people suspect that they might not be good mothers or they might not be good people, so it’s not attractive socially from the society, it’s not really attractive to be a successful female scientist, so I sometimes think, why should I talk young women into being a scientist if they then end up being sort of disliked or not accepted by their contemporaries and so it’s a tricky business actually. |
| Q1 | What drove you into science? |
|  | I think a very big curiosity. I’m very curious and I like to understand things and not only science but also other things where I just try to find out why things work or how things work. Science and nature caught my attention as a small child already. I was growing up in a city but we had a garden and I loved the garden and then often on vacation I was at a farm and I loved these animals and plants and so on, so I was attracted very early on and then we had a very good teaching actually at my … I don’t know whether my teachers really had much of a role because I was determined very early, but then I also did music and I did languages and Literature and so on. I have broad interests actually other than science, but this is really true, this curiosity.  Yes, so I mean just to solve problems, to express yourself?  Christiane Nüsslein-Volhard: To find out, yes I’m a curious reader too, yes I want to understand things, yes. |
| Q6 | I would like to come back to that just now but I was thinking of, after the Nobel Prize, did life change in any way in the sense that you could take bigger risks in your scientific work or were allowed, so to speak, from the surroundings to? |
|  | Not really. I thought that getting the Nobel Prize was a big interruption in my career, I thought and it was very distracting. It takes a lot of time you know, it just takes time to be honoured, you have to travel and you have to give speeches of things you have, oh it’s so often that you get bored to tears when you hear your own voice. And it’s really taking a lot of your time and there’s no way that during this time you can start something new, I mean you just profit from what you’ve done and there is no time to develop new ideas.  I suffered a little bit during this time, I really thought that must end and I now stop a bit, you know shield myself a bit more from this type of redundancy because you have to have leisure to develop ideas, this is absolutely important and this is something I find people do not realise enough. Also scientists are very ambitious, they work and work and work and they go to the lab and they write this and they write that and they run from conference to conference and I sometimes wonder when they have time to have a new idea.  … creativity can only come on an empty mind …  I think sometimes they just work on old ideas and creativity can only come on an empty mind, but somehow there must be some wandering around: oh what could I do now and hey, let’s think about this or s. But if you’re always are occupied with travelling or with having to do something, so someone else tells you what to do, you are the programme, you can’t really develop original thoughts and so this is why I now sort of take my time. I take time off and I take long weekends and I stay home and I think and write and read and this is really quite fun.  … and sing, I believe?  Christiane Nüsslein-Volhard: I sing yes sure and I garden, I have a large garden and I really recreate myself by doing gardening and thinking about something else so that when your mind gets free from all the burden of the daily troubles and then you can start putting something fresh in, you know. |
| Q14 | So is that the link between science and art for you or culture? |
|  | Yes I mean, I have a strong likeness of culture and also I mean my grandmother was a painter and we do music in the family quite a lot and I think that’s very important. What was also important, I thought about that recently, also maybe as a follow-up of an interview but I was asked what my parents did and so on and looking at my brothers and sisters, we had a wonderful education because my parents were so practical, they did books themselves and we did a lot of handicrafts and I knew how to knit and sew and cook and we learnt a lot to do things ourselves, to make things ourselves so we all have some dexterity in doing things ourselves and this is also very important for Science, because you could quickly see how things would work and organise something, make it work, yes. |
| Q23 | I was thinking about what you said of being able to get new ideas and thoughts and create something that has not been created before. You changed from the fruit fly to the zebra fish and I read in some of the articles that people were saying, yes that’s outrageous and you can’t do that and you know, are people very conservative and do you have to fight to be able to, you know, new challenges? |
|  | If you look at the career paths of many scientists, they tend to start with something and just go on and on and on and on and on and they would not change topic because they always think there is something else to do, which is true, they follow a predetermined path. Whenever you have a problem there is another problem coming up, you can always go on and I changed dramatically after my thesis work when I went from bacterial transcription by chemistry to fruit flies. This was a wonderful challenge because it was all new and it really challenges you to think freshly about things. I think that was the most creative time of my life and it was great fun and I also experienced at that time that I, compared to other people working in this field, I came up with ideas. They were blocked in their minds to do this because they thought, oh this is not done, we don’t do that in our field and you can’t do that, and I said: Why not?  And then I did things which were completely unconventional and it helps changing fields because you can be unconventional for some time. Later on you are again bound in all this. This is how it’s done and you can’t really change very much. In the fish I think I didn’t really change that dramatically, I just changed the animal but not the question and changing the animal of course was a big challenge too and it was fun for me to develop the tools to do what we had done with flies, also with fish and it took a long time actually and we had some years without success.  We had success but without sort of products and publications and so on and you have to be able to afford that and I’m lucky I’m in this Max Planck society where this is essentially encouraged that you start something new, do some risky projects without having to fear that you lose your funding, so we can do that and one should do that and should encourage people to do that, but some think they can’t afford it because they might have a gap in their track record in the publications and then they won’t do it.  … and funding, yes.  … funding policy should be such that people can run risks …  Christiane Nüsslein-Volhard: Yes. So, on the other hand you can also say that funding policy should be such that people can run risks and if they have done something. I think, when I started with fish I was pretty well known, I had been successful and people sort of entrusted, the Max Planck Society at least, they said okay, she’s done fine, she’s not stupid and why not support that and let her do something new and I think that’s perfectly okay, but maybe in the United States, I wouldn’t have gotten the funding because they immediately want you to, the next half year already to write another paper or show that you’ve done something when it’s not yet time. |
| Q25 | What is the greatest challenge at the moment for you on a professional level? |
|  | At the moment I have changed the way my lab is run and I think, more and more I just provide the atmosphere for young groups to do their own projects and I do the coordination. I listen to them and I help them and I challenge them with stupid questions or smart questions or with criticism or so. But it’s less and less my own ideas which are done and this is because I have a great interest now also in history of science and also in teaching, not teaching in schools, but I’m writing a book and I’m also on ethical councils and I’m thinking a lot about what people should know and develop in biology and in genetics and how to explain it to them and so on.  So I spend much of my time now writing this book, reading other books and trying to understand things or sort of make a synthesis from things which are not from other fields. I don’t know, actually in my field, I mean if you ask what my scientific goals would be which I probably will not follow up myself but sort of appointing people who would work on these topics is evolutionary biology actually, how organisms change, making this switch would lead to a change of the species and this is a very interesting topic and in my Institute there are other groups which do similar things and we try to look at some of the mechanisms now with this viewpoint and this is very interesting actually.  It is certainly because we still yet don’t know really.  Christiane Nüsslein-Volhard: No, we don’t know and actually it’s true, I said that this morning, we know the fish, we know the worm, we know the fly, but we don’t know the links between and we don’t know, when we go back to the branches in evolution, we really don’t know what happened there when they branched and how they divert and what is the major drive for evolution.  The coelacanth fish is just one of those amazing examples that intrigues me.  Christiane Nüsslein-Volhard: Which?  The coelacanth, you know, I don’t know what it’s called in German, the fish with the legs which has always been one of the, yes.  Christiane Nüsslein-Volhard: Aha.  I would like to say thank you but I just want to say, you talked about encouraging German students, so you become a bridge builder, don’t you, in many ways, I would say?  Christiane Nüsslein-Volhard: I don’t know, I mean I can’t tell from my own viewpoint. Yes.  I can see you as a bridge builder between this and because I think it’s so easy to get into just one question, not to see the whole. Great, thank you very much for a very interesting talk. Thank you very much.  Christiane Nüsslein-Volhard: Okay, thank you |
| ID | **0570** |
| Biographical | I was born in South Bend, Indiana on June 8, 1947, one of that large bumper crop of babies born in the United States after World War II. My family moved to Birmingham Alabama in 1953 when I was six. Although Birmingham was already a major industrial center in the South, the city still had the small town character of most Southern cities at the time. My brother, my three sisters and I could go exploring in the woods near our house, and collect frogs, turtles and crayfish from the local streams and lake. I went to Catholic grade schools and, when I was fourteen, took a 6:45 bus every morning across the city to make it to the only Catholic high school by 8:30. Though I did well in my science and math courses, I did not see myself in a career in science. I played piano and read books, but spent most of my time painting and drawing pictures. I dreamed of becoming an artist when I grew up.  In the summer between my junior and senior years, I went to Lawrence, Kansas, to a program funded by the National Science Foundation to encourage high school kids to become scientists. For the first time in my life I was with kids who were smarter than I, who cared about science, and who talked about books and art. I felt as though I had finally found a group to which I belonged; in these surroundings I was able to conquer the shyness and insecurity that plagued me in my own high school back in Birmingham. In the laboratory associated with the Zoology course, I dissected animals for the first time, from fish up the vertebrate ladder to fetal pigs. I was invited back the following summer to work in the neurobiology lab of Nancy and Dennis Dahl. My work involved more dissection, this time removing vagus nerves from large land tortoises, stripping off the outer sheaths and recording the electrical depolarization when they were stimulated. The Dahls’ generosity in opening their lab to a high school senior still amazes me. I can’t believe I produced much useful data, but the experience was enough to convince me that I wanted to become a scientist. By the time I started college at Notre Dame, there was no doubt in my mind that I would major in biology.  In my sophomore year at Notre Dame, I needed money and found a job preparing fly food in a Drosophila laboratory run by Professor Harvey Bender. In Bender’s lab, I encountered my first fruit flies and learned basic genetics. Though I liked working in a lab, genetics did not excite me as much as the embryology courses I was then taking from Kenyon Tweedel. Tweedel seemed to have a continuous supply of living embryos from a variety of different species. I will never forget the thrill of seeing cleavage and gastrulation for the first time in living frog embryos. I immediately wanted to understand why cells in particular regions of the developing embryo behaved the way they did. What were the mechanisms that made them different from each other? What forces drove such dramatic rearrangements in the cytoplasm and the shape of cells?  In my last years at Notre Dame, I became increasingly active in the student effort against the war in Vietnam. I collected petitions, joined in protest demonstrations and applied for conscientious objector status to avoid being sent to Vietnam. It was, however, very unlikely that my local draft board would grant me such status, given that I had not been raised in one of the traditionally pacifist religions. In spite of my somewhat uncertain future, I decided to begin graduate school in biology and was accepted to Yale University. Bender was worried about my draft status and wrote to Donald Poulson, the only Drosophila geneticist he knew at Yale, telling him about my problems and asking him to look after me while I was in New Haven. When I arrived in New Haven, Poulson had a place set up for me in his lab. He was so very kind that I didn’t have the courage to tell him that after three years of washing fly bottles at Notre Dame, I never wanted to see another fly, much less work on flies for my thesis.  In the 30’s and early 40’s, Poulson had described the basic embryology of Drosophila and had characterized one of the first mutants with an interesting interpretable phenotype during embryonic development (the neural defects associated with deletions of the *Notch* locus). Until that point, I had thought all developmental genetics of flies involved eye colors and bristles and other aspects of adult morphology. It had never occurred to me that flies had embryos, or that Drosophila embryogenesis was characterized by the same kinds of spectacular cell movements seen in the classically studied embryos of vertebrates. I learned all that from Poulson.  In my second year in graduate school, I switched to Walter Gehring’s lab to learn *in vivo* techniques for culturing embryos. Gehring had just set up his lab in the medical school, so it was still very small, much smaller than what it was to become after his return to Basel two years later. Because I was his only student, working directly with him was a wonderful opportunity to learn how experimental science is done. For my first experiments in his lab, I set out to investigate whether cells at the blastoderm stage were already determined to form specific discs. My plan was to remove single cells from defined regions of the blastoderm and culture them in adult abdomens surrounded by genetically marked “feeder cells.” My last years in New Haven and almost all my time in Basel were spent dissociating embryos and trying different culturing procedures, but I was never able to get single isolated cells to survive. Fortunately, at some point along the way, I had decided I needed to know what normal cells did in embryos that weren’t homogenized or subjected to my in vivo culturing techniques. It was those experiments, initially planned as controls for my more ambitious cultures, that eventually constituted my thesis. I used X-ray induced mitotic recombination to mark clones derived from single cells. In contrast to the restricted clones produced by irradiation of larvae, such clones extended between the wing and leg of the adult fly, indicating that the blastoderm cell that gave rise to the clone could not yet have been determined with respect to either disc. On the other hand I could never find clones that overlapped adjacent legs. Because legs were derived from different segments, my results suggested that if blastoderm cells were determined for anything, they were determined for segments rather than discs.  In my last year in Basel I started a collaboration with Elisha Van Deusen and Larry Marsh using pole cell transplantation to make genetically mosaic ovaries. We wanted to use such mosaics to determine whether particular maternal effect mutants block gene activities in the germ cells themselves, or whether they identified genes that were active in the overlying follicle cells. Although most of the mutants we tested did not have interesting phenotypes, there was one, *fs(1)k10*, that caused an abnormal pattern in the egg shell. Since the shell is secreted by the follicle cells during oogenesis, we expected the defect to depend on the genotype of those cells. To our surprise, the mutant was germ line dependent. Those transplants provided the first evidence for an organizing principle that emanated from germ cells and controlled patterning of the overlying follicle cells. The embryos that developed in *k10* eggs were also abnormal, but in a way that I did not understand at the time. It took [Christiane Nüsslein-Volhards](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1995/index.html)‘s work on *dorsal* for me to re-interpret it in terms of dorsal ventral polarity.  I met Christiane (Janni) Nüsslein-Volhard two months before I left Basel to begin my postdoctoral work with Rolf Nöthiger in Zurich. Janni had come to Basel to learn Drosophila embryology and we thus had many interests in common. Even after I had left for my postdoctoral work in Zurich, I would come back to Basel, in part to finish experiments, but also always to have dinner with her. We would talk science and plan experiments we eventually wanted to do together.  In much of my work in Zurich, I continued to use the cell lineage techniques of my thesis work, but now to analyze the development of sexually dimorphic structures. Janos Szabad and I developed efficient procedures for making germ line mosaics using *K10* and mitotic recombination. In collaboration with Trudi Schüpbach, we also studied the cell lineage of the embryonic epidermis. Those studies paralleled a similar analysis that Janni Nüsslein-Volhard had begun with Margit Lohs using laser ablation. Both studies suggested that segmental units might be established as three to four cell wide stripes at the blastoderm stage. By far, however the most important thing that happened to me at Zurich was my deepening relationship with Trudi Schüpbach, who became my close friend and occasional scientific collaborator, but also an enormous emotional support throughout my life. We eventually married, in Princeton in 1983. Life with her, and with our three daughters Ingrid, Eleanor and Laura, has kept me busy and provided a needed balance to the demands of the lab.  In 1978, I moved on to my first independent job, at the European Molecular Biology Laboratory in Heidelberg. The lab had just been built and was intended as an international meeting ground for scientists from the various member nations. Although there were no permanent contracts at the time, the position as group leader gave me independence to pursue my interest in embryos, without major teaching obligations or being required to explain every step in my experimental plans to get the necessary funding. The job was as extraordinary opportunity, one that I regret is not given to more young scientists at the beginning of their careers. The most attractive feature of the move to Heidelberg, however, was that the EMBL had also offered a similar position to Janni. This gave us the chance to realize many of the experiments, and test many of the speculations developed over the long dinner conversations in Basel.  Although we tried to keep our own individual research projects going, most of our time at the EMBL was spent on the joint mutagenesis experiment. Because handling large numbers of flies was essential if we were going to saturate the fly genome for mutations affecting embryonic development, we first had to test genetic selections to kill off specific genotypes at particular generations, and establish techniques for making large numbers of microscope preparations. We also continued to discuss developmental issues, recent models for patterning in embryos and, as the mutagenesis screens got underway, the interpretation of the particular defects observed in the various mutant lines. Those years were probable the most exciting, intellectually stimulating ones of my entire scientific career. A special feature of those mutagenesis experiments was that almost every day we could expect to encounter a new phenotype, a phenotype that would force us to re-evaluate some long held assumption about embryonic development.  I moved from Heidelberg to Princeton in 1981. Since then I have taught genetics and development courses at the graduate and undergraduate level. The Heidelberg experiments continue to provide a rich source of inspiration for further research. After arriving in Princeton, Trudi Schüpbach and I carried out similar large scale mutagenesis screens for maternal effect mutants. The loci identified in those screens, as well as in a comparable screen made by Janni’s lab in Tübingen, allowed Drosophila oogenesis to come to rival embrogenesis as a ideal system for studying patterning. I have also continued to be interested in segmentation genes, as well as genes affecting segmental identity. Peter Gergen, Jym Mohler and Doug Coulter began their analyses of *runt, hedgehog* and *oddskipped* in my lab at Princeton and the extradenticle gene was analysed by Mark Peifer and Cordelia Rauskolb. Our work on the *armadillo* was started by Bob Riggleman and Paul Schedl, and was continued by Mark Peifer.  Much of my current work centers on genes controlling cell shape changes during gastrulation (with Sue Zusman, Suki Parks, Dari Sweeton, Mike Costa), and genes for the establishment of the early cytoskeleton (work with Lesilee Rose, Eyal Schejter, Marya Postner). The mutagenesis experiments in Heidelberg were less successful in identifying genes directly involved in such specific morphological changes. We have consequently designed alternate genetic procedures involving translocations to identity such genes and have initiated an analysis of their roles within the cell. Overall the Princeton years have seen an increasingly cell biological turn to my research. My work has always had a strong visual component (probably to assuage my suppressed teenage desires to be an artist or painter). What I did not realize until late in my development as a scientist is that morphology and cell biology are actually the same scientific areas, or at least that the latter provides the molecular explanation of the former. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0570** |
| Interview |  |
| Q6 | You seem to have almost consciously avoided the changes that can come with laureate status. |
|  | Yes. If your life is okay, if your life is successful. I lived in the lab, I do stuff, I do experiments actively at the bench myself. At the time when I received the award I did that, I worked five or six hours a day, still at the bench. I teach, I have a family. I don’t have much more time in my life, but the way my time is spent is pretty good for me. I’m happy that way, so why would I want to change things? I was curious, I had very few active decisions, thoughtful decisions, after receiving the prize, but one of them really was this conscious choice that I would not be a Nobel Laureate, in an odd sense.  We came back from Stockholm and I didn’t know what to do with all the stuff. We went to the local bank and we never had this, but we had a little bank box thing. We rented one of those boxes with keys, a deposit box, put all that stuff in it, in 1995, and I haven’t seen it since. It’s there someplace, and I think we still have the key, God, I hope we have the key. It’s there, but … Because I like the way things were before. |
| Q6 | I imagine the prize gives a certain sense of security, and yet you didn’t need that really, I suppose, in the first place. |
|  | I think it’s a nice thing that people recognise what you do and recognise the value of what you do. It also brings a certain power, not real power, but in the sense of a certain ability to influence or your opinions matter. Newspapers sometimes will call you up. Or if people want you to participate, if you go to a local high school science fair and you walk around and talk to people it brings them pleasure because of who you are. But …  There’s a danger in that as well.  Eric F. Wieschaus: Yes. The reality is that from a personal gratification standpoint, everyone who’s received a Nobel Prize has already has that to some degree. You don’t get a Nobel Prize out of the blue because suddenly the Swedes figure out that you did a cool experiment that nobody else has recognized. Reality is that by the time I received the award, the experiments were already highly regarded and people understood their impact and understood that they were important. I had as much recognition as any scientist would really want to have in their life. The Nobel Prize is something that’s really an important thing in my life, and it did give me security. It did give me a certain sense of position in the world that I didn’t fully appreciate, but it is a nice thing to have happened, but it would be very sad if it were a necessary part of my life. I suppose that’s what my choice was, the absolute belief that this thing was not necessary.  One hears of people who don’t receive the prize, who seem to have been concerned with the idea of winning it and that must be a burden.  Eric F. Wieschaus: Yes, that would be sad because like all things, it’s a /- – -/.  We’re sitting here on a beautiful spring day in Princeton, which has been your home for what, 28 years?  Eric F. Wieschaus: Something like that, yes. |
| Q43 | Obviously it suits you. What is it about the place that’s so right? |
|  | It’s a small town, a great university, great students, wonderful opportunity to do science. I am happy with the size, the department that I’m in has maybe 35 people, 35 scientists, all of whom I respect and all of whom I interact with. We teach together, we work together. There is a strong sense of intellectual community that’s satisfying for me here. It’s an easy town to live in. I have a family, my wife is also a professor in this department. We don’t collaborate or do science together, but it’s because we’re both living in this small town, we are able to manage our lives and get things done. Get home in time to throw a dinner together for the kids, all of those things that made our earlier lives, when we were a little bit younger and in developing our careers, a lot easier just simply because we could have a family here and we could do our science in a fully committed way. And that worked out really well for us. |
| Q43 | Does the smallness of the department and indeed of the small-town feel contribute to your ability to stay in science? Because one of the unusual things about you is that you still do several hours bench work a day. |
|  | I think it clearly does. If I had to commute 40 minutes from a house into the laboratory, my life would be more complicated, I wouldn’t be able to do science. When our children were at home either my wife or I would come back into the lab almost in the evening after we finally got the kids to bed, from nine to nine to one or something like that and get us an extra four hours in, because we live 5-10 minutes by bike, away from the lab. You can hop on the bike and get in and all those things make it easier. I just found it an easy place for me to figure out what it was. It was small enough that I could control it. There weren’t that many variables. At lab I have teaching. I have my university responsibilities administratively, but all those things were kind of definable. I could say, I could do this and this and this, and I could manage. If things were bigger, maybe if there were more opportunities, maybe things would’ve been different, but I felt comfortable with being able to manage things here. |
| Q13 | It’s actually quite a rare talent to be able to be able to manage the opportunities and not to get drawn away into all the administration and the kind of empire building and stuff. That must be a temptation? |
|  | Ah, noted. No, no. I got into the business because I like doing science. I like being in the lab. I have this crazy sense that every time I’m doing an experiment it’s as exciting as the experiment that I did yesterday. I know that’s not true. I know that I’ve had great experiments and good experiments, but any experiment when I’m doing it, at the time that I’m doing it, seems like it’s going to be a great experiment. There is no attraction to me beyond, other than doing science. I like teaching actually and the reason to be good teacher, but I’m conscious of the cost because teaching means that you have to organize yourself, get up, give formal lectures for an hour and an hour and a half. It costs to do, for you to be a teacher, and that’s a different kind of cost. When I go into the lab, it’s like the totally natural thing for me to do. I plot down in front of a microscope and start sorting flies or checking expression patterns or thinking about things or designing crosses. That’s natural. It’s the only thing that I do that doesn’t take any effort at all ever.  What a blessing.  Eric F. Wieschaus: Yes, absolutely. |
| Q1 | Did it come naturally? Was that when you were growing up, were you a scientist as a child, do you think? |
|  | Perhaps, I don’t know. You look back and you try to figure out who you were as a child. My family are not scientists, they’re not academics. I grew up in Alabama, in Birmingham in the 1950s and 1960s. I didn’t know that people could be scientists. My father worked in the steel industry and then he and my mother eventually had a construction company and they built things. I didn’t know the possibilities. I wanted to be an artist. I painted, I drew, there’s a part of my character that’s very driven towards visual things that even plays into my science heavily. I know that in part, me being an artist was the same part of me that eventually became and me becoming a scientist. Fortunate for me was that I had certain chance things. I was able to go to a summer science program when I was in high school and actually left Birmingham, Alabama and took a train to Lawrence, Kansas to the University of Kansas and lived there for a summer when I was like 16 or 17. For me, it was wonderful, that nerdy little high school kid, and then suddenly going off to Kansas and living in a dormitory with, I suppose, other nerdy little high school kids. It was suddenly a social situation that was different than the so typical social situation.  When you’re a young teenager in high school, it’s a traumatic thing, regardless of whether you’re the most popular person in the class or the least popular, or somewhere on the spectrum in between because everybody at that age is terribly insecure. You’re not the coolest kid, you want to hang around with the cool because they’re clearly cliques and all that. In high school, this period from 14 to 18 is a difficult traumatic time or difficult time, not traumatic time, but difficult time for everybody in growing up. I think one of the reasons I ended up being a scientist was that I went from that typical middle school, high school malaise, and was taken out of that situation by chance and for summer moved out to Lawrence, Kansas, and lived in a dorm with all these other kids that were equally socially maladapt, probably.  Yet there we had this … It was like a great social environment and it was actually even interesting and I did all this science and I tend to care intensely about things that I do. I think internally I have a … There must be some competitive aspect to my character in terms of wanting to do, but I don’t automatically walking into a room or walking into a classroom where I didn’t think that I was the best student there. Yet I was very trended, I was very successful there because I go in and I do everything with this kind of emotional intensity that raises my performance and my ability to get things up to a high level. Then I was invited back to for another year and that was a reinforcement that yes, you can do things.  You can do things well, and this is a socially attractive circumstance to live your … You could do this for your life and people will pay you for this. It seemed I’ll do this. Yes, absolutely. |
|  |  |
| Q1 | You found your clique. |
|  | Yes, of course. I can’t say that I necessarily planned to be a scientist, but I had the good fortune of having broad experiences and recognizing and being able to follow the things that I like. I was smart enough, I guess, to recognize this is something cool, this is something that matches me, this is something about who I am. |
| Q3 | Illustrates how important it is to give opportunities to people at that stage in their development. A science camp type thing. |
|  | Absolutely. And it’s opportunities out of their normal life. You grow up with certain expectations and you grow up with an understanding of the world that is always limited in some sense. Being able to leave home, go someplace else, see other things, make other choices. I think it’s hard for me to say growing up in Alabama at that time, it’s probably special in itself but I think it would be true regardless of where you grew up that if you grew up in New York City, your experiences are still going to be limited regardless of where you are as a child. The opportunity to go away and do something kind of semi on your own, but in a somewhat protected environment is a great thing. |
| Q8 | One sort of boundary you crossed was to move across to the East coast to do graduate work, and you chose Yale. Was that an easy choice? |
|  | This was 1969. I only applied to two places, to Yale and Harvard and this was because it was 1960, this was in the middle of Vietnam war and I was, I guess, politically active or semi politically active. This was in the anti-war movement. In Notre Dame, which is the university which I was at at the time, the movement had started pretty much on the two coasts. It was beginning to go in on my campus and the opportunities that I had as an undergraduate were to be politically active. I wasn’t really involved in the truly exciting things that were happening, and so when I went out to interview at the two places, Harvard and Yale, I got to Yale and met with many professors and talked with these people and it all seemed very exciting. It was like science and I could do this. It would be like graduate school and this would be exciting.  I took the bus from New Haven, which is where Yale is up to, to Boston. The day that I was in New Haven, the undergraduates at Harvard had taken over the university and the whole university had closed down. I arrived at Harvard for my interviews and they’d all been cancelled, and there was nobody in the biology department except for one young professor, so I actually spent that day with him. We walked around and saw the … and participated in some of the demonstrations, they were all very exciting. Then I laughed and I thought this Harvard must be an exciting place to be.  But then I have this side to my character where I … Harvard is exciting, but if I’m going to do science, I should probably go to Yale, and so I picked over Harvard. Next year of course the demonstrations were all at Yale, so it turned out to a great choice because I would’ve missed the demonstrations at Harvard anyways. Whereas the following year, 1970, was the big year for demonstrations in New Haven. I was there for that, but I didn’t miss anything. It was a good choice, many fortunate things throughout my life. |
| Q60 | How about your choice of your research question? Because you found this area of embryogenesis, pathing of embryogenesis in flies, as a graduate student and have kept that question throughout your whole career. Which in a way is very fortunate, to have found a question that occupies you so well. |
|  | I suppose the really cool thing if you’d say what would you like to recommend. If you could recommend stuff to young students it’s really good if you find something that really fascinates you and it’s really hard. Because if it were really fascinating, and it was hard, you might solve it and then you’d have to find something else. Whereas for me, because the whole issue of embryonic development and pattern information and morphogenesis and form is so complex and operates at so many different levels, that the moment you decide for me, it was a decision looking at embryos that I knew that I wanted to understand. The process: how it is that a fertilized egg, single cell that looks simple can divide into many cells and then reshape itself into something as complex as our bodies is a process that … You can watch it, you can see it and if you watch it, you can’t help but be fascinated by it.  Can’t help to say, this is what I want to understand. What’s true is that you can understand it at a whole variety of different levels. In the famous experiments, the Nobel experiments, those are largely directed at trying to get entry points into the whole process of embryonic development by identifying genes that play specific roles at specific times at specific events, genes that are required for certain cells to do certain things at certain times. The idea of those experiments, if you knew all the genes, you could make a map or a logical scheme in a way for how the process occurs. But I think it’s still true that those genetic experiments that identify genes, they give you a map, but they don’t really explain things. They give you a strategy for understanding things and processes, but that’s all that it is. What you need, there’s still all these other levels where you use your previous experiments, you use those genes, you use your previous observations to build a better understanding of a biophysical understanding or a cell biological or biochemical understanding. But it all grows out from that map. |
| Q38 | On this idea of being fortunate enough to choose a hard question that’s intriguing, there’s a talent involved in finding the entry point, in finding something. That allows you to access the question at all. The example that you raised with the Nobel Prize awarded work was a good one because there you undertook an experiment which was seemingly well, possibly impossible at the time, but certainly there was no guarantee that you were going to get the result you looked for, which was classes of genes that would control segmentation. So there’s a bravery and talent involved in choosing the right question. |
|  | Yes. I suppose it’s brave. Some people have called it brave and other people describe the experiment in ways that are different than the way that you see it yourself. I don’t waste time. It matters to me when I do things in the lab that they work and part of that is an ability to judge. Not only what’s interesting, but what’s interesting and what’s doable right now. What can I do right now? What’s the opportunity to maybe push forward a little bit on a problem to see this is something that is doable at this moment. I’ve come to realize that is something that drives me, the practical aspect of success, of doing successful experiments, more than the big question. This is a hard thing to parse out, but you could imagine, and I know there may be scientists who see and are driven by the big question and see things in terms of big questions. I’d like to believe that I have a little bit of that myself, but I don’t. I think probably I don’t, I probably don’t have it. That’s not my strongest suit. Maybe I bring some vague sense of big questions with me wherever I go. But my strongest suit, I think, as a scientist is being able to walk into a lab and see a novel or unexpected way of doing something or solving a problem, or being able to go in and say, this may seem hard to do, or this may seem convoluted, or this may seem chance, or this may seem brave, but I can do. And that’s a trivial I can. The questions here, and if I can measure this and get this thing done, I will learn something and something that’s really cool and interesting. My whole scientific career in part has always been driven by this sense of I can go into the lab and do something and produce something. I suppose, why I’ve never wanted to have a big lab. I never had a big enough vision to manage an army of postdocs and graduate students to solve something, to push forward, for the frontiers of knowledge, for that lack of vision, if you will.  Because what I like doing is going in and doing things myself, or working closely with people, a small number of students or postdocs in my lab to solve some problem, do something that no one’s ever done before. Bring level of understanding to a new level. I like the idea and this isn’t always true, but it’s substantially true that most of the papers, virtually all the papers that come from my lab, have parts in them that I’ve done. They can be small parts, they can be trivial parts. I’ll do anything to push an experiment for all amount, hand section 500 embryos. If I have to, for five afternoons in a row, the most boring part of an experiment, I won’t do the necessarily do the analysis myself, but if I can leap in and say, This is doable, we can push things forward, I’ll do this part right now. I feel comfortable with that way of being a scientist. |
| Q11 | It’s a true collaboration between you and your students, then, you really working. |
|  | Yes. They never do what I want anyway. You might as well, kind of join, best to join forces. Sometimes when you ride these airplanes they have these little magazines and there’s little business management courses. I think, someone could explain to me how to run this operation in a more efficient way, that’d be cool. |
| Q11 | On the top of collaboration, your work with Christiane Nüsslein-Volhard was obviously a wonderful sort of symbiotic relationship. What was it that the two of you brought to this? Are you just extremely similar or did you have differing skills? |
|  | I think we’re very in certain respects, we’re very similar. We’re both ambitious. We’re both somewhat self-contained in that we like and evaluate our success heavily by our own appraisal of what it is that we do. It matters to us. Each of us, it matters to us a lot. It matters to everybody what the world thinks and we’re social people in the world. Not totally, but we both have an internal standard for the quality of our work and a sense of gratification that the most important thing is to meet our own standards and to be happy when we’re happy with our experiments. Both intensely interested in science. She’s also visually oriented, so we both have certain common tools and strategies. For example, a lot of the immunogenetics experiments that we did in Heidelberg involve not only breeding thousands and hundreds, lots of fly stocks and collecting embryos, but a lot of it depended on our looking at them, and that we both took pleasure. We both take pleasure in beauty.  There’s this lovely picture of the two of you looking down the same microscope.  Eric F. Wieschaus: Exactly. I look at that picture and I see two things. One, that’s certainly true that we were both looking at embryos and enjoying the looking at the embryos. But the other thing, my memory of those times is we’re also competitive in the sense. The reality is that we had set up in any given time, thousands of inbred lines we were collecting embryos from, we work all through the morning trying to identify which stocks were appropriate to make microscopic slides up for examining the embryos. We prepared those and then in the evening, or the next morning, we would have a box or stacks of slides with embryos from each individual, fly embryos from individual mutant lines that we thought potentially would have a gene mutated or a gene would’ve been mutated that caused some interesting effect in development.  But most of it was just garbage or not interesting things, and so we would sit there at this dual microscope and you take a slide and we would both look, we put it on, and then our natural competitive sides, because if there was something there you wanted to be the first person to see it. I wanted to see it before she … She’s really good and she’s incredibly sharp eyes and intuitive. For me, it was like, you put the slide on and then you’re looking through stuff. A lot of it is on average, only one slide in 50 is going to be interesting. Yet you want to be the person who’s look. And it’s true that the way this’s competitive, we all have our favourite stocks in part and our favourite genes and our favourite phenomena.  I would love to tell you that this depended heavily on some inner insights, scientific evaluations for why *runt* is a particularly cool pair-rule gene or what /- – -/ is important for, but the reality is, always in the background for our scientific choices is this memory of the competition. If I happened to have identified *runt* before she did, embryos before recognizing them on the slide as something interesting and unique, then I, of course, I came to believe that that gene plays some truly central role in the process, because you’d like to imagine. We work very well in that way. I think we are also personally very close friends in that I think we understand each other very well, scientifically, but also personally in terms of … And value each other. Even though we see each other once or twice, I visit Tübingen once a year or so, we don’t see each other that much. We don’t collaborate anymore, we haven’t collaborated for 20 years. She’s still one of my closest friends in the world. |
| Q38 | You were both in your first independent investigator roles when you did that work and I suppose one might have played it a bit safe at that point and just tried to get something under your belt to get the jobs. But obviously just that wasn’t … |
|  | I wasn’t smart enough to play things safe. No one advised us to play things safe. One thing that is probably true is that we didn’t talk to old scientists that much. That’s probably why the silly thing about me giving you this interview and God, if they’re any young scientists out there, they shouldn’t be watching this interview. This is pretty serious.  You feel like a young scientist to talk to.  Eric F. Wieschaus: I think basically it’s probably good to … We didn’t talk to many established scientists. We were aware that most of them thought that what we were doing was stupid or was not likely to work because it would evolve into lots of epiphenomena or things would be too complex or there’d be too many genes or not enough genes. Everybody that we knew, senior scientists that we knew in our field were … I can’t say they actually advised us not to do those experiments, but we knew that we were doing them and they weren’t there to be some obvious reason for that. It wasn’t that we were clever, they probably saw dangers or flaws that we probably didn’t see, which is I suppose a good thing about our age. The fact that we were also very self-sufficient and very interdependent, so talking to her was enough. I didn’t really have to take other people’s opinions very seriously. |
| Q11 | There’s a parallel there with Brown and Goldstein, another great collaborative pair, who also say that each other’s approval was what they sought, in a way. |
|  | Yes, right, and that’s certainly true. Getting Janni’s approval is not easy and are not always easy. Particularly if things are … If you’re trying to do that with flawed experiments, that usually doesn’t work. It does set standards and you make choices because there’s enough people out there who are eager to impose or suggest standards to you that you as a scientist have the two choose who matters, whose opinions matter to you. I think we both benefited from making the right choice there. Her opinions matter to me and my opinion mattered to her. |
| Q23 | Let’s turn to the choice of the flies and model organisms. You say you don’t like wasting time and I suppose the fly is the ideal model in that sense that the development lasts 10 days. You can ask a question, get an answer and move on. |
|  | Right. As an undergraduate, when I was learning science, I had my first exposure to flies. I needed money. I got a job in a fly lab making fly food and washing bottles, dirty fly bottles and maintaining fly stocks, stuff like that. I worked in a lab and eventually was able to begin doing genetics experiments. My professor Harvey Bender, who ran this lab, was interested in various aspects of fly genetics. To a certain extent they /- – -/ on adult characters, eye, colour, I think are eye morphology. I thought that was interesting. I like genetics. I learned genetics well, but I didn’t want to do that for the rest of my life. I, as an undergraduate, had taken courses in embryology and I’d seen frog embryos and fish embryos and chicken embryos, and that was the most beautiful thing that I’d seen.  I can remember sitting in the lab after everybody had got home and you do these fertilizations. You can do an in vitro fertilization with frog eggs, and you can see cells divide and you can see stuff happening, and I wanted to know that. I spent a summer, then at the end of my undergraduate period in the embryology course at Woods Hole I got to see many more embryos. That’s what I wanted to do. I wanted to look at embryos and I didn’t want to work on flies. When I went to graduate school. I would’ve been happy never to have seen another fly embryo in my life. The complication in my life, this was a chance thing, but in going to graduate school, my situation was somewhat chancy because this was in good 1969. I grew up in Alabama. Because of my opposition to the Vietnam war, I had applied for a conscientious objector status. This in my local draft board is a very conservative part, no one had ever done this before, and you had to apply for this status based on religious convictions, and at the time I was a Roman Catholic and I believed that my moral convictions were grounded in my … I had tried to apply for this thing, and I failed. I was in the middle of all these legal procedures and I was into reading prison literature because I was convinced that I was going off to prison, but I’d also applied to graduate school and was admitted to graduate school. All this was going on.  Harvey Bender, who was my boss in this fly lab liked me and cared about my future and was concerned about me going to graduate school with this whole huge burden of the Vietnam war and the conscientious rejection and all this stuff, my legal debacle in Alabama. He wrote to the only person whom he knew at Yale, which was Don Poulson, and told him there was this young person coming as graduate student and would he take him under his wing? When I arrived at Yale, Don Poulson, who was about 60 at the time, came and up to me and took me under his wing and took me into his laboratory and was very kind, so kind that I didn’t have the heart to tell him that I never wanted to see another fly lab. I never wanted to see another fly lab or flies in my life. It was good that that happened. I didn’t know who Don Poulson was, Don Poulson was 60 or something at the time. In the 1930s, as a graduate student at Cal Tech, he’d gone to Cal Tech to biochemistry, but got sucked into a fly lab at Cal Tech, and in the 1930s did all of the embryology of *Drosophila*, all the basic descriptive work, and also all the original work showing that genes controlled the way embryos developed.  He was the only person … This was an important set of experiments, but this was not where science was in 1960. I ended up in his lab, at that point. I didn’t know that flies had embryos. I said this often, I don’t know where I thought flies came from, maybe from rotten flesh and spoiled lasagne or something. Some people thought so. I didn’t realize that flies had embryos or that if you looked at a fly embryo, it would be every bit as beautiful as a frog embryo or a chick embryo, and I learned that from Don Poulson. |
| Q24 | You inherited this sort of semi-secret stock of knowledge? |
|  | Yes. Then Poulson didn’t want a graduate student. He was being kind to me, but he didn’t want a graduate student. My memory of Paulson mostly is him reading his papers. Then I would see him, this old man, backing into his office when I was coming with all of “This”, and “You said this”. Poulson, after about a year and a half, arranged for me to switch labs and move into the laboratory of a young assistant professor who’d just been hired at Yale, Walter Gehring from Switzerland. Poulson, I think with a lot of relief arranged for me to go over to Walter Gehring’s lab. Walter’s lab at the time was a great, lucky thing, he’d just been hired. His lab was empty and I was his first graduate student.  He just found a technician himself. There were just three people in the lab, and I worked with Walter for the first year side by side, we would transplant cells and do things. His lab gradually grew, and then after about a year and a half, he decided that he was going to leave New Haven in Yale and go back to Switzerland and asked me if I wanted to finish my graduate work in Switzerland with him in his lab. I said, Yes. I’d never been out of the United States before, New Haven was the most exciting place that I’d ever been in up to that point that I got on an airplane and flew over to Switzerland, stayed in Europe then for 10 years. But the whole fly connection, why I ended up working on flies was just extraordinary good luck, because the ability to do genetics on an embryo was the crucial thing that was needed at the time. Many people did genetics and many people did embryology, but by chance, there I was, one of the few people in the world, a small, small little set of people in the world who knew that flies had embryos that were beautiful. Who knew enough fly genetics to think about how one could approach the problem from the standpoint using the past 60, 70 years of *Drosophila* genetics to solve something that interested me more deeply, which was not genes and was not genetics, but how embryos developed.  Again, it’s the peculiar interplay of chance and talent in having the right tools at the right time the right question is.  Eric F. Wieschaus: And saying, I want to do this thing. This thing is doable. Go for it. |
| Q26 | We’re sitting just up the corridor from your small lab. I wanted to finish by asking you about the students you choose to work with you. What do you look for when you’re picking people? |
|  | I think it helps if they’re smart, at some level you’ve got to bring that to the table. I tend to abandon students fairly quickly in the lab, I would rather that they do experiments that they care about. On the other hand, this is odd. I don’t run a lab so that other people can do experiments that they care about, I’m not that generous. I want to care about their experiments and participate in them at some level. The best thing in my best students always started out with a certain level of independence, but also working with me and then ended up someplace totally different than I would’ve predicted with a set of results or a set of experiments that I didn’t really anticipated, made me rethink what it was that I thought we were doing.  That’s really what you want from students or postdocs in your lab, that they do something that I can take part in because I, like I said, I don’t run my lab so that other people get the opportunity of doing science. I run my lab because I want to do science, but I want to work, so they have to be able to convince me that it’s something worth doing and that I’d be happy to sort flies for them or collect embryos or do some part of this thing. But I’m happiest if they assume responsibility for it. I think that’s the critical thing. I suppose what it means is that I don’t want to assume responsibility. I suppose that really means is I don’t want to assume responsibility for their failure. If they fail, I don’t want it. I don’t want the responsibility of making somebody else’s career. I don’t want to provide a vehicle and a responsibility for doing this and this and then the thing will work if you do what I say. I would rather work with people who, even though they’re at a different stage in their career, are essentially independent scientists with whom I can collaborate. |
| Q26 | It’s the ability to spot those people because you don’t have a high three-foot screening where you’ve got lots of students and you can just pick the ones you like. |
|  | Yes, I think one of the things it’s probably also true that it’s not even a screen, it’s also a matter of adaptability because everybody you work with is different. It’s not like I would look for a certain set of qualities and then only choose people who have those qualities. It’s more that I have to choose some among the large range of qualities that are out there that I could see there’s a potential for me to interact with or to shape myself in response to them. I probably don’t really shape myself that much.  Sounds good.  Eric F. Wieschaus: In a certain sense, I do, I shape myself with a response to them. I am a reactive person, meaning I talk with people and I respond and I’m empathetic. I’m not internally driven enough to expect the world to go through all on my own little tracks. I do adjust my behaviour all the time when I am talking to people. I’m a social human being. In lab it is not so much that it has a certain format of person who will interact well with me, because I kind of change how I talk with or work with people depending on, because science is so peculiar that it is so unpredictable what are the qualities that are required at any moment for any particular problem? I know scientists and this extraordinary heterogeneity of scientists who are successful and some of them are shy and some of them are loud and some of them are showy and some of them are risk takers and some of them are all of these qualities among the really successful scientists that I know.  Some of them seem really, really smart, and some of them don’t necessarily seem so smart, but they really are. This whole heterogeneity of scientists out there. In part what we do as scientists, and this is the thing that I think most people don’t understand about science is how much of a social activity it is.  That’s true. The image is of the lonely person.  Eric F. Wieschaus: The lonely person in the lab and that’s not … The way science works is heavily through a whole variety of different kind of social interaction, some of which are competitive. Either you have your competitors, you have your semi competitors, you have your friends, you have your supporters. All of this kind of a social network in science that reinforces and forces all of us to maintain high standards for our productivity, for experiments, subjects us to criticism at a whole variety of levels. In part, in running a lab, what you want to have is a social structure that mimics that flexibility. You’d like to have people in most successful labs run that way and that they have different kinds of personalities in them. They are extraordinarily supportive places where scientists interact with each other and support each other and criticize each other’s experiments, like a little mom and pop store atmosphere. Small business, a lot of interaction, criticism, sometimes bad emotional blood, more likely like a family where you get a bunch of personalities in a room and they have to keep this boat afloat. |
| Q55 | People are always talking about the role of science in society, but this is the society of science. |
|  | It is something that when I was a child in Alabama, I didn’t know existed. I didn’t know what to be a scientist was. I think that one of the things that I learned at Kansas or going off and being able to work in a laboratory is, at Kansas or being able to work in laboratories at Notre Dame, is how extraordinary gratifying it is for the social aspect that we’re probably all stuck back in our human evolution back. We don’t evolve rapidly if we’re all still biologically stuck back in this hunter gatherer, small tribe stage in terms of our personal interactions. We gravitate towards that social structure and the science, the laboratory academic science, the way we do it now is probably a pretty close approximation for little tribes and little groups of people out there trying to find nuts and edible fruit out in a jungle at that same level. It’s what we’re evolved for.  It’s a lovely idea. There’s a lovely guy called James Curnow who makes furniture. He wrote a book about a challenging time in his life when he decided that he wasn’t going to make any money doing this. He came back to the idea eventually that all he could do was make the furniture he believed in, and somehow things would be right. It sounds like the approach to start, isn’t that different for that? You do the experiments you think are right.  Eric F. Wieschaus: It’s hard nowadays. Maybe I was more naive and I didn’t know as much as young people know now, because of the web, because everybody knows the job market, everybody can follow my postdocs. My graduate students are probably wiser and probably base their decisions on more information and more calculation than I do or ever did. In a way that’s good, but in a way it’s bad because you can’t know everything. The one thing that it’s very hard to know is your own personal quality. What’s hard is you can make the calculation on the average job prospect, and you can make your calculations by what people tell you you should do on average, but that’s not going to get you anywhere. The strength that you bring to science is your own personality, your own weird combination of abilities, my visual orientation or my curiosity or some intuitive ability with math at some level, those weird things that you piece together that makes you *dR* and different from anybody else. That weird combination, that unusual combination that’s distinct for each individual scientist makes it very hard to calculate career choices based on averages.  All this extra information that’s out there that is in theory helpful, I think might interfere with what’s the strongest thing, strongest determinant, which is this internal personal drive and internal personal necessity of matching who you are in terms of gifts and abilities and desires with a particular scientific problem, with a particular career choice. I think I had the benefit of being internally driven and making almost all of my choices based on that.  And not having the impediment of too much information.  Eric F. Wieschaus: And not having the impediment of too much information. Absolutely. I look at some of the things that I did and I would be very shy to recommend those to anybody, but they were the right things for me. I think that internal sense is something that you have to rely on, when you’re young, as well as when you’re old. You have to rely on it throughout life, I think. If you’re going to make choices that are going to contribute to your happiness or your success, you have to rely on that internal sense of who you are and what matters to you.  That’s a good piece of advice.  Eric F. Wieschaus: Yes.  I couldn’t have been happier with that. It was marvellous stuff. Thank you very much.  Eric F. Wieschaus: Yeah, absolutely. So what do we do now?  We stop. Okay. |
| ID | **0571** |
| Biographical | My father, Alfred Gilman, could play almost any musical instrument and frequently did so at neighborhood parties; his father owned a music store in Bridgeport, Connecticut. My mother, Mabel Schmidt Gilman, was an excellent pianist and gave lessons; her father was a professional trombonist, also in Bridgeport. Despite this heritage, my musical career ended after a few years of mediocre performance with the Yale University Concert Band during my days in college.  There were more substantial influences. My father had turned to science, receiving his Ph.D. in Physiological Chemistry from Yale in 1931 for “Chemical and Physiological Investigations on Canine Gastric Secretion”. He then joined the faculty of the Department of Pharmacology at the Yale Medical School, where he and Louis S. Goodman, a young M.D., became colleagues and close friends. A major new textbook of Pharmacology *The Pharmacological Basis of Therapeutics*, was the fruit of the Goodman and Gilman collaboration, first published in 1941. I too was born in 1941 (in New Haven, Connecticut) and named Alfred Goodman Gilman. Perhaps my fate was sealed from that day; as my friend [Michael Brown](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/index.html) once said, I am probably the only person who was ever named after a textboook.  The bulk of my childhood was spent in a suburb of New York City, White Plains, while my father was first on the faculty of The College of Physicians and Surgeons of Columbia University and then the founding Chairman of Pharmacology at the new Albert Einstein College of Medicine. I remember exciting trips to the city with my parents and elder sister Joanna to visit museums and, particularly, the Hayden Planetarium. In the early 1950’s I made a reservation for a trip to the moon and was quite positive that I wanted to be an astronomer. Alas, I eventually learned that astronomers do little star gazing, and biology began to look more appealing. These feelings were clearly nurtured by trips to my father’s laboratory, where I was able to watch experiments on canine renal function. There were also elaborate pharmacological demonstrations prepared for the medical students. All of these experiences were very visual. It is perhaps surprising that I eventually turned to biochemical approaches to pharmacology; it is not much fun to watch someone pipette.  My parents were less than enthusiastic about the local high school, and I was “sent away” in 1955, not smiling, to The Taft School in Watertown, Connecticut for grades 10 – 12. New England boys’ “prep” schools were not much fun in the 1950’s. There was much I did not enjoy, from compulsory rising bells to compulsory religion and compulsory athletics. I was surely the worst 120-pound lineman on the intramural tackle football team. But the education was superb, and I learned how to learn. Chemistry, physics, and math were extraordinary, and I was even forced to write – an essay every week. My final victory was from my English teacher. “Not bad, Gilman,” he said, “it still sounds like a lab report, but not bad.”  After Taft, college (at Yale University) was relatively easy and a lot more fun. I majored in Biochemistry and was inspired by the best series of lectures ever delivered – by Henry A. Harbury, who taught half the course. The room was always overflowing, in part because the medical interns and residents arrived to hear protein chemistry and thermodynamics come to life; I swear it’s the truth. I also had my first real opportunity to work on my own in a lab – that of Melvin Simpson. My project was wildly overambitious, to test [Francis Crick](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html)‘s adapter hypothesis, but the experience was an enormous treat because of Simpson’s warmth and strong encouragement. I met my eventual wife at this time, and she spent many late nights in the lab with me as I manually fed planchettes into the radioactivity counter. Perhaps she should have smelled the competition.  The summer after college (1962) I worked in Allan Conney’s lab at Burroughs Wellcome in New York and, thanks to Conney’s generosity, I published my first two papers. There was no question in my mind that research was for me as I headed to Case Western Reserve University in Cleveland in the fall of 1962, following the lure of cyclic AMP and a novel M.D.-Ph.D. program. My initial interactions with [Earl Sutherland](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1971/index.html) are described in my Nobel lecture and need not be repeated here. My experience in Cleveland was most notable, socially, for my marriage to Kathryn Hedlund and the births of our first two children and, scientifically, for interactions with Ted Rall, my thesis advisor and now close friend. His commitment was epitomized by the excuse, usually necessary, when I arrived home for dinner at nine: “I just went into Ted’s office at five o’clock for a few minutes to talk about an experiment.”  Rall was working on cyclic AMP in the brain, while I toiled with the thyroid gland. The brain looked a bit more interesting, and I was particularly struck by the molecular biologists who had “solved” their field and were defecting to the nervous system *en mass*. Clonal cell lines and genetic approaches seemed to be the answer, and I asked to work with [Marshall Nirenberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1968/index.html) via the Pharmacology Research Associate Training Program of the National Institute of General Medical Sciences. My experience with Marshall (1969 1971) was enormously broadening, despite the fact that I was “forced” (for a while) to work on cyclic AMP. I also met friends who were to have a great influence later, particularly [Joseph Goldstein](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/index.html), who had not seen the neural light and was working in the residual protein synthesis section of the Nirenberg laboratory. I had the fortune to develop a simple and sensitive assay for cyclic AMP while in Bethesda. It helped make second messengers accessible to everyone, and it surely made my name visible as I looked for a job.  Continuing what was to become a habit – when moving, always move south – I became an Assistant Professor of Pharmacology at the University of Virginia in Charlottesville in 1971. The position was a particularly attractive opportunity to join old friends from Cleveland, including Joseph Lamer (the Chairman), Robert Haynes, [Ferid Murad](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1998/index.html), and Bob Berne. The environment was intellectually supportive and, slowly but surely, good things began to happen. Crucial were the advent of ligand binding assays for receptors, the development by Gordon Tomkins and associates of S49 cells (which were killed by cyclic AMP), and the arrival in 1975 of a superb new postdoctoral fellow, Elliott Ross. Elliott’s hope was to get help from genetics while unraveling the biochemistry of a complex piece of membrane biology. The cyclic AMP system interested him, and he had planned to join Tomkins. Gordon’s untimely death forced Ross to a second choice, and I was the beneficiary. Ross’s contributions were enormous, as described in the Nobel lecture, and his success inspired others to join the group, particularly including his friend from Cornell, Paul Sternweis, and [John Northrop](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1946/index.html).  [Joe Goldstein](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/index.html) and [Mike Brown](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/index.html) approached me to move to Dallas in 1979, but I was totally immersed in research and my other major preoccupation, editing the sixth edition of *Goodman and Gilman’s the Pharmacological Basis of Therapeutics*. Amusingly, [Martin Rodbell](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1994/index.html) almost took the job, but, when he eventually declined, the Dallas crowd came calling again – this time with a *real* talker in the lead, Donald Seldin. Very few say no to Dr. Seldin, and I arrived in Dallas to chair the Department of Pharmacology in 1981. I have been extraordinarily happy in Dallas and have benefitted greatly from close interactions with colleagues like Brown and Goldstein and from the opportunity to recruit those whom I knew to be superb – Ross and Sternweis. I have derived great satisfaction from building what I consider to be an excellent department, and I hope that our faculty feel as encouraged as I did in Charlottesville. It is easy to be a successful Chair in Dallas; our administration, particularly President Kern Wildenthal and Dean William Neaves, and local philanthropists ensure it.  My wife and three children, Amy, Anne, and Ted, have always been strongly supportive and wonderfully understanding of the intense competition from my affair with science. My children have not benefitted from the lavish fatherly attention that I did. Despite me, they are well on their way to happy and productive lives. I am very proud of them and of their super mother, who has made up for my deficiencies. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0571** |
| Interview |  |
| Q83 | I’m happy to be here. Your part in the work was the identification of the nature of the transducer, hypothesised by [Martin Rodbell](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1994/rodbell-facts.html), as the protein complex which we now know as the ubiquitous G-proteins, and I’d like to come back to the time of the discovery a little later, but to start off with, I’d like to discuss your scientific beginnings a little. You had quite early exposure to science, and biomedical science in particular, through your father. |
|  | I’m reminded that, there’s an expression of, I guess, particularly wealthy people that were both with a silver spoon in their mouth. A former governor of Texas, Anne Richards once, in commenting on her opponent George Bush, said he was born with a silver foot in his mouth, I think. I was born with a scientific silver spoon in my mouth.  A silver spatula.  Alfred G. Gilman: Yes, and my father was a Ph.D. in biochemistry, he turned to pharmacology, he was on various medical school faculties and he was a terrific father and showed me the pleasures and joys of science as a kid. I’d go down to his lab and watch things and had a wonderful time.  You were even named after the textbook?  Alfred G. Gilman: That is interesting, yes. They had no idea what they were doing at the time, but I was born the same year as my father and Lou Goodman first wrote this textbook, *The Pharmacological Basis of Therapeutics*, so I was given my father’s friend’s name Goodman as a middle name and that has enormously confused generations of medical students for quite some time now as to how that came to be. They imagined all sorts of strange relationships.  And you took over the editing of the textbook.  Alfred G. Gilman: Yes I did, in the mid 1970s. |
| Q1 | Did you know when you were a child that you wanted to be a scientist then? |
|  | Yes, I wanted to be an astronomer and some of my favourite memories of being a kid, we lived in suburbs of New York city, going into the city and visiting museums but especially the hidden planetarium in New York. I remember with great excitement, signing up for a trip to the moon. I can’t remember how, I was probably well maybe 10 years old, so this was maybe in the early 50s and they had a book you could register for a reservation and it seemed quite fanciful at the time.  Biology then came to supplant astronomy at some point.  Alfred G. Gilman: The thing is, a friend of mine had similar thoughts as a child and she once mentioned, but I figured out that astronomers don’t spend all their time looking at stars and interest turned, yes. I became much more interested in biology in high school and college. |
| Q11 | Then Yale and then you made what on reflection was the fairly momentous decision to go and do the MD Ph.D. programme at Case Western with Earl Sutherland, but you refused the first time. |
|  | That’s correct. You know, that was another good example, really, of an advantage I had, I think. [Earl Sutherland](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1971/sutherland-facts.html), who won the Nobel Prize in, and you can probably tell me better than I, maybe the mid-60s, no, probably the mid-70s. He discovered cyclic AMP along with Ted Rall and maybe in 1956-57 he had gone to Cleveland and started this new programme, MD Ph.D. programme. It was quite unique; he knew my father well. He recruited every student into that programme individually, you know, there was no advertising, no marketing, he just got to know people one way or another and it was a small programme and he recruited it.  I think he knew he would see my father in meetings and my father liked to talk about his family, so Earl knew that I existed. He sent me a note and asked me if I’d be interested in looking at the programme and I got the letter when I was a junior in college and I looked at it and said Seven years in Cleveland, no thank you, and I responded back, politely I hope, that I wasn’t interested, but he tried me again in the fall of my senior year and I thought, oh, what the hell, I’ll go check this out, and I did and was very excited about it, so I did it.  So what ‘the hell’ led to your first exposure to second messengers and a career.  Alfred G. Gilman: That’s about right, yes. My big concern was that he was Chairman of a pharmacology department, I was majoring in biochemistry at Yale and I didn’t want to just, you know, follow along in my father’s footsteps too precisely and my father was much more of a physiology and I was more interested in biochemistry. I said to Earl, My only real concern here is that this is pharmacology and he patted me on the back, said don’t worry, he said, pharmacology to us is just biochemistry with a purpose so I think that was the clinching line for him. |
| Q11 | And what was the question that they were asking at Case Western that really got you going? Were you even at that stage interested in the big questions such as how do hormones work? |
|  | That’s correct. You know, that was another good example, really, of an advantage I had, I think. [Earl Sutherland](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1971/sutherland-facts.html), who won the Nobel Prize in, and you can probably tell me better than I, maybe the mid-60s, no, probably the mid-70s. He discovered cyclic AMP along with Ted Rall and maybe in 1956-57 he had gone to Cleveland and started this new programme, MD Ph.D. programme. It was quite unique; he knew my father well. He recruited every student into that programme individually, you know, there was no advertising, no marketing, he just got to know people one way or another and it was a small programme and he recruited it.  I think he knew he would see my father in meetings and my father liked to talk about his family, so Earl knew that I existed. He sent me a note and asked me if I’d be interested in looking at the programme and I got the letter when I was a junior in college and I looked at it and said Seven years in Cleveland, no thank you, and I responded back, politely I hope, that I wasn’t interested, but he tried me again in the fall of my senior year and I thought, oh, what the hell, I’ll go check this out, and I did and was very excited about it, so I did it. |
| Q3 | So what ‘the hell’ led to your first exposure to second messengers and a career. |
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| Q23 | And what was the question that they were asking at Case Western that really got you going? Were you even at that stage interested in the big questions such as how do hormones work? |
|  | That was Earl’s question, how does a hormone work and the system he was studying, he had grown up under the tutorage of [Carl and Gerty Cori](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/), so a train of Nobel’s. He was in St Louis at Washington University which was in many ways the birthplace of so much in biochemistry in the United States. Earl was particularly interested in epinethrine and glucagons and how did the action of those two hormones result in hypoglycaemia, that was the increase in blood sugar. It was a biochemical parameter that could be measured.  We gave a hormone to an animal, blood sugar went up, what was in between and Earl ultimately took that problem to understanding that the hormone worked at the outer surface of the cell, stimulated somehow the generation of this so called second messenger, cyclic AMP, which was his key discovery and that cyclic AMP went on inside the cell to stimulate the enzymatic reactions that cause the breakdown of stored sugar or glycagon, broke down into sugar and released into the body. So that was the problem and Earl brought it to a very substantial level and others included us picked up from there.  So you picked up on the question of what lay between the outer surface and cyclic AMP?  Alfred G. Gilman: Really, yes. |
| Q2 | And that fascinated you from the beginning? |
|  | That was the black box. The inside part was pretty well worked out, the details of what went on inside the cell, but what happened at the cell surface, how that information got from outside to inside was a mystery.  Were you aware when you sort of pondered taking on this question that there was a great lineage of august figures behind you or was it just …?  Alfred G. Gilman: I guess intellectually I was, but I’m not sure emotionally whether that was, probably not a big factor.  Because there’s so many questions to ask, it’s lovely to find your questions so early and then stick with it, it shows great foresight but also great luck.  Alfred G. Gilman: I’m not sure, you know, how well the question was framed at that point. When I took my first job, the first grant I wrote, the title was *The Role of Cyclic AMP in Neurons and Glia*.  Hedging your bets.  Alfred G. Gilman There was more of focus on deciphering specificity in the nervous system and just who was doing what to what cells types and what those interactions looked like. This was in the very early 1970s and there was certainly a piece of it interested in the receptors and how that all worked but questions were phrased more broadly and less specifically. I think I probably became a lot more specific as data and experimental success led you on one path or another. |
| Q4 | Because I suppose there are a lot of people, young scientists, who are fishing around for the right question to ask and are very worried about the finding of that right question, which will lead them on the correct path. |
|  | I think one shouldn’t be concerned about being too specific about that question too early. You need to find an area of importance and something where there are big questions, hopefully more than one and to begin to hone in on an area first. I don’t think that the questions need to get too specific too soon.  There’s a balance between not getting too specific and being too broad and therefore being a bit dissipated, I imagine.  Alfred G. Gilman: Yes, yes. |
| Q25 | Marshall is a very creative and free thinking man. The reason I ended up in his lab was because he made a huge switch in his field of interest and just that alone takes a great deal of courage. He won his Nobel Prize for deciphering the genetic code and was particularly interested in how information got from genes to proteins and mechanisms as protein synthesis but in the late 1960s, the field of molecular biology was looking mature to some, which is sort of funny, but many molecular biologists had that point in time said that we’ve figured it all out now and neuroscience, neurobiology is the big frontier and so let’s go there and that’s an important lesson to be learned there.  First of all, they were of course wrong, molecular biology wasn’t quite done but it was a great move for many of these guys to move onto the next big challenge and Marshall was one of those and it was his move into studying the nervous system, particularly the use of cultured cells to do that, that attracted me to his lab so I went there with that notion. His imagination was always very inspirational, he was quite different from other mentors I had, he would imagine that you could discern things and learn things in ways that were not obvious to me and it was mind opening.  So how did he do that?  Alfred G. Gilman: He saw paths that were, I think tenuous, that would take courage to pursue. He had it, he had the courage.  And was he able to instil some of that courage in the people working for him?  Alfred G. Gilman: I think so, I hope so. That was a time of great talent at NIH, National Institutes of Health. The Vietnam war was on and that is unfortunate, the set of circumstances that it was, provided a lot of motivation for a lot of young physicians to go into research careers, rather than to go into military service and so there was huge talent at NIH, it was sort of the heyday of NIH in many ways, so there were a lot of bright young people there, working in those laboratories and they profited hugely from mentors like Marshall and many others that were there. |
| Q61 | How interesting, so there was a generation of doctors who wanted to look at basic science for a while? |
|  | I recall also, I was one of the very early MD Ph.D. graduates. The path for many at that time was to get a medical degree and that’s the path I thought I was going to follow, to get an MD and then get research training afterwards and many, many people did that, that’s the way that academic departments of medicine were populated with researchers, was via that route and there was a lot of motivation for people to go that route at that period of time. Let me go back a little bit though because we’ve neglected someone who was very important.  Earl Sutherland recruited me to that programme in Cleveland, but he left very shortly after I got there and my Ph.D. advisor was his young colleague, Ted Rall who was the one I did all my work with and I owe an enormous amount to him and he was a spectacular mentor. I was married early during that period of time and that programme and a classic line in our household when I get home at 8 or 9 o’clock for dinner was, make my excuses to my young wife saying, I just stopped in Ted’s office to say a couple of things around six and that was 8.30 before we stopped. So he was incredibly generous with his time and advice and we just had a wonderful relationship. |
| Q26 | Was he very selective in the people he brought into the lab to work with, I imagine he must have been if he was going to devote such time to their relationships? |
|  | It was a relatively small lab and most labs were relatively small in the 1960s, it was sort of before big science or bigger science. |
| Q26 | It must have been both exciting and overwhelming to have somebody focus on you to that degree, when you’re so young. |
|  | It seemed natural. It was the way it worked and that was the way it was in that department, it was the Department of Pharmacology at Western Reserve, now Case Western Reserve. I think there were many things that were done on a smaller scale then and there was a lot more time. There was a lot more time to think, a lot more time to interact more closely with people.  What about in the way that you did experiments. Was that very different from now, somewhat?  Alfred G. Gilman: Everything was much less automated, much more manual, much more hands on. It was reasonably primitive by today’s standards.  Primitive, but you understood what you were doing, you understood what the technology was delivering.  Alfred G. Gilman: Yes, there wasn’t that much technology but we certainly understood what it was delivering.  And do you think that makes a difference?  Alfred G. Gilman: I’m not sure exactly what level you’re asking the question. We could not envision then things that can be done in a matter of a day or a week now. The notion of purifying a protein was daunting enough, let alone having the sequence of a protein, there were two or three examples at the time and so on and probably not much else. The notion of understanding how proteins worked and the level of detail, the notion of understanding what a protein looked like, how it interacted with the … These were pretty difficult to fathom at the time. |
| Q26 | But maybe more accessible to young students as well, that you could undertake experiments that other people were doing in their labs without having to go out and get a big grant to get the equipment etc. |
|  | That’s true but the equipment was also expensive and … the grants were much smaller. I’m sure that everything scales. But the question at the time and Earl Sutherland phrased this question … The technical way to ask the question was the beta-adrenergic receptor, the enzyme that made cyclic AMP. To put it in more allayed terms was, was there just a single component in the cell surface membrane that allowed the information to get across.  Or were there a chain of events?  Alfred G. Gilman: Yes, chain of events or was it all one thing and it was very difficult even to think about how to answer that question. Today it’s trivial to think about how to answer that question but it wasn’t at the time. |
| Q3 | Many things, yes, so I was going to ask, what made you come and stay? |
|  | Let me say first, I had a wonderful 10 years at the University of Virginia, it was a terrific place to launch my career. It was, I think, a pretty nurturing environment with a good, excellent Department Chairman Joe Larner, who recruited me there. He had been in Cleveland, I had known him as a student and I got a great start there. Dallas offered opportunities on a grander scale. This is a very ambitious place and it’s ambitious to excel, particularly in terms of research. It’s ambitious, I think, in all the finer senses of the word to have fantastic research programmes of highest quality, answering major questions and I think it’s reasonably entrepreneurial, people who do well are well supported by the institution in ways that I couldn’t imagine ever changing. There really is strong institutional support for people who succeed and I think that was obvious in the way that people’s careers were going here, particularly my good friends [Joe Goldstein](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/goldstein-facts.html) and [Mike Brown](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/brown-facts.html) who were instrumental in recruiting me here. |
| Q11 | And Joe and you had been post-docs together. |
|  | Joe and I were both in the Nirenberg lab all though he was still in the protein synthesis section which was being led by Tom Caskey at the time, so Joe and I knew each other and we were on separate floors, sort of in different areas of interest but I knew Joe. Joe had been a medical student here, he went off to clinical training in Boston and in Seattle, research training, pardon me, in clinical training in Boston and then research training at NIH in Seattle and Joe and Mike had gotten together and were doing fantastic things and were having great careers here and were a shining example of success and how successful people were treated in Dallas. Joe Goldstein called me to ask me about the position in maybe 1979, I think, and I was very busy and told Joe I wasn’t interested.  The story gets sort of amusing because then they really successfully recruited Marty Rodbell, of course with whom I shared the Nobel, and Marty accepted the job here but then for personal reasons had to back out at the last moment. Seldin came back to me and called me one day on the phone and Don remains an extraordinarily forceful personality with incredible vision and great gift of gab and he called me up, said would you do me the courtesy of just giving me 15 minutes on the phone and I got the next word in I think about 1½ hours later and I was pretty well hooked, perhaps, at that point. Made a visit and it all went very quickly. But this was and still is a young school, they had a great vision of growth and great plans for success and it was very attractive and a terrific decision I made to come here. Schools continued to grow enormously and have been very successful |
| Q11 | Certainly so and they seem to have an unerring accuracy for recruiting future Nobel Laureates to their faculty. |
|  | You know I’d put a lot of that good decision making in the hands of relatively few people who are gifted. Don Seldin had the gift from the very beginning and he is the man, I think, if you wanted to pick a single individual who really got the school going in the proper directions and fostered its growth, he’s the man and the stories are famous. He had really nothing to work with, it was a pretty primitive place and he would go into the medical school class and identify bright young talent and take that talent under its wing and with his strong persuasive powers, sculpt its career and there are many famous examples of that, Joe Goldstein being the best. Joe came here. He was born in South Carolina, went to William and Mary, I think, as an undergraduate, came here to medical school thinking that he might be a neurosurgeon and Don Seldin turned him into a molecular geneticist so that’s it, that’s persuasion and there are many other examples but the ability to identify talent like that is something quite unusual and Don had it and Joe has it and Joe and Mike especially have played a huge role in sculpting the school further and others of us have joined along the way. |
| Q32 | I guess the standalone medical school faces certain challenges of not having the surrounding media for research, but that’s also a problem that has been addressed. |
|  | I think, in terms of the history of this school in Dallas, I think it being a standalone medical school has at times been an advantage and at times it’s a disadvantage. We have profited in this city enormously from generosity of the Dallas community and philanthropy has played a very important role in the growth of the school. |
| Q6 | Did that increase greatly once Nobel Laureates were there? |
|  | It certainly helped. I think that made a big impact and there are certainly some major donors who were perhaps sceptical of the school’s future and the Nobel Prize puts a seal of approval, quite like no other on an enterprise and so yes, I think that was hugely important and the first one which involved two individuals, Joe Goldstein and Mike Brown, the first one, was incredibly important, the second one was wow and then there was a little bit of frosting on the cake, so I think it has had a huge impact. Dr Wildenthal, our president, loves to show a slide of the four of us together and proudly proclaims that no other president of a medical school in the world perhaps can show that he’s got four still active Nobel Laureates on the faculty. So, that’s been a great help and so philanthropy in Dallas has been hugely important to us.  Modern communication makes it a lot easier, you can move electrons a lot faster than people …  At the same time, I think particularly now in this century, the need for interactions of medicine that interfaces with virtually all the other sciences are critical. 20th century medicine was young and unsophisticated and perhaps couldn’t benefit as much as one might hope from strong interactions with chemistry, chemistry perhaps, yes, but physical sciences, computational sciences, engineering sciences not as much, but that’s changing dramatically now and we need all those interactions and being a freestanding medical school is a disadvantage in that regard, but we’re working hard to fix those things. Modern communication makes it a lot easier, you can move electrons a lot faster than people and so communication helps a great deal. In addition, we have two components to general academic campuses at the University of Texas system in this area, you know, University of Texas at Dallas and University of Texas at Arlington, they both have strong science programmes, particularly in engineering and computer science and we’re establishing strong ties with them and will all go very well for the continued growth of this place. |
| Q43 | What do you think the school misses most at the moment? What does it need? |
|  | I don’t think there are any really glaring weaknesses. There are areas where we are stronger than others. The laboratory based sciences are our traditional strength and we’re very good at it. Things that we’re really trying to build now include greater strength in clinical research and translational research on the one hand and on the other these interfaces, particularly with engineering, computationals, computer science, chemistry and physics. |
| Q62 | So on the former, have you got drug discovery efforts, for instance, going on here on campus? |
|  | Yes and that’s a very nice outgrowth of one of our first moves to establishing interfaces, so Steve McKnight who’s chairman of biochemistry here has built a very strong, basic chemistry programme within biochemistry. Some are very pleased to look at this department and say Steve has put the chemistry back in lab chemistry, and there are half a dozen really superb young chemists in that department. And these are young people who I think have had the courage and vision to say, no I don’t want to be part of a traditional chemistry department, being here is like being a kid in a candy store because you’re in the midst of all this biology, so you’re sort of swimming in a possibility of interactions and collaborations.  One by one, these young folks have come here and taken advantage of it and really done very well with it so, you know, companies have been spun off, drugs are in clinical trials and it’s easy to see how this has come about from interactions of strong biochemists and molecular biologists on the one hand and the chemists on the other. Targets have been identified, screens have been run and targets of, you know, drug candidates have been discovered and optimised and the process is moving on, so it’s going very nicely and now we’re building the capabilities to move those things further down the stream and really do much more in terms of clinical trials ourselves. |
| Q62 | Right and is it a disadvantage? I suppose it is a little bit of a disadvantage that there isn’t very much major pharma based around here. |
|  | I think that is a disadvantage and we have tried to and are trying to catalyse the growth of biotechnology in Dallas, it’s been slow, it’s been slow almost everywhere except the coast and just really in a few major cities on the coast and there’s a huge focus. I think it’ll happen, it’ll come. |
| Q62 | I suppose there’s an effort in biotech and drug discovery to put the clinical back into their efforts so you stand in a good position there. |
|  | Alfred G. Gilman Drug discovery is a whole huge and interesting and difficult subject these days but obviously many alliances of biotechnology companies with big pharma to accomplish those things and also with academia. |
| Q25 | In terms of forming alliances, I know that you have put your heart and soul, for a while, in the Alliance for Cellular Signaling. A massive collaboration to work out the entire repertoire of signalling molecules within two cell types. What did that experience teach you about the necessary prerequisites for forming such collaborative networks? |
|  | They taught me a lot about management for one thing but the Alliance has been very successful in some ways and not as successful in others, as I might have hoped and it’s still ongoing and on a slightly smaller scale, which has probably served it reasonably well to scale down some of its ambitions and efforts. Collaboration in biology is a very interesting subject at the moment, I think. Other sciences have gone further in that direction, I think physics being the best example, where it’s been driven by various specific needs for instrumentation and equipment that costs millions and millions, if not 100s of millions or billions of dollars and then collaboration is an absolute necessity and if it’s a necessity, people do it. In biology and biomedical science, successful grand collaborations have been driven by very specific … and the most obvious is the sequencing of the human genome and that was a very specific project and a business-like plan that you could put together and do it.  … it’s more problematic to get people working together at a discovery level than at a more technological level …  At the more fundamental and more discovery oriented biology, it’s still a little harder, I think, to get people together. A lot of that I think is still very much driven by individual genius, individual creativity, individual motivation and egos and egos are certainly a part of this and it’s more problematic to get people working together at a discovery level than at a more technological level. It’s going to come and it will happen more as people begin to get more into the really big problems of biology, how do really complex systems work? The magnitude of the problems is extraordinary and the difficulty is extraordinary and concerted efforts are going to be necessary and they’re happening but I think they’re just more difficult from really sort of a fundamental management point of view.  It is the trend for people to form these networks increasingly …  Alfred G. Gilman: It is a trend.  .And yet a lot of those networks don’t quite fulfil the goals they set out with.  Alfred G. Gilman: I think it’s very early to tell, in terms of the success of many of them, but I think obviously there’s growing success for sure in terms of putting unconventional or not unconventional but interdisciplinary people together and really letting things happen based on interactions that haven’t happened before. We are working now on a concept, I hope it may happen, it’s too early to tell but a concept of an Institute within the University of Texas system for example that would need not be confined to the University of Texas but that would be one possible mechanism, but to create a really interdisciplinary institute that would get into big problems of systems biology and cross fertilisation between biology and engineering sciences, for example. We think the way to do that now would be really to bring really interdisciplinary people together, rather than creating an interdisciplinary Institute composed of a specialist here and a specialist there. The communication barriers remain huge and it’s still very tough for a physician to talk to an engineer. |
| Q20 | You know the engineer says what’s that squiggly stuff and the doctor says that’s DNA. |
|  | Yes, so it’s a challenge, but there’s a growing number of rare breeds of people who can transcend themselves and putting those people together in a proper environment, I think there’s potential great gain to be had there and we’re talking about trying to approach problems. All of these problems in biology span huge scales and this is part of the issue so, one way to think about it is that biology build machines or organisms or people whose dimensions are in metres. We build these out of pieces whose dimensions are nanometres, so you know there’s a scale of 9, 10, 11 orders of magnitude and there’s a temporal scale too and motions of molecules that happen in nanoseconds and drive events that are measured all the way to lifetimes of organisms or even evolutionary timescales.  So, there are even more orders of magnitude there and finding people who are driven by the notion of finding out whether things that they can measure that happen in nanoseconds of milliseconds, how relevant are they to events that play out over minutes, days, weeks, years or lifetimes. That’s an interesting way of thinking and I think people who are driven to thinking those sorts of ways will make each contribution.  It’s a very appealing concept to work with, the idea of existing on such a scale that …  Alfred G. Gilman: It’s a daunting concept to work with and the technical challenges are enormous, I mean the ways that you measure things that happen in milliseconds and the ways that you measure things that happen in years. |
| Q62 | In your mind that’s one key to the systems biology problem that people have to get away from only thinking about the system that they all study, which may be for instance a very small scale. |
|  | Another way of thinking about it is the value of understanding how something came to be, not just what it looks like but why does it look that way and what was the process that created it, so really thinking in evolutionary terms. If you can understand why a system was built the way it was and what constraints evolution put on the way that the thing was built, I think, and this isn’t all completely intuitive and obvious but I think that you will acquire deep insight into how something really works if you understand how it came to be, rather than just what it looks like when it was finished. |
| Q20 | Given that question, you then as you say, need to get people together in the same institute, they need to work in close proximity. |
|  | I think people working at different ends of that spectrum, of different ends of the spacial scale spectrum and the temporal scale spectrum.  Sounds a very attractive prospective.  Alfred G. Gilman: I hope so and many of these ideas are not mine, they’re circulating around widely but we’ve been talking about the idea of creating this institute and particularly talking with some of my young colleagues here who’s minds are still very flexible and who think very well in these directions and I’ve been trying to learn from them. |
| Q34 | Is that the major thrust of your current efforts as Dean of the medical school? |
|  | It’s one and I think really trying to work on two major things simultaneously, one the translational and clinical side, say in the laboratory research particularly here is in strong shape, we need to push translational medicine and clinical research much further in that way and also the more fundamental interfaces in the other, so we want to span that scale too. |
| Q6 | I also wanted to ask you about the effect of the Nobel Prize on your career, in a sort of general sense. It’s a difficult question but I imagine that obviously, it had a very positive effect, it may also have had some detrimental effects on your research I imagine? |
|  | It can be a distraction. It’s a ticket to travel the world, if you want one, and it’s an opportunity to do many things. It’s an opportunity to be heard, whether you have anything to say or not, some people do and some people don’t and I think people handle it very differently and if you want to stay focussed in your laboratory as many do, you need to acquire a very fine sense of how to say no and because you’re going to be turning down hundreds of invitations. If you want a bully pulpit, you sure have one and many people are doing terrific things with that. Just yesterday evening I was at a dinner with [Peter Agre](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/2003/agre-facts.html), who won the Prize in Chemistry a few years ago now.  2003 I think.  Alfred G. Gilman: I think 2003 is right and Peter has very well thought out and well expressed feelings about the role of science and public policy and the fact that science is not being heard adequately, I think by politicians and public policymakers and he is outspoken on that subject and I think very well spoken on that subject and the Nobel Prize gives him a lot of bully pulpit, gives him a lot of credibility. He’s even thinking of running for public office and I guess I hope he does but if he does, I sincerely hope he succeeds at it, but I’m not sure whether the American public is ready for a Nobel Laureate as Senator from the state of wherever, but it would be interesting. Some states are more ready than others.  The Nobel sort of imprint tends to allow one to comment on things way outside one’s subject area.  Alfred G. Gilman: Yes and some people, you know, occasionally one goes too far but good judgement and all things unless it’s useful.  But you took the other course, you decided not to use it for that but to use it rather for …?  Alfred G. Gilman: Well, I’d say for the first half dozen years ago after my good fortune, really stayed very well focussed on my own laboratory. Other opportunities then came along and I decided to pursue some of them. The most drastic obviously being becoming Dean of the medical school and now Provost here and in some ways there’s a little bit of guilt perhaps for leaving the lab but I’ve enjoyed what I’m doing now a lot. I focussed on the laboratory for the better part of 40 years. I’m a pretty competitive individual really, and I like to think that whatever I’m doing I’m doing my best at it and I don’t necessarily think that I’m as creative a scientist at the age of 65 as I was at the age of 45.  Frankly I don’t think anybody is, brains get a little fossilised. Opportunity to do something really different came along and I decided to take a little try at it and then decided I very much enjoyed it and it’s a very different sort of life. I’ve learned more about how this school and how medical schools and universities work in general in the last two or three beta-adrenergic receptor years than I learned in the prior 30. Interact with a much broader sphere of people, cross a much bigger range of interests and disciplines and I’m enjoying that. I think there’s a little lingering guilt but there’s also some real pleasure in the new activities. |
| Q83 | Is there any lingering sense of a career that you might have done other than the one you’ve chosen? |
|  | Oh sure. We can go back to astronomy and astrophysics and I don’t think I didn’t have a talent for it but, unravelling the mysteries of the universe is a reasonably noble goal. I was a not very talented clarinet and saxophone player as a youth, a career as a musician would have been quite wonderful. Huge numbers of things left undone for sure that everybody would like to do. I also am a pretty focussed individual and maybe excessively so, get very caught up in what I’m doing and I’d like to go back through it all again and spend a little more time with my family and my children than I did. I wasn’t as good a father as my father was to me.  Are they, do you think an understanding family?  Alfred G. Gilman: They’re a very understanding family.  Yeah, they must be very proud?  Alfred G. Gilman: I hope so. I have a wonderful wife and three superb children, who are all doing very, very well.  Did any of them go into science?  Alfred G. Gilman: No. Perhaps they saw someone who was a little too focussed. My kids like to say that when they came to me with a science question based on their schoolwork or other, they wanted the five minute answer and they got the 45 minute answers. Maybe I just didn’t know when to shut up.  They sound like many medical students in the making.  Alfred G. Gilman: Yes, could be. None of them is in science. |
| Q12 | When you have students coming through or when you had students coming through the lab and now you have whole faculties to look after and you see people making their choices and you want to help them go the right path, is it possible to reflect on what sort of mentor you are to people? |
|  | That’s really hard I think. Mentoring has become a very, very popular subject. I hear the word constantly and I will admit to sometimes having mixed feelings about it because I think there’s a lot of discussion of mentoring programmes and formal programmes and teaching people to be mentors and of course then evaluating the quality of people’s mentoring activities, etc, etc, etc and I sometimes think it’s getting maybe a bit too programmed and looks a bit too much like a business plan and I think a great deal of it is still very spontaneous and one on one activity.  When I hear we must find someone, a mentor, frequently my first reaction is people need to find their own mentors. Yes, they should be helped and I don’t mean to sound like a bad guy about it but I think there’s still a good deal of spontaneity that’s required here and that it needs to be comfortable from both sides and it’s just not something that necessarily can be assigned. At the sort of level that you get mentored as a Ph.D. student, it requires a reasonably decent personal interaction and close relationship and that’s the most effective sort of mentoring. |
| Q12 | I suppose it’s a question of time. It’s the spontaneous coming out like for dinner? |
|  | Yes and you know this is the biggest problem. I mean I sound like an old curmudgeon at this point but the pace of life is much, much faster, everything is faster and if access to information is instantaneous, that’s all great and wonderful but it consumes us and there is not as much time available for and there’s certainly not as much time spent on personal interactions and thought and reflection and everything is just much more fast paced and the biggest complaint I hear from everyone, especially faculties is there’s too many demands, you’re asking us to do too many things and that’s probably true, we are. |
| Q63 | Where did the extra demand come from though, because basically what medical schools do now is what they did 40 years ago? |
|  | Frankly, a lot of it’s economic. On the clinical side, can our clinical faculty teach, can they do clinical research, can they do laboratory research and can they also be clinicians? A lot of that pressure is how they earn their salaries and we go from there to the entire economics of the healthcare industry and if you have a few weeks we could bring in a whole bunch of people and talk about that but it’s enormously complex and there’s a lot of conflicts there and just how people can exist and survive in an academic setting and have clinical activities and research activities and earn their salary for it. |
| Q3 | It comes again to that word you use, focus. It’s finding people who can maintain their focus despite all this stuff going on around them and presumably those individuals shine out, it’s easy to spot? |
|  | Yes and an example is they have to make choices. If I want to have an active research career and be a clinician, I’m going to earn less than the person who’s just going to be a clinician, in order to focus exclusively on being a clinician. On the basic science side, there’s a lot of pressure to generate funding for your laboratory research, the money’s got to come from some place. In the United States we’re very well blessed with public funding for science, more so than in any other country in the world but that funding is tight at the moment.  The competition for it is ferocious, only 10 or 15% of new grant applications are successful and that means you write more of them and worry more over each one of them and spend a lot more time competing for the money, than doing the actual research. There are also many issues of accountability for what we’re all doing, rules, regulations, compliance, more forms to be filled out, more regulations to be satisfied and these are distractions too, they’re important ones but they’re distractions and people are increasingly frustrated by them. |
| Q23 | Do you think that the situation in future years, funding in this country, is going to be similar? What do the auguries look like? |
|  | It’s cyclical and things get better or they get worse. The concerns of the moment are the level of funding for sure. Another major concern is the number of young people who are going into scientific careers. There’s a paucity of US educated students who are going into basic science careers and many probable causes for it. A public education system that is I think weak as far as science education is concerned, there are many reflections of that in terms of scientific awareness in this society, so that is a big issue and I think the perceived level of competition and compensation in careers in science is probably a bit of a turnoff as well. So the United States is relying more and more on foreign born scientists, who are coming to be trained here and happily, many are staying here and that’s a clear trend and so those are big issues too. |
| Q25 | In terms of the outreach to children and getting children interested in science, it is strange, isn’t it, because the US has a very high level of competence at reading at very young ages and then suddenly it seems to fall behind on scientific education? |
|  | I’m not aware of the reading statistics, I’m glad to hear that something seems to be going well but, you know, most of the data I see shows US school children well behind many, many other countries in the world in terms of educational competence and there’s growing concern about the problem and various programmes that will hopefully be effective in correcting it.  But I still fail to see a real public commitment to public education in this country and I think there’s sad reflections of that in terms of things that just jar badly with … sensitivities and beliefs. The percentage of people in this country who believe in evolution is horrifying. The number of people who think that human beings and dinosaurs co-habitated the earth – they didn’t. The number of people who think that the earth is 10,000 years old – it isn’t. The scientific evidence there is irrefutable. Other issues of global warming may be more debatable but not that much more, I don’t think and the level of scientific ignorance in this country or even suspicion of science is way too high. |
|  |  |
| ID | 0572 |
| Biographical | I was born on December 1, 1925 in Baltimore, Maryland where I attended public schools and graduated from the accelerated course at Baltimore City College, a public high school of special note because it took selected students from around the city. An all boys school, it resembled a private college preparatory school in both its scholastic standards and by giving sufficient college courses to qualify after graduation to enter the second year of a university. Special attention was given to languages (Latin, Greek, German, French); the sciences were understated. In fact, the only class in chemistry was given by a teacher who seemed to know Lavoisier personally since he was given the highest status in that course. As a result, my interests tended toward languages, especially French, which greatly influenced my direction when I entered Johns Hopkins University in 1943. On the other hand, I had acquired a great interest in chemistry despite the high school teacher. That interest was acquired through a special boyhood friendship with two individuals from my neighborhood. We were gifted students, highly competitive, and interested in math and chemistry. The three of us shared these interests throughout our boyhood and were together from elementary school to Johns Hopkins. We separated during the war when each of us went into different wartime situations. I was drafted into the Navy, the other two stayed at universities under the auspices of Uncle Sam, the expression used for those taken in the armed services.  I happily went into the armed services from Hopkins. I was bored with the courses given during wartime; most of the young, enthusiastic teachers had left for the services. More importantly for me, most of my friends had gone to war. As a Jew, fighting Hitler was the highest priority. However, in the Navy I spent most of the time in the South Pacific where the fighting was with the Japanese. I was a radio operator attached to the Marine Corps until I contracted malaria in the jungles of the Philippines. After recovering, I practiced my profession on several ships and traveled, as a result, to Korea and China. I mention this aspect of my life because my interactions with so many different types of people under trying conditions provided me with a healthy respect for the human condition. In fact, this experience buttressed the wonderful childhood atmosphere that I experienced in my home and in my neighborhood where my father’s grocery store served as a focal point for contact between people in the area. I believe all of these experiences conditioned me for the life I have led as a scientist.  When I returned from the war and re-entered Johns Hopkins, I was again attracted to French literature and became an avid reader of contemporary French writers, particularly [Gide](https://www.nobelprize.org/nobel_prizes/literature/laureates/1947/index.html) and those promoting the existentialist philosophy. My father was interested in my going to medical school. Pre-medical school was not at all interesting to me in part because of the intense competition among students for obtaining the highest grades, so necessary at the time to enter medical school. The turning point for me was a small class given by James Ebert, then a graduate student in the Biology department. Lengthy discourses on science philosophy and his deep interest and knowledge of embryology along with his enthusiasm for biology in general probably were the principal inducements for me to consider a career in the biological sciences. Moreover, the Biology department was filled with great professors like Bentley Glass and Vincent Dethier. When graduation time came, I went to Dr. Glass for advice. He told me to enter the field of Biochemistry. Not having taken advanced chemistry courses, I spent an extra year taking every advanced course in chemistry available at Hopkins. I knew at the end of that year that science was my forte.  I met my future wife, Barbara Ledermann, in 1949. She had come to America from Holland where she survived the war in the Dutch underground. Her sister and parents disappeared in the ovens of Auschwitz. During the war she learned photography and maintained her training as a ballet dancer. She had come to Baltimore and by chance was given a part in Moliere’s “School for Wives” in a production by the Johns Hopkins “Barnstormers”. In a short time she had acquired a number of friends interested in theater, art, and music. I had never met so many interesting people. Given my proclivity for literature and my somewhat limited experience in classical piano, the scene that unfolded was overwhelming. I knew she would be the perfect companion. We married in 1950. Not only had I entered the world of Science, my life now became intensely immersed in the Arts.  Having disappointed my father with my choice to become a scientist I gave him another shock by departing with Barbara for the U. of Washington in Seattle. Hans Neurath had just taken the chair of Biochemistry. The department was young with only a few graduate students and youthful professors ([Ed Krebs](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1992/index.html), Don Hanahan, Frank Huennekens, among others). I chose Hanahan as my thesis advisor and became immersed in lipid chemistry, particularly in the metabolism of phospholipids. I learned from Hanahan how to assay for the actions of phospholipases in ether solution. Not realized at the time, my life as a biochemist was to be immersed in membranes. My thesis concerned the biosynthesis of lecithin in the rat liver. Unfortunately for me, Eugene Kennedy was working on the same subject and succeeded in demonstrating that CTP rather than ATP is responsible for the biosynthetic pathway. That experience taught me a good lesson; never rely on the purity of biological chemicals, as I had done. That lesson helped greatly in the later discovery of the role of GTP in signal transduction.  I received my Ph.D. in Biochemistry in 1954. We immediately left Seattle for Urbana, Illinois where I became a post-doctoral fellow under Dr. Herbert E. Carter, then chairman of the department of Chemistry at the U. of Illinois. It was a wonderful place to be at that time, not only because of the great chemists in the department but also because the department of Microbiology had such notables as Gunsalus, [Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) and Spiegelman who enlivened seminars with their egocentric views and vivid arguments about everything. I took on the research problem of the biosynthesis of chloramphenicol, an antibiotic of note that interested Dr. Carter. The molecule contained a nitro group appended to its benzene ring and two chlorides in the aliphatic side chain. My interest was how inorganic chloride was taken up into the side chain. I had some good ideas toward the second and final year after spending a great deal of effort trying to crush the mycelia into cell-free extracts. Finally it came down to the understanding that chloride was taken up into an activated (radical?) carbon at the two position of acetylacetate derived from the metabolism of phenylalanine! That problem was ultimately solved. The challenge was exciting, it was time to move on. Dr. Carter asked me at what university would I wish to teach. I replied: none. I had experienced teaching his lecture courses for the first year students: few of the students passed my exams. Devastated I decided never to teach. I chose research as my metier. Dr. [Anfinsen](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1972/index.html) at the National Heart Institute accepted me for a position in his laboratory to work on “clearing factor”. By the time I arrived, Dr. Edward Korn (an old and dear friend at NIH) had established clearing factor as lipoprotein lipase, an enzyme that hydrolyzed the triglycerides in chylomicrons, the principle form of fat circulating in the bloodstream. Using emulsions of coconut oil as substrate, the enzyme required the presence of serum lipoproteins. My interest was to discern the nature of the lipoproteins on the surface of chylomicrons. Fortunately for me, Dr. Donald Frederickson and other scientists in the Heart Institute had extensive experience with serum lipoproteins; he and scientists at the Rockefeller Institute in New York supplied me with copious quantities of human chylomicrons. Using a newly developed “fingerprinting” method I established that at least five different proteins (designated alphabetically as A,B,C..etc) were present. Years later these five proteins proved to have very significant roles in diseases involving lipoproteins. For me, this was a fine exercise in protein chemistry that I had gained from Neurath’s department combined with my invaluable experience with phospholipids.  In 1960 I reached the conclusion that I wanted to return to my initial interest in cell biology: embryology. Fortunately I was granted a fellowship in Professor Jean Brachet’s department at the Free University of Brussels. A delightful man of great erudition and wit, Brachet was my perfect opening into the culture of Europe. I learned many new techniques; especially useful was an ultrathin x-ray film process to record localization of tritium-labeled molecules in cells. My family, meanwhile, lived in the Hague, enjoying the remaining family of Barbara: the Citroens of which Paul Citroen was a great Dutch painter. Traveling to and fro by train between Brussels and the Hague proved too much after 6 months. Luckily I found a suitable laboratory in Leiden, headed by Dr. Peter Gaillard, a pioneer in the techniques of cell culturing. In that lab I acquired expert training in the use of cultured heart cells for discerning the uptake of tritium-labeled chylomicrons. The year in Belgium and Holland, however, proved to be most important because of the cultural impact of European civilization on my life. I have been wedded to Europe since then.  On returning to the States I found myself in the Institute of Arthritis and Metabolic Diseases headed by DeWitt Stetten who gave me a position in the Laboratory of Nutrition and Endocrinology. With my experience in cell culturing, I became interested in discerning whether lipoprotein lipase was synthesized and released from fat cells. Korn had already established that the enzyme was present in adipose tissue. After months of trying several means of disrupting adipose tissue, I discovered that collagenase (actually an impure preparation containing many proteases) rapidly digested the tissue matrix, releasing the fat cells. Since fat cells floated to the surface of the incubation medium, it proved a simple matter to separate and purify these cells from the mostly vascular cells in adipose tissue. Little did I realize that this simple procedure was to change the course of research and the rest of my scientific career!  Dr. [Bernardo Houssay](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html), the great physiologist and Nobelist from Argentina was visiting the laboratory (one of his post-doctoral students was Robert Scow, section head of my lab) and learned of my feat. However, he questioned whether the cells were metabolically viable and said I must demonstrate to him that the cells were susceptible to insulin action. A few days later I showed him the results of insulin action on glucose utilization. He was ecstatic and proclaimed that this would be a landmark in the history of endocrinology. I was nonplussed but heartened by his enthusiasm. Insulin action, particularly its site of action on the cell, became a driving force. Testing the effects of my old favorites, phospholipases, I found that they mimicked the effects of the hormone on glucose utilization and protein synthesis. I had considered their actions to be restricted to the surface membrane. These results suggested that insulin may act by stimulating phospholipases thereby altering the structure of the surface membrane. As importantly, these data provided indirect evidence that the insulin receptor is located on the surface of fat cells. Prompted by teachings of Dr. Robert Williams of the department of Medicine at the U. of Washington, I decided to pursue this research by gently removing the fat from the cell while retaining many of the structural and metabolic aspects of the cell. This preparation I termed fat cell “ghosts”. Importantly, they were responsive to a variety of hormones in terms of their actions on glucose utilization.  In the mid-sixties, [Earl Sutherland](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1971/index.html) gave a lecture on his “second-messenger” theory of hormone action in which cyclic AMP was demonstrated to be a product of the actions of a variety of hormones on adenyl (adenylate, adenylyl) cyclase. I believe his lecture had a great impact on a number of us at NIH. Certainly, it caused me to turn to the “cyclic AMP” paradigm. Until that time I worked in the lab with Ann Butler Jones as technician. In 1967, just prior to embarking on a sabbatical in Geneva, we were joined by Lutz Birnbaumer. He proved to be a prime source for the next two years of the important information that led ultimately to the concept of transducers and the principles of signal transduction that I projected in lectures and in writings. News of our investigations rapidly spread. When I returned from Geneva, Michiel Krans and Stephen L. Pohl joined in our efforts with fat cell ghosts and later with rat liver membranes.  Meanwhile I had been asked by Albert E. Renold, a great endocrinologist and a noble man, to take over his Institut de Biochimie Clinique in Geneva while he was going on sabbatical in the laboratory of Robert Williams. That was the beginning of my long love affair with the city of Geneva and my many friends and colleagues there. Later I was to be Professor in the Laboratory of Biochemistry at the University (1981-83) where I carried out research on the structure/function of glucagon. During the period 1967-68, I carried out very interesting research on the effects of hormones on ion and amino acid translocations in fat cell ghosts with Torben Clausen who was serving a post-doctoral period from the U. of Aarhus in Denmark. We both learned from that experience that hormones originally thought to act monotheistically actually are pleiotropic agents; i.e., they can do many different things by separate routes. Certainly in my mind, endocrinology was no longer just a science; it was imbued with existentialism!  There is no point in recounting the story of the discovery of the role of GTP and magnesium ions in hormone action. That story evolved in our lab with many contributors over the past two decades of harmonious and exciting times. Looking back it was a period in which my life experiences had kaleidoscoped into a wonderful sense of creativity shared with not only my immediate colleagues but with scientists from all over the world. My life as a scientist has been joyful in large part because of my wife and our four children (Paul, Suzanne, Andrew, and Phillip) who succored me during those long days and nights of intense thought and often of frustration when ideas were scarce. In many respects, my career and my experiences with people and events have been seamless in that I cannot separate one from another. Without doubt, the thread of one’s life should be within the matrix of the total human experience. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| ID | **0573** |
| Biographical | I was born in 1943, the only child of John and Edna Roberts (née Allsop) in Derby, England. My father was a motor mechanic and my mother a homemaker. We moved to Bath when I was four and so I consider myself a Bathonian. My elementary education was at Christ Church infant school and St. Stephen’s junior school. At St. Stephen’s I encountered my first real mentor, the headmaster Mr. Broakes. He must have spotted something unusual in me for he spent lots of time encouraging my interest in mathematics. He would produce problems and puzzles for me to solve and I still enjoy the challenge of crossword and logical puzzles. Most importantly, I learned that logic and mathematics are fun! After passing the “dreaded” 11 + exam I moved on to the City of Bath Boys (now Beechen Cliff) School.  At this time I wanted to be a detective, where it seemed they paid you to solve puzzles. This changed quickly when I received a chemistry set as a present. I soon exhausted the experiments that came with the set and started reading about less mundane ones. More interesting apparatus like Bunsen burners, retorts, flasks and beakers were purchased. My father, ever supportive of my endeavors, arranged for the construction of a large chemistry cabinet complete with a formica top, drawers, cupboards and shelves. This was to be my pride and joy for many years. Through my father, I met a local pharmacist who became a source of chemicals that were not in the toy stores. I soon discovered fireworks and other concoctions. Luckily, I survived those years with no serious injuries or burns. I knew I had to be a chemist.  I am a passionate reader, having been tutored very early by my mother. I avidly devoured all books on chemistry that I could find. Formal chemistry at school seemed boring by comparison and my performance was routine. In contrast, I did spectacularly well in mathematics and sailed through classes and exams with ease. During these years at school I also discovered chess, which I loved, and billiards and snooker, which became a consuming passion. At age 15, I easily passed the O-level examinations and then began to specialize in the sciences taking Mathematics, Physics and Chemistry. For exercise I discovered the sport of caving and would spend most weekends underground on the nearby Mendips.  From age 16 on I found school boring and failed A-level Physics at my first attempt. This was necessary for University entrance and so I stayed an extra year to repeat it. This time I did splendidly and was admitted to Sheffield University, my first choice because of their excellent Chemistry Department. After Chemistry, Physics and Mathematics in the first year, I opted for Biochemistry as a subsidiary subject in the second year. I loathed it. The lectures merely required rote learning and the laboratory consisted of the most dull experiments imaginable. I was grateful when that year was over and could concentrate wholly on Chemistry. I graduated in 1965 with an upper second class honours degree.  As an undergraduate, David Ollis, the Professor of Organic Chemistry, really caught my imagination. His course emphasized problem solving, not memorization – more puzzles! Fortunately, he accepted me as his Ph.D. student and I began to explore the neoflavonoids found in a piece of heartwood from a Brazilian tree. Two pieces of luck followed. My tree contained more than its fair share of interesting new compounds and I was put in a lab with an exceptional postdoctoral fellow, Kazu Kurosawa, who proved a gifted teacher. Not only did he suggest the right experiments he explained why they should be done. Within one year I had essentially enough for my thesis and an understanding of how to do research. I had the luxury of spending the next two years following my nose, reading and experimenting.  During this time I came across a book, by [John Kendrew](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1962/index.html), that was to change the course of my research career. It described the early history of crystallography and molecular biology focussing on the MRC Laboratory in Cambridge. It was my first exposure to “molecular biology” and I became hooked. For postdoctoral studies, I looked for a laboratory doing biochemistry that might accept an organic chemist and provide a pathway into molecular biology. Luckily, Jack Strominger offered me a position, not in Wisconsin as I had thought, but at Harvard where he had just been appointed Professor of Biochemistry and Molecular Biology. It was on January 1st, 1969, that my family walked across the runway at Logan Airport with an outside temperature of 4°F and a massive wind blowing, to start a new life.  The next four years were wonderful. Mostly, I learned, although at first I was in a fog. Everyone spoke in acronyms: DNA, RNA, ATP, UDP, GlcNAc. Luckily two Australians, Aubrey Egan and Allen Warth, lived close to my apartment and we would drive in and out of the lab together each day. Those half hour commutes became my biochemistry classroom. Slowly I learned the jargon. A third Australian, Tom Stewart patiently guided me into the world of tRNAs since it was his project that I was to pick up. I was assigned the job of sequencing a tRNA that was involved in bacterial cell wall biosynthesis. In 1969, only a handful of tRNAs had been sequenced previously, mostly by chemical techniques introduced by Holly and his contemporaries. However, within a few months and much reading, I decided that a new method, being pioneered in [Fred Sanger](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1958/index.html)‘s lab in Cambridge, was much better. In late 1970, I had succeeded in making enough pure tRNAGly to start sequencing and set off for a one month sojourn in Cambridge to learn the techniques. What a wonderful time! I don’t remember sleeping, but I do remember the excitement of meeting Fred and the other famous researchers, many of whom had featured in Kendrew’s book. This was a heady experience that validated my decision to be a molecular biologist.  On my return to Harvard, my small sequencing operation was the first in the Boston area and many researchers came to learn the techniques. My own sequencing was successful and I managed two Nature papers during this postdoctoral period. When it came time to leave Harvard I wanted to return to the UK and applied for a job in Edinburgh. In the meantime, I was approached by Mark Ptashne, who told me that [Jim Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) (“the” Watson) was looking for someone to sequence SV40. I had not met Jim previously and I was over-awed when he offered me the job after a 10 minute meeting, during which I mainly listened! It was a challenging project made all the more exciting by Jim’s description and his offer of a good salary, money to support a lab and all necessary set-up money. With a month to decide and no word from Edinburgh, I decided the offer was too good to turn down. In September, 1972, I moved to Cold Spring Harbor.  Earlier in 1972, I attended a seminar at Harvard Medical School given by [Dan Nathans](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1978/index.html). He described an enzyme, Endonuclease R, that could cleave DNA into specific pieces. This was to shape much of my subsequent research career. Sanger had developed RNA sequencing because there were plenty of small RNA molecules to practice on, but no suitable DNA molecules. I realized that Nathans’ restriction enzyme gave an immediate way to isolate small DNA molecules. Surely there must be more restriction enzymes with different specificities. DNA sequencing seemed within reach and I was exhilarated. Upon moving to Cold Spring Harbor, I set out to make preparations of Endonuclease R and the few other restriction enzymes known at the time. We also began a systematic search for new ones. I also made some DNA, since I had never worked with it before!  A key factor in our restriction enzyme success was a highly talented technician, Phyllis Myers, who joined me in 1973. She became the keeper of our enzyme collection and a valuable resource to scientists around the world. We constantly sent samples to other researchers and were inundated with visitors. Every meeting at Cold Spring Harbor brought a few people carrying tubes of DNA to see if we had an enzyme that would cut it. Three quarters of the world’s first restriction enzymes were discovered or characterized in my laboratory. I made a lot of friends in those days!  Plans to sequence SV40 DNA were abandoned shortly after reaching Cold Spring Harbor. Instead we turned our attention to Adenovirus-2 DNA. Ulf Pettersson had brought this system to the laboratory shortly before my arrival and it seemed a good model system because it was similar in size to bacteriophage lambda, where many spectacular advances in prokaryotic molecular biology had taken place. We began to map the DNA. Similar work was being carried out in Joe Sambrook’s lab at Cold Spring Harbor and eventually led to the only joint publication I have with [Phil Sharp](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1993/index.html).  In 1974, Richard Gelinas, whom I had first met at Harvard, joined my laboratory to characterize the initiation and termination signals for an Adenovirus-2 mRNA. The idea was to sequence the 5′-end of an mRNA, map its location on a restriction fragment, and then sequence the upstream region. This would be the promoter. Shortly after beginning the project, mRNA caps were discovered and we developed an assay for capped oligonucleotides. All seemed well until we came up with the startling finding that all late mRNAs seemed to begin with the same capped oligonucleotide, which was not encoded on the DNA next to the main body of the mRNA. We had excellent biochemical evidence for this, but real proof was elusive. In March, 1977, I hit on the right experiment to show that our proposed split structure for Adenovirus-2 mRNAs was correct. Louise Chow and Tom Broker, two talented electron microscopists, agreed to collaborate with us on the crucial experiment. We hoped to visualize the split structure by hybridizing an intact mRNA to its two different coding regions. Based on a guess about the location of the coding region for the 5′-end, we made appropriate DNA fragments. The reason for our guess turned out to be wrong, but luckily the fragment worked anyway! Finally, by direct visualization we could see the split genes in the electron microscope.  Our own work turned to an analysis of the sequences involved in RNA splicing. Joe Sambrook and Walter Keller cloned the common leader sequence at the 5′-end of late Adenovirus-2 mRNAs and Sayeeda Zain in my lab sequenced it. Later we undertook the complete sequence of Adenovirus-2 DNA. This required a lot of computer software development and I was fortunate to have Richard Gelinas and Tom Gingeras spearheading this effort. In 1978, this was still a relatively new activity and not considered particularly biological. I had trouble convincing Jim Watson that computers were essential for modern biology and for several years we operated remotely through Stony Brook University. Eventually, I managed to get funding from NIH (Phil Sharp was chairman of a site-visit team that reviewed this grant) and we are still active in this area. My most recent work has been in the area of DNA methylases as outlined in the Nobel Lecture.  In 1992 I moved to New England Biolabs, a small private company of 150 individuals making research reagents, most notably restriction enzymes, and carrying out basic research. In 1974 I had tried unsuccessfully to convince Jim Watson that Cold Spring Harbor should start a company to manufacture and sell restriction enzymes. He declined, thinking there was no money to be made. Soon after this I met Don Comb, the president and founder of New England Biolabs, who had a small basement operation going with himself, his wife and one technician. They were about to start selling the first restriction enzyme. I told him about our rapidly growing collection and was appointed their chief consultant. I am now joint Research Director with my good friend, Ira Schildkraut.  The main theme of my work in biology has centered on the belief that we must know the structure of the molecules we work with if we are to understand how they function. This means knowing the sequence of macromolecules and cataloguing any modifications such as methylation. For proteins, 3-dimensional structure and post-translational modification are crucial. This latter area is a target for my future work. Throughout my life in science I have been fortunate to have friends and family who will bring me back to earth and remind me that there is much in life to be savored besides Science. I enjoy music very much and love to collect and play games, especially video games. I am indebted to my wife Jean, and my children, Alison, Andrew, Christopher and Amanda who have been a source of great joy and comfort. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0573** |
| Interview |  |
| Q64 | Three days ago, there was a major announcement, a major event in science, you could say, a joint announcement by groups in the United States and the United Kingdom about, I would say, a high-quality DNA sequence of the entire human genome and the significance of this event was underlined by the fact that two heads of state, Bill Clinton and Tony Blair, had joined the press conference. We are happy to have here among us two Nobel Laureates in Physiology or Medicine, Professor or Doctor Richard Roberts and Hamilton Smith who have been involved in various capacity in the human genome project. In fact, one of you was actually present at the White House during this press conference. Would you like to take it on from here? |
|  | Hamilton Smith: I’m actually an employee of Celera Genomics, which is a company in Rockville Maryland that has been single-handedly determining the human genome sequence in what many have called a race with the rest of the world, with the public efforts which carried on in the United States, England, Germany and Japan and I think some other countries. The White House ceremony was an attempt to get a cooperation between the public effort and the private effort, not a collaboration but a cooperation where we would agree to not say bad things about each other’s approaches or data or personalities and that we would try to do joint publications in a scientific journal, sometime near the end of the year 2000. Not papers that have joint authorship between the groups but separate publications where we present our accomplishments. I think it’s been a very good thing actually to do this, it takes the focus of the press coverage away from the warring parties and gets it back to what’s really important, namely getting the sequence and getting it out to the public.  The ceremony itself, President Clinton gave a short talk of about 4-5 minutes and then, by a TV hook-up in England, Tony Blair came on and said a few words in his best oratorical style and then President Clinton introduced briefly Francis Collins, who’s head of the public effort in the US and of course there were words said about the DoE part of the effort and there were nice things said all over the place. It was really a pretty good show and then Craig Venter was the last speaker. I was wondering when he went up to the microphones, whether there was anything left to be said but Craig, I think, handled this situation extremely well and got across how Celera fits into this accomplishment. So, we had a press conference afterwards. I think it was not only a truce between the public and private efforts but also an announcement that each of the groups had achieved their goals. The public human genome project announced that they had completed a working draft of the genome which represents about a 90% coverage of the genome but without a complete assembling of the genome and Celera announced that they had a 99% random coverage of the genome with an assembly of those sequences, so that genes are laid down linearly along the chromosomes. |
| Q23 | Now that we have two independent groups who have come to an agreement about the general structure of the human genome, maybe you are able to answer the question, how many genes are there in the human genome. It’s a question you get when you lecture in this field and I’ve heard widely varying figures so, now if you get the question, what would your answer be? |
|  | Hamilton Smith: I think at this moment we still are in considerable doubt, but at Celera we’re also sequencing the mouse genome which will be complete sometime before the end of the year, to the extent that we can compare the mouse sequence to the human sequence. The protein coding regions of the mouse and human are sufficiently similar that they can be aligned, whereas the so called junk DNA, the 97% of the genome which doesn’t code for …  Richard Roberts: You’re talking about this stuff I discovered, are you?  Hamilton Smith: Yes, something like that.  Richard Roberts: The junk.  Hamilton Smith: Yes, the junk.  Hamilton Smith: … is more dissimilar, so it should be possible to simply read the two genomes in six frames and with high probability overlap the protein coding regions and get a fairly precise count of how many genes are present and that’s really the strategy that we’re pursuing. We have the mouse sequence, or we will have the mouse sequence and we’re the only ones in the world that will have it, so I think Celera will have the most accurate annotation. |
| Q23 | Because people are betting on the number and there is a need for an authoritative answer to this question from the gambling point of view and from the human centred views that we entertain. To drive these large projects, the human genome project, obviously there have been precursors, people have got news from physics now that they are enormous projects, big physics and you now have big biology coming around, so once the human genome project has been completed, how will we proceed? I think we would agree that the most important thing now is to find out how the genome functions and we now enter then a type of research where we want to study the ultimate products, the proteins. Since there are many ways in which you can process the information from the DNA and the genome, at the RNA level, there are many more proteins to be found. This field of studying the proteins made in biological systems is called proteomics, so do you see any such big proteomics coming along and what can be done in terms of technology to speed up the analysis of the much larger number of proteins than the number of genes? |
|  | Hamilton Smith: I mean, I can say pretty much what we are planning at Celera. Celera I think is unique in its ability to do very large scale surveys. We don’t like really doing anything unless we can do 100,000 a day of whatever it is, so this is a way Craig Venter thinks and it allows us to do things that can’t be done easily in the university setting or in most other companies. What we’re planning of course is to move into proteomics using new instrumentation from PE Bio systems, mass spectrometers that can analyse tens of thousands of samples per day of protein. The plan would be to, the big interest initially I think is to see the spectrum of proteins that are being made in specific tissues, normal or diseased tissues, cancer, whatever. The plan would be to separate these proteins from say a cancer tissue on two-dimensional gels and then each single protein spot on the gel would be analysed in the mass spectrometer. Essentially hit by a laser blown into fragments of the protein which would then be matched with the genomic sequence and by computer, one should be able to predict the protein peptide spectrum that you would get for each of the genes in the human genome. Let’s say there are 50,000, so that we would get a virtually instantaneous identification of the particular gene product for each of the spots and we could say then that a given tissue is expressing certain genes and we form a database of this kind of information and again we sell that to our subscribers. This is sort of a first step of something that we can easily see ahead that we could produce this. I don’t know where we’re going beyond that but maybe Rich could.  Richard Roberts: The real problem with proteomics is that much of the technology that you need to relate function back to the gene is not in place at the moment, so one issue is well what is being expressed, how much is being expressed if we look at particular tissues, if we look at the brain, if we look at skin, if we look at liver, what kinds of proteins are taking place? At the moment we are able to look at what messenger RNAs are taking place, but we know also from other experiments that the amount of protein very often does not match the level of RNA, so we need both to be able to look at RNA and to look at the protein. One way to look at the protein is to use the kind of technology that Ham just talked about. |
| Q65 | You made a point in one of the sessions at this meeting that once you study microbial genomes and there is a project called the minimal genome project which tries to define what’s the minimum number of genes. Wouldn’t such a system be the most suitable in finding out the function of various genes, because the human with this much larger genome and many genes is incredibly more complex? |
|  | Richard Roberts: Right. I think there are two separate issues, one issue relates to what is it that really makes life, what do you need, what is the minimum set of instructions that you need to make a living cell? And one way to do that is to take the very smallest cell that we know that is free living, as Clyde Hutchison is doing, and try to remove the genes that look as though they’re not necessary, get down to the minimum set, understand that in completion. Then one will at least know what is the minimum thing you need for life but that’s likely to be less than 500 genes and those 500 genes are a small set of what is present in a human cell. So, I think what will come from say the minimal genome project will be a working definition of kind of what is the minimum of life but there’s so much more to life than that. We need to know what is the precise biochemical function of each of the gene products, what reactions does it catalyse? That is something that for most proteins is not easy to do and we’re working ourselves at the moment on a bunch of proteins that are present in every organism for which the genome has been sequenced so far.  We think that this particular protein transfers methyl groups from S-Adenosyl methionine onto something, but we don’t know what and it’s not easy to find out, it’s not easy to prove that. But it is an interesting protein, it’s present in every genome but we don’t know what it does, no-one has stumbled upon it by genetics or by biochemistry yet, to know what it does and there are many such proteins. In the human genome, there are going to be thousands of these proteins for which we need to define function so what we need is to find high throughput ways, fast ways in which we can get clues to function. One high throughput way is to use computation to try to do that, so you look through the protein sequences, you try to find the little protein sequence motifs that in other proteins we know interact with ATP or they interact with DNA or they’re RNA binding proteins or whatever, so this can give you a clue, but you need to do the biochemistry afterwards to show that the clues that were given were correct or not and we don’t have good methods for doing that at the moment.  Hamilton Smith: Another approach to the minimal genome is the synthetic approach which I think is intriguing, creating “life” in the laboratory. The idea there would be again working with the mycoplasma genitalium is sort of the basic tools or parts for it. Having some idea from the other studies as to what genes are essential, one could actually make a synthetic chromosome that contains the set of proteins that have been identified as essential and then put that synthetic chromosome into a cell from which the natural chromosome has been removed and then see if you get something that will grow in the laboratory. Of course it probably won’t work the first time, maybe not the 100th time either, it could be somewhere to cloning Dolly and in the beginning you had to do hundreds of them before you got a successful attempt. But it would be a spectacular event if one could create a new genome.  Richard Roberts: I guess, when you start to think about the real importance of microbiological research, within the context of the human genome, the methodology that will need to be developed to understand how something as simple as mycoplasma genitalium work is going to methodology that can be applied to the human genome. So if we can learn to do this thing properly and if we can learn to do it in a fast manner for the small bacterial genomes, where in principle everything is a lot easier, we should be able to apply that methodology to these much more complicated systems too and in the meantime of course, we will find out much about what is really important in order to make life. What is it about these proteins and these genes that really makes something living as opposed to just a collection of chemicals in a test tube. |
| Q16 | If we look at the biomedical benefits of the DNA sequence of the human genome, I’m sure when [Jim Watson](https://www.nobelprize.org/prizes/medicine/1962/watson/facts/) went to congress, he had many ideas on what the benefits would be and tried to convince the congress and I noticed also that Bill Clinton mentioned cancer, the cure of cancer would be something that would be following after the sequencing. How do you see the immediate consequences in the biomedical field of our knowledge of the human genome sequence? |
|  | Hamilton Smith: I don’t think I can foresee all of the benefits or consequences, we’re going to have to work into it gradually, but I it seems clear that it would facilitate much of the work that’s going on. A lot of work over the past few years has gone into hunting for genes in the genome and sub-cloning them and so on and so forth. This should short circuit all of that, I mean you should be able to in many cases find a gene or several duplications of the gene in the genome and proceed from that sort of jumpstart. I think an example would be, there are several groups of proteins that have demonstrated therapeutic benefits, for example the interferons and already we have an example by the genome sequencing of a new interferon which was previously not detected. With the whole genome you can look and often find members of a protein group that you didn’t know about, so these are new potential products. We could discover new epogen type proteins as well or growth factors that can stimulate certain tissues simply by analogy to ones that are already known. |
| Q16 | Will it be possible to sequence a genome of individuals in the short time, in such a short time that it would be important in medical practice, in designing the therapy one is planning for a certain disease? |
|  | Hamilton Smith: Not with current technology, it’s too expensive. Eventually I think that we will need some sort of a physical method for single molecule sequencing. Once that arrives, we might be able to tackle the whole individual, but one of the big areas of effort now is large scale genotyping using various arrays of genes. My dream would be to be able to take a single drop of blood from an individual and within a few hours, determine 100,000 single nucleotide polymorphism mutations in that individual, I shouldn’t say mutations but indifferences in that person’s genome. In other words develop an immediate genotypical profile for an individual that could be used in judging what treatments would be best for that individual or what possible genetic diseases that person might encounter in life. I think that’s coming, probably in the near future.  Richard Roberts: I guess the real point that you’re getting at here is that one would like to take individuals and get some idea of their genetic makeup. One way to do that is to get the complete DNA sequence, but in fact you can get a lot of information without looking at the complete DNA sequence because as a result of these things called single nucleotide polymorphisms, we know that approximately every 300 bases or so, along with human genome, there is a region that varies, quite often from one individual to another. By just looking at those regions, in essence just sampling a one three hundredth of the genome instead of looking at the whole thing, one can actually tell a lot about the genetic propensity of various people.  For instance, we know that there are genes that if they go wrong, if they have some particular polymorphism, they have one sequence as opposed to another, that that leads to problems and the first classic example of this was sickle cell haemoglobin where we knew that a single base change in the DNA sequence for haemoglobin rendered the haemoglobin not quite so effective. This was a mutation that had been well kept within the human population in Africa because when you had heterozygous for this condition, when you had one sickle cell gene and one normal gene, you had resistance to malaria which, if you live in Africa, this is quite an important thing to have. That has been maintained in the population, even though the selection no longer applies among blacks who have moved from Africa into the US or into England or into Western Europe and they maintain this mutation because evolution is slow, it takes a long time for it to get out of, and there are many diseases for which this kind of thing is true. |
| Q34 | You mentioned the probability of finding an SNP /- – -/ that the human genomes that have been sequenced a body, say a single group and then the sphere group have been different and can you already now see evidence of SNPs if you compare your sequences with each other? |
|  | Richard Roberts: Yes.  They shouldn’t be entirely equivalent, I would imagine.  Richard Roberts: No, basically what’s happened so far is that the main sequence that’s come from Celera is from one individual. There are other individuals who are being sequenced at Celera at a level sufficient to identify single nucleotide polymorphisms. The public human genome project, they have sequenced many individuals, a much larger number than Celera have been dealing with and so there are single nucleotide polymorphisms that are apparent within their data already and there is in fact something called the SNIP consortium which are a group of labs who are specifically looking for single nucleotide polymorphisms. These have been funded by both government agencies and by commercial companies and this data is all being placed in the public domain, so the answer is we know of a lot of snips already but we don’t know enough to do a complete genotype on someone.  Hamilton Smith: Nor do we know which of those snips really are clinically relevant, I mean the large proportion of them are probably pretty neutral changes. We don’t know how many would be medically significant or genetically significant.  Richard Roberts: But this is what will come out of the next stage of the human genome project where one tries to assign function and identify the genes, because many of these we know that these are important for this disease or for that, we will probably find homologs of some of these genes and we don’t know whether they’re important yet, so that will need to be tested. In many ways, we’re really at the beginning of the human genome project, not at the end, so even though we have announced we’ve gotten through this first stage, it very much is a beginning. Biology has undergone this revolution in the last few years where it’s gone from being really an observational science, in which people have been looking at phenomenon and trying to understand them and trying to figure out what was going on, to become a hard science like chemistry or physics where we can really now look at a complete genome and put some bounds on the problem. If we want to explain how a small bacterium works, we can say we’ve found there are 4,000 genes or 5,000 genes, we need to explain this organism in term of these 5,000 genes, if we’re going to do a genetic experiment in which we change one of these genes and we know what to look for, we know we have to look and see what happens to all of the other genes, in order to begin to understand. I think we’re very much at the start of biology, which is a wonderfully exciting time for us, you know I mean this is the time I would love to be a graduate student again, this is the time to be a graduate because there are many discoveries to make, many more Nobel Prizes coming out of this field.  Hamilton Smith: In science, one tends to go from simple to complex and then hopefully back to simple again. We’re in the complex phase right now. |
| Q12 | But now, if you are a graduate student today looking for what to do during a career in biology and you see these large enterprises doing all the sequencing, so all the sequences will be available, you can’t get the PhD out of sequencing anything as an individual. |
|  | Richard Roberts: We would hope not.  So your supervisor buys a licence maybe, to have the detailed sequence for a certain genome, so does that leave the individual graduate student then with trying to define the role of specific proteins or signalling systems?  Richard Roberts: That’s certainly one possibility. Basically what you have is this enormous textbook, except that instead of being a textbook with diagrams and clear headings telling you what everything is, you’ve got a textbook, it’s full of words but we don’t know what the headings are and we don’t know how to put in the diagrams to explain how this little bit relates to this little bit. This is for the graduate student to start to work out.  Hamilton Smith: Each gene with an unknown function is a PhD degree, if you can figure it out. |
| ID | 0574 |
| Biographical | A sense of place was and remains an important part of my life. I was born in a rural community in the northern hill country of Kentucky. My earliest memories are those of a child playing around the house on our family farm, located in a bend of the Licking River near McKinneysburg. My mother, Kathrin Colvin Sharp, had grown up in that same house and her family had been part of this community for many generations. My father, Joseph Walter Sharp, grew up nearby within walking distance of the nearest town and county-seat, Falmouth. Both parents came from large families and I was surrounded by grandparents, aunts, uncles, siblings and cousins.  My formal education was entirely in the public schools of Pendleton County: McKinneysburg Elementary, Butler Elementary and High School and Pendleton County High School. Even though my studies never interfered with sports or fun, I managed to gain an appreciation of math and science.  All through my childhood, my parents strongly encouraged me to attend college. With that in mind, they taught me to save my money for college tuition, and, even more important, they allowed me to earn it by raising cattle for the market and growing tobacco. The rural background of my childhood made me feel more comfortable attending a small institution in a familiar environment. Therefore, I entered a small liberal arts school, Union College, in the foothills of eastern Kentucky. Union is in Barbourville, the county-seat of Knox County, and in those days it was one of the gateways for the youth from the mountains in the eastern part of the state to emerge into a larger world. While at Union, I majored in chemistry and mathematics and decided that I wanted to continue to study and learn about science, particularly chemistry. I also met and married a lovely girl from New Jersey, Ann Holcombe (Sharp).  A young professor at Union, Dr. Dan Foote, became a good friend and encouraged me to apply to the Department of Chemistry at the University of Illinois. This old and distinguished department must have recognized some hidden promise as I was offered a fellowship and soon began graduate studies under Victor Bloomfield in physical chemistry. Victor was an excellent mentor as he encouraged both my scientific as well as cultural growth. He provided funds for my participation in national scientific meetings and broadened my perspective on society and culture by being a long-haired liberal, well-read and artistic friend. Fortunately, I was deferred from the Vietnam draft for a number of years and was able to finish graduate school. My thesis dealt primarily with the description of DNA as a polymer using statistical and physical theories. My attempts at experimental science at this stage were juvenile. In spite of my youth on the farm, I was never very skilled in manual tasks; in fact, I soon lost interest in any complex “hands on” manipulations.  The 1966 volume of the Cold Spring Harbor Symposium on *The Genetic Code* stimulated my interest in molecular biology and genetics. A subsequent letter to Norman Davidson at the California Institute of Technology resulted in an offer of a postdoctoral position in 1969 and my immersion into a vibrant research program in molecular biology. Ron Davis, a graduate student in Norman’s lab at the time, had previously developed the heteroduplex method for visualizing deletions in phage genomes with the electron microscope. Jerome Vinograd in an adjacent laboratory had discovered the superhelical structure of animal virus genomes. In this environment, I began the transition to experimental molecular biology by using the heteroduplex method and electron microscopy to study the structure of plasmids of the sex factors and drug resistant factors of bacteria. I was particularly interested in how sex factor plasmids acquired genomic sequences from the bacterial chromosome. We found that both sex and drug resistance factors contained transposable elements. This experience taught me many things, including the power of novel methodology and how a simple experiment can transform the understanding of an important problem.  At the end of my stay at Caltech, I opted to extend my postdoctoral period and begin to study the structure and pathway of expression of genes in human cells. The expression of genes of animal viruses with DNA genomes was the only experimentally approachable system at that time, and this led me to a further postdoctoral year at Cold Spring Harbor Laboratory under the mentorship of [Jim Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html). Here, I entered a close-knit scientific commune of extremely talented people who lived and worked together in an isolated environment for nine months, and then were immersed in a continuous scientific meeting for the remaining three summer months.  At the Lab Joe Sambrook, a staff member, I, and others used hybridization techniques to map sequences in the simian virus 40 genome that were expressed as stable RNAs in both infected cells and oncogenic cells transformed by this virus. These were important results for understanding the biology of this papovavirus and helped move the laboratory into a very rapidly advancing field of research – the molecular and cell biology of tumor viruses. Luckily, or perhaps by design at a higher level, Ulf Pettersson, an expert in the growth of human adenovirus who had done graduate studies with Lennart Philipson in Uppsala, Sweden, was a fellow postdoctoral associate and my office mate at Cold Spring Harbor. Adenoviruses are common causes of respiratory and other types of infections in man; however, when infected into newborn rodents, they can cause tumors. The high levels of both replication and viral protein expression made the growth cycle of this virus ideal for the study of gene structure and regulation. Furthermore, the then recent discovery of restriction endonucleases offered the prospect of fragmenting the viral genome of 35,000 base pairs into tractable units. Ulf, I, and others generated the first restriction endonuclease maps of this virus, and Dr. S. Jane Flint and I began to analyze the regions of the genome expressed as mRNAs in both productively infected cells and in adenovirus transformed cells. This was an exciting period in the molecular biology of adenovirus with the discoveries (a) that only one specific fragment of the genome, the E1 region, was responsible for oncogenic transformation; (b) that restriction endonuclease length polymorphism could be utilized to generate genetic maps; (c) the mapping of specific genes on the viral genome; and (d) generation of a viral map of sequences expressed as stable RNAs.  [Salvador Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html), the Director of the then recently established Center for Cancer Research at the Massachusetts Institute of Technology, called in 1974 to inquire if I would be interested in a position at the Center. After a brief visit to MIT I accepted. Fortunately, I was assigned laboratory space on the 5th floor, which was shared with [David Baltimore](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html), Nancy Hopkins, Robert Weinberg and David Housman. Salva was a visionary who protected his young faculty from unnecessary interruptions, thus allowing their research programs to flourish in an ideal scientific environment. He was also a role model for how a scientist could shape and lead a community. That summer, Jane Flint moved with me to MIT and we continued our analysis of adenovirus transcription, focusing on quantitating the levels of RNA from all parts of the genome in the nuclear and cytoplasmic compartments of the cell. We found that the nuclei of cells productively infected by adenovirus contained abundant sets of viral RNAs which were not transported to the cytoplasm. We speculated that these long nuclear RNAs were processed to generate the cytoplasmic mRNAs. This stimulated our interest in comparing the relative structures of nuclear precursor RNA and cytoplasmic mRNA from the adenovirus genome. We were joined in the latter part of these studies by a postdoctoral fellow, Dr. Susan Berget. For Sue, these studies were the beginning of a much more interesting series of experiments which form the first part of the lecture.  As mentioned above, Ann and I were married in 1964 while still undergraduates at Union College. Our three daughters arrived on a schedule which approximated a seven year itch: Christine Alynn was born in 1968, while I was still in graduate school, Sarah Katherin was born in 1974, just before we moved to New England, and Helena Holcombe was born in 1981. Ann teaches a preschool class in Newton, Massachusetts, the town we have made our home since moving from Cold Spring Harbor. My family and are deeply enamored with New England. We enjoy its rural towns, coastal beauty, and the changes of seasons.  Through the years at MIT my environment has remained relatively constant, though changes have occurred. David Baltimore and Robert Weinberg left the Center in 1983 to found the Whitehead Institute, which is associated with MIT. Salva retired from MIT in 1985 and I assumed his position as Director of the Center for Cancer Research. In 1991, I relinquished the Directorship to Richard Hynes and became the Head of the Department of Biology. The development of biotechnology has both enriched and complicated my work. [Walter Gilbert](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1980/index.html) of Harvard and I, along with a number of European colleagues, founded the biotechnology company Biogen in 1978 in Geneva, Switzerland. This organization and the friends who have worked for it have remained an important part of my life since.  My collaborators over the years have been: (listed in alphabetical order) A. S. Baldwin, S. M. Berget, A. J. Berk, K. Berkner, B. Blencowe, M. A. Brown, S. Buratowski, C. Carr, R. W. Carthew, C. Cepko, D. Chang, D. Chasman, L. A. Chodosh, G. Chu, R. G. Clerc, J. D. Crispino, D. J. Donoghue, A. Z. Fire, D. E. Fisher, S. J. Flint, M. Garcia-Blanco, A. Gil, S. Gilbert, P. J. Grabowski, H. Handa, U. Hansen, S. Hardy, S. Harper, T. Harrison, M. Horowitz, P. S. Jat, R. Kaufman, J. Kim, R. Kingston, J. Kjems, T. Kobayashi, M. M. Konarska, T. Kristie, A. I. Lamond, F. Laski, J. LeBowitz, K. LeClair, F. Lee, I. Lemischka, A. M. MacMillan, R. Marciniak, P. McCaw, R. Meyers, C. Moore, M. Moore, M. Morton, M. Murata, R. Padgett, J. Parvin, J. L. Pomerantz, C. Query, M. E. Samuels, J. Sedivy, S. Seiler, B. Shykind, H. Singh, H. Skolnik-David, M. Timmers, A. Virtanen, J. Weinberger, and Q. Zhou.  In 1980, Dr. Sharp received both the Eli Lilly Award in molecular biology and the U.S. Steel Award from the National Academy of Sciences. His awards are too numerous to list but some include MIT’s James R. Killian, Jr., Faculty Achievement Award (1993), the John D. MacArthur Professorship (1987-1992), the first Salvador E. Luria Professorship (1992-), the New York Academy of Sciences Award in Biological and Medical Sciences, the General Motors Research Foundation Alfred P. Sloan, Jr., Prize for Cancer Research, the 1988 Louisa Gross Horwitz Prize, the 1988 Albert Lasker Basic Medical Research Award, the 1986 Gairdner Foundation International Award, Canada, and the 1980 Dickson Prize from the University of Pittsburgh. In 1985, he was the Harvey Society Lecturer and on May 4, 1991, he received the honorary degree of Doctor of Humane Letters from Union College, his Alma Mater. He is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, associate member of the European Molecular Biology Organization and Fellow of the American Academy for the Advancement of Science, the American Philosophical Society, the Institute of Medicine of the National Academy of Sciences, and a member of the editorial board of the journal *Cell*. He is co-founder and Chairman of the Scientific Board of Biogen, Inc., and member of its Board of Directors.  Dr. Sharp has a distinguished record of public service, which partially includes having served as a member of the President’s Advisory Council on Science and Technology, as co-chairman of the Director of NIH’s Strategic Plan, as a member of the Committee on Science, Engineering, and Public Policy (COSEPUP), as a member of the Search Committee of Director, National Center for Human Genome Research, and more recently, as a member of the Search Committee for the Director, Office of AIDS Research, NIH. His career publications in peer reviewed and other journals are over 255 |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview  Interview | 0574 |
| Q56 | You start your autobiography writing these words “A sense of place was and remains an important part of my life” and I wanted just to ask you what did you mean by this sentence. |
|  | I mean by the sentence that I have always found that I am comfortable in identifying myself with certain special places. I grew up on a farm in Kentucky, a family farm, a small farm, and I identify with that place. I go back every year and it’s always relaxing and home. I worked at MIT for 30 years almost and it’s an outstanding institution, does tremendous research and education and I’ve been in the same office all that time. It’s a place, I go there, it’s one of those pleasant places that I have. So, I tend to identify with certain places and enjoy working there. |
| Q56 | But MIT’s very far away from a farm. |
|  | Very far away from the farm and very different backgrounds, very different places and histories, but both special in the sense that one place it’s special, that was my place and then at MIT it’s a special place to do science and engineering. It’s a spectacular research institute. |
| Q43 | So how come you did this big step from the farm to this institute? |
|  | It was a step driven by curiosity. I clearly did not want to spend my life being a farmer. I enjoyed the time when I was young, but it wasn’t intellectually stimulating and the world was very confined and as I looked out on the world and thought about what I would like to do, I would like to continue learning and science gave me the opportunity to continue learning, even today. As I flew across the Atlantic Ocean I was taking research papers written by colleagues in the field and learning from them and it’s just terribly enjoyable being able to understand in detail how other people think and how problems unfold and adding your own little bit to it and creating something new and that’s a wonderful life. It’s just an enjoyable way to spend one’s time. |
| Q33 | When you look backwards can you see when one could, for the first time, see a Nobel Prize winner in the future in you? |
|  | Oh, I had no idea about a Nobel Prize. When I was about 10 or 11, I started getting fascinated about science and mathematics and the area of study that I excelled at, other people admired my ability to do it and then as I rose through science and at each stage did well and moved to MIT I knew I was in a research community that was absolutely at the forefront of what was going on in the world and I had great colleagues in my environment to talk to about, you know, cutting edge research and there I began to do research that I knew was important. Now, there’s many, many great scientists out there who cannot be blessed by a Nobel Prize; there just aren’t enough around and never did I think I was going to necessarily see a Nobel Prize but I knew I was doing very good science and enjoyed that and that’s what life is about, it’s doing good science. If you’re a scientist that’s what you want to do and have people appreciate it. It’s wonderful when people appreciate it. |
| Q11 | Yes, and this was genetics that you were in? You were two that got the prize, Richard Roberts. |
|  | [Rich Roberts](https://www.nobelprize.org/prizes/medicine/1993/roberts/facts/) and his group worked at Cold Spring Harbor and my group worked at MIT and in parallel we made this discovery of the split gene structure. |
| Q42 | So you worked day and night? Was it the big race there? |
|  | We worked day and night. We didn’t actually know at the time we were both on the same thing. It was at the end when we started to talk to people about this new discovery that we realised that there was another lab who was talking about a new discovery too and as we got together and compared our results it was clear that we had come to similar conclusions at about the same time. |
| Q55 | The last announcement about HUGO, the human genome project, also revealed that we have much less genes that you were hoping for? |
|  | I mean from a biologist’s point of view the fewer the better because we would like to understand how those genes function in the physiology of what makes us work as a human being and the estimate at the end of the day was that there are 35,000 genes.  Instead of 100?  Phillip Sharp: I use the term estimate because of this mosaic gene split structure, this split gene structure, it’s very difficult to identify those little bits of information that are genes.  Hidden in the garbage?  Phillip Sharp: They may be hidden in the garbage. There could be many other genes but even with the genes we know, because of this split gene structure, that a gene is split up into 10 or 20 different pieces, we now know that as the gene is expressed, different pieces of that gene can be joined together to make the protein, and this gives you the ability to use combinations in different cells in the body. For example, there’s been recently described the gene in the brain of a fruit fly, a simple fruit fly, one gene, and that gene has the ability to be expressed in 38,000 different proteins.  Because of the split genes?  Phillip Sharp: The split genes and alternative splicing, 38,000. There’s more variations in the way that gene can be expressed than there are genes in the whole genome. When we look at 35,000 genes we know more than half of them are alternatively spliced. We look at a complexity that’s much larger than 35,000. We’re looking at complexities of hundreds of thousands of possible variations in gene expression that could give rise to the complexity that you see in the different cells and different functions of our bodies. So, though we have what is thought to be 35,000 genes, we know that those 35,000 genes can generate a great deal more complexity than just 35,000 genes. But, even with 35,000 genes, if you take one here and one there and one there and one there and mix them in different combinations at different times you can make an enormously complex machine. So, we have a lot to understand yet in biology. The genome is not the end of biology. The genome is actually just the beginning of biology. It is going to set us on a whole new plane or rate of discovery that will make it fascinating for decades to come. |
| Q34 | So what is the next challenge in biology do you think? |
|  | The next challenge in biology. Well, there’s so many challenges, and so little time. The challenges of how we are formed. We’re making great progress on how development of a complex organism such as ourselves, with skin and hair and all these other different tissues develop from the 35,000 genes. We’re going to understand that and that’s going to underwrite a lot of development of new drugs and treatment for diseases but then we look at the real challenge and ultimate challenge. There’s nothing that a human biologist would like to study more than the brain, the human brain. It’s a fascinating organ. |
| Q34 | So this is a new field you’re moving into? |
|  | It’s a new field I’m moving into and I’m leading the development of institute at MIT but if you think about that as an area of science first you’ve got the biology and physiology and how the brain works. I mean that’s a fascinating substance unto itself but then as we understand more about how the brain functions and what’s the physiology and part of emotion and intuition and all these other things. It has implications for culture, it has implications for communication, it has implication for education, it has implications for economics. It’s just a wonderful interface between biology and the rest of society and culture. So I see, as one of the great challenges of the future, developing a more complete understanding of how the brain functions and how we modify it by our educational cultural experiences and use that to do creativity and that’s a fascinating field and I think young people are going to flock to it, it’s going to change us, the way we view ourselves, it’s going to change the way we view culture and history. It’s a wonderful field and I’m hoping by taking the responsibility of being director of a new institute at MIT to expand that field at MIT and get a lot of bright young people working on it and enthusiastically making progress. |
| Q34 | You’re also involved in a biotech firm since very long time ago. Biogen. |
|  | Biogen. I was very fortunate early on. I entered science just at the time of recombinant DNA so the early stages of my career recombinant DNA developed that I assume in my research programme the manipulation of DNA and this was a new tool and frequently when a new tool arrives in science it changes science and it certainly was the case for recombinant DNA. It gave us the ability to take DNA from different species and put them together. |
| Q34 | When was it? |
|  | It was in the 1975-76-77 period in which that technology really became quite widely spread. I’d learned about it in the early 1970s and participated in it but then in 1976-77 we knew we had this technology, we knew we could make new pharmaceuticals and that they would benefit man and a group of scientists, myself and [Wally Gilbert](https://www.nobelprize.org/prizes/chemistry/1980/gilbert/facts/) out of the US, Charles Weissmann and Bernard Mach out of Switzerland, Heinz Schaller and Peter Hofschneider out of Germany and Ken Murray and Brian Hartley out of England all got together and stared a company with a bunch of capitalists who gave us money to do it and the company’s called Biogen and it’s still a very significant biotech company. It’s located in Boston and there are some remarkable things that Biogen’s done. It holds the intellectual property patents for hepatitis B vaccine and most of the people in Europe and in the US and many parts of the world have been vaccinated with that vaccine. It holds the patent for alpha interferon and it’s one of the major treatments for hepatic infections from hepatitis B and C and it’s really changed a lot of people’s lives and it now is selling the major drug for multiple sclerosis called avonex. The first type of drug made interferon and several companies have it and Biogen’s the market leader, but it’s changed people’s lives because it gives a significant fraction of people better control of that disease, which is a horrible disease. I’ve been fortunate to being able to touch many people’s lives by having participated in developing a technology and then helping translate it into the private sector and then have it used to improve the quality of people’s lives around the world. So that’s been a great experience and I’ve learned a lot from that experience and how business works, how societies work and all those sorts of things and it was a tremendous time in science. |
| Q57 | In the context of genomic research there has been quite large criticism against commercialisation of science. What do you think about that? |
|  | In the genomics research there’s been this specific issue that we have human genome sequence and do we patent it and do we patent specific parts of it, how assessable to the scientific community around the world is this sequence going to be and I think the scientific community has come down on the side strongly that it will be available and that people will be able to do research with it. The other side is that to develop a pharmaceutical requires easily between $400 and $800 million. |
| Q57 | From the basic research to the product? |
|  | From the basic research to the approval for sales. Now those two numbers just appeared in the press in the US from a news study and it’s not important to go through the details; they’re both very large numbers and to be able to husband those resources, apply them and get new drugs requires the ability to use patents to recover those investments because you make the investments long before you actually sale. Now, I’m not justifying the industry. It’s a very profitable industry, there’s no question about, highly profitable industry but in addition it does deliver drugs, right, and most of the drugs that we use today, almost all of them without exception, they have been developed through that mechanism and I’m confident people will not make those types of investments without being able to patent and recover their investment with some profit after they make it. Now, societies are going to debate just what the amount of profits reasonable and how long those patents should be used for creating a monopoly but there have to be some mechanism to allow recovery of those costs. |
| Q34 | So this will be the future of biotechnology? |
|  | I mean that’s the way pharmaceuticals have been structured for the last decades and in biotechnology it will also be the case. Biotechnology is predicated on new science, new things happening so fast that large organisations find it difficult to incorporate those new things and I think the addition of the genome sequence and our abilities to use new ways of studying cells and physiology is going to mean that there’s going to be a continual rapid advance in biological science creating many opportunities and therefore biotech will continue to be a thriving subpart of the pharmaceutical world for at least a decade or more and will bring us new treatments for diseases and infections and other things. |
| ID | **0575** |
| Biographical | Memories of my early childhood are clouded with uncertainties because I was essentially separated from my parents since the early age of seven. I was born in Shanghai, China on April 6, 1920. My father had come there from Vienna, Austria after earning doctorates in law and business. My mother, born Renée Tapernoux, had arrived from France with her parents via Hanoi. Her father had left Switzerland as a young man to become a journalist for L’Aurore. This journal published the letter by Emile Zola entitled “J’accuse” in which he denounced the government cover-up during the Affaire Dreyfus which tore France apart at the turn of the century. When the case against Dreyfus collapsed in the early 1900s my grandfather left for French Indochina, then called le Tonkin. He later went to Shanghai where he founded the “Courrier de Chine”, the first French newspaper published in China. He also helped to establish “l’Ecole Municipale Française” where I first went to school.  At age 7, my parents sent my two older brothers and me to La Châtaigneraie, a large Swiss boarding school overlooking Lake Geneva. My oldest brother, Raoul, was the first to leave to attend the ETH, the Swiss Federal Polytechnical Institute in Zürich where he was awarded a degree in engineering. My brother Georges went to Oxford and read law.  In 1935, I entered Geneva’s all boys Collège de Calvin from which I obtained my Maturité Fédérale four years later, even as the specter of World War II loomed evermore menacing. While in school, I formed a lifelong friendship with my classmate Wilfried Haudenschild who dazzled me with his tinkering abilities, off-the-wall ideas and mechanical inventiveness. Together we decided that one of us should go into the Sciences and the other into Medicine so that we could cure all the ills of the world.  Another important event marked my High School days: I was admitted to the Geneva Conservatory of Music. I had heard Johnny Aubert give an unforgettable rendition of Beethoven’s 5th Piano Concerto. I decided on the spot that I wanted to study with him. After an audition in which I nervously presented Mendelssohn’s Rondo Capriccioso and Chopin’s A-maj. Polonaise, he took me on, and that spelled the beginning of many enthralling years. Music had always played an important part in my life, to such an extent that I even wondered whether I should not make a career of it. But finally I thought it better to keep music purely for pleasure.  It was my goal to become a microbiologist but Fernand Chodat, the Professeur of Bacteriology, argued that there was little future in that field, which was probably the case in Switzerland at that time. He advised me to get a diploma in Chemistry saying that, in any case, test tubes were of more use than a microscope to modern microbiologists.  I therefore entered the School of Chemistry just at the start of World War II. Two years of quantitative inorganic analyses seemed endless. Organic chemistry finally arrived like a breath of fresh air, if not a reprieve on life. I earned two Licences ès Sciences, one in Biology, the other in Chemistry and, two years later, the Diploma of “Ingénieur Chimiste”. For my thesis, I elected to work with Prof. Kurt H. Meyer, Head of the Department of Organic Chemistry. “Le Patron” as we affectionately called him, was a most impressive person. At the time when most scientists showed little understanding of natural high polymers, Kurt Meyer had already authored several books on the subject, starting with the epochal “Meyer-Mark: Der Aufbau der hochpolymeren organischen Naturstoffe” and “Makromolekulare Chemie”. His main interest lay in the structure of polysaccharides, particularly starch and glycogen. To unravel the structure of these molecules, enzymes were needed: alpha- and beta-amylases, phosphorylase, etc. Therefore, the lab was divided into two groups: the enzymologists under the guidance of Peter Bernfeld and carbohydrate chemists under Roger Jeanloz. I decided to work on the purification of hog pancreas amylase. Within a couple of years, we succeeded in crystallizing alpha-amylase from pork pancreas and soon after that, from a variety of other sources including human pancreas and saliva, two strains of *A. oryzae*, *B. subtilis* and *P. saccharophila*. It is at that time that Eric A. Stein joined the laboratory, beginning a marvelous 15-year collaboration and a lifelong friendship.  It had always been my intention to go to the United States to pursue my studies in Biochemistry. In those days, that field was in its infancy in most European universities to such an extent that I was asked to present the very first course in Enzymology as a Privat Docent at the University of Geneva in 1950. Two events hastened my departure for the USA: the untimely death of Kurt Meyer following an asthma attack and my being abruptly issued a US immigration visa. Apparently, the US consulates abroad were clearing their files before the complicated McCarran Act would come into effect. I had decided to go to CalTech on a Swiss Post-doctoral Fellowship that Professor [Paul Karrer](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1937/index.html) succeeded in securing for me on a moment’s notice. Some friends who knew of my arrival in New York had arranged for me to give some seminars on my way to Pasadena: Maria Fuld at Pittsburgh and Henry Lardy at Madison. To my utter surprise, I was offered a job in both places. Then, upon my arrival at CalTech I found a letter from Hans Neurath, Chairman of the Department of Biochemistry at the University of Washington, inviting me to come to Seattle, apparently for the same purpose. I thought that the Americans had to be crazy since at that time, academic positions in Europe were one-in-a-million. I visited Seattle with my wife and thought that the surrounding mountains, forests and lakes were beautiful, reminiscent of Switzerland. The Medical School was brand-new and when I was offered an Assistant Professorship, I accepted and have never regretted that decision.  There were only seven of us on the faculty and we quickly became close friends. I remember the amused expressions of my colleagues seated in the back row of the class listening to my fractured English when lecturing the medical students. I also remember [Ed Krebs](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1992/index.html)‘ broad smile whenever I lapsed into French. What Ed didn’t realize, though, is that within two years, while my English didn’t improve very much, his deteriorated completely!  Within six months of my arrival, Ed Krebs and I started to work together on glycogen phosphorylase. He had been a student of the [Cori’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html) in St. Louis. They believed that AMP had to serve some kind of co-factor function for that enzyme. In Geneva, on the other hand, we had purified potato phosphorylase for which there was no AMP requirement. Even though essentially no information existed at that time on the evolutionary relationship of proteins, we knew that enzymes, whatever their origin, used the same co-enzymes to catalyze identical reactions. It seemed unlikely, therefore, that muscle phosphorylase would require AMP as a co-factor but not potato phosphorylase. We decided to try to elucidate the role of this nucleotide in the phosphorylase reaction. Of course, we never found out what AMP was doing: that problem was solved 6-7 years later when [Jacques Monod](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html) proposed his allosteric model for the regulation of enzymes. But what we stumbled on was another quite unexpected reaction: i.e. that muscle phosphorylase was regulated by phosphorylation-dephosphorylation. This is yet another example of what makes fundamental research so attractive: one knows where one takes off but one never knows where one will end up.  These were very exciting years when just about every experiment revealed something new and unexpected. At first we worked alone in a small, single laboratory with stone sinks. Experiments were planned the night before and carried out the next day. We worked so closely together that whenever one of us had to leave the laboratory in the middle of an experiment, the other would carry on without a word of explanation. Ed Krebs had a small group that continued his original work, determining the structure and function of DPNH-X, a derivative of NADH. I was still studying the alpha-amylases with Eric Stein. In collaboration with Bert Vallee, we were able to demonstrate that these enzymes were in reality calcium-containing metalloproteins.  In those days, we waited all year for the next Federation Meeting or Gordon Conference. It was an occasion for me to get together with my friends on the East Coast: Herb and Eva Sober and Chris and Flossie [Anfinsen](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1972/index.html) from NIH, Bill and Inge Harrington from Johns Hopkins, Bert and Kuggie Vallee from the Brigham and Al and Lee Meister, then at Tufts and later at Cornell, and many others. I have forgotten much about the meetings themselves. There was the excitement of hearing about the latest breakthroughs, the frantic preparations for talks that had to be given, and the numerous notebooks filled with information, questions and problems that had to be solved. I will never forget, though, the marvelous time we had together speaking far into the night about anything and everything. Some of these friends are gone today but their memory is still vivid.  I have two sons, François and Henri, from my first wife Nelly Gagnaux, a Swiss National who died in 1961. I married my present wife Beverley née Bullock from Eureka, California, in 1963. She has a daughter Paula from a first marriage. All three of our children are now married and my two sons each has a son.  I received the Werner Medal from the Swiss Chemical Society, the Lederle Medical Faculty Award; the Prix Jaubert from the University of Geneva and, jointly with Ed Krebs, the Senior Passano Award and the Steven C. Beering Award from Indiana University. I received Doctorates Honoris Causa from the University of Montpellier, France and the University of Basel, Switzerland and was elected to the American Academy of Arts and Sciences in 1972 and to the National Academy of Sciences in 1973. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q1 | Then the first question. How did you come into your research field and what were your initial steps in the field that lead you to your future career? |
|  | How I went into science, that came very early when I was about 15 years old, I had read books on Louis Pasteur and I decided I wanted to become a microbiologist, and I remember for my 16th birthday I asked, as a present, for a microscope and my brother who was at the Polytechnical school in Zürich bought in a second hand store, beautiful in fact, lights, the old lights microscope with a emersion objective. I wanted to solve all the problems of the world and this is how I went in fact into that field. Then when, before I went to the university, I went to see the professor in microbiology and he said: you know, there’s no money in microbiology. If you want to become a microbiologist you have to get a diploma of something, pharmacy or chemistry, pharmacy didn’t interest me so I went into chemistry and this is how I ended up. |
| Q6 | You finally came into the Nobel Prize laureate field and you did this 1992 in physiology or medicine for reversible protein phosphorylation. How did that feel? |
|  | It came as a big surprise. In fact I, I got a phone call in the middle of the night, my wife was a little bit ill so she was sleeping in another room and the phone rang and I grabbed it and somebody said ‘Dr Fischer’. The first idea was somebody wants to sell me a new roof on the house. I said ‘Yes’, he said ‘Are you Dr Fischer from the University Washington? I said ‘Yes, why does he’ … and he said ‘Congratulations, you just got the Nobel Prize’ and it had no reality. I said ‘I don’t believe it’, he said ‘Oh yes, believe it, you and Dr Krebs are sharing’, and the moment he mentioned Ed Krebs’ name since we had been working together for 40 years, it put everything in the right ball park, so that woke me up. I put the light on and it was 3.45 in the morning. It was CBS New York. |
| Q1 | That’s the usual time, because there is a time difference and this time difference from the decision to reaching the West Coast, US, makes that early in the morning for you. But I meant how did you come into exactly that field, because it must have been a long story before that too. |
|  | It came from the fact that Ed Krebs, my colleague, had been working with [Carl Cori](https://www.nobelprize.org/prizes/medicine/1947/cori-cf/facts/), the [Cori’s](https://www.nobelprize.org/prizes/medicine/1947/summary/) in St Louis, on phosphorylase, muscle. We in Geneva, my mentor was Kurt Meyer and we had been working on potato phosphorylase and the muscle enzyme is activated as you well know by compound called AMP, adenylic acid, but not the potato one. The Cori’s thought it was a form of co-enzyme and I thought it can’t be because co-enzymes are preserved through evolution as you know better than anybody else. We decided to investigate the system and we started working, we thought we would be working for a few months on that and very rapidly we found that the enzyme was activated by a totally different mechanism. That’s how we entered the field of phosphorylation. |
| Q41 | And then you had a long series of discoveries, would you like to describe some of them you think are crucial? |
|  | That was the first, that the protein could be activated and inhibited by phosphorylase and dephosphorylation. When we worked in crude muscle extract there was an absolute requirement for calcium, but when we purified the enzyme there was no involvement of calcium and the question is why do we need calcium in the crude extract? There were a lot of our enzyme, phosphorylase, there was a lot of magnesium ATP required, why do we need calcium? The only possibility is that the enzyme, we knew it had to be an enzymatic reaction, we knew it had to be what we call a kinase, the only possibility was that kinase also existed in inactive and active form and calcium was involved in that and that turned out to be correct. That was the beginning of a cascade system, activation of an enzyme that activated another enzyme that breaks down glycogen. |
| Q23 | How do you feel now with something like 10% or whatever of all protein being regulated by phosphorylation? It must be a wonderful feeling to have found this first and then know that everything depends on it. |
|  | This is really serendipity. You know where you start in research and you never know where you will end up. This is the beauty of basic research and yes, now there’s an explosion of kinases and the very very big development in the field was the discovery just 20 years ago that a very important carcinogenic virus, [Rous](https://www.nobelprize.org/prizes/medicine/1966/rous/facts/) sarcoma virus, brings about tyrosine phosphorylation and involve tyrosine phosphorylation in transformation and oncogenesis. The field developed, at first people thought: Oh, it’s a nice system, but they are working on it why. Then when we found that calcium was involved that got all the muscle physiologists interested because muscle contraction is triggered. Then it was found that nerve conduction, phosphorylation, that got all the neurologists excited and then when it was found a transformation is brought about by tyrosine so that was the explosion. |
| Q41 | You feel that you have an incapacity to follow all the different fields? |
|  | Absolutely not. This is the importance of going to meetings, the importance of friends who call you. I’m retired now, in fact since seven years, but I closed my laboratory about three years ago and I’m delighted I have because now I can read science for the beauty of it without saying: Oh, I have to tell Al he should do that, I have to remember that. Now I just read science and follow science for the pleasure of it. |
| Q14 | That’s very good. This matter with sociology on science, did the Nobel Prize change your life? Did you come into lots of committees, you’ve got other commitments? |
|  | In many little ways, nice ways, I certainly can’t bitch about it. It has been an extraordinary experience, not only for me, but we have always been very very close friends with Ed Krebs, but more than that. The two families went to Stockholm, they have become close friends. Within my family they have become much closer, you know we are bound by this sort of a *confrerie*, brotherhood, if you want. It has been a really extraordinary experience. A little bit disturbing too. Disturbing because – and I was wondering why – you wonder you know why? Why were we selected? Somebody this morning spoke about that, science, you never do science alone. You do science with collaborators; the whole field is carried out by many many groups. We would have never been able to do what we did without very very bright collaborators. There is a difference between the Nobel Prize for instance and the gold medal in the Olympic games. For the Olympics you train like crazy for several years with one goal in mind, you compete, you beat all the other guys and by golly when they give you the gold medal you know why you got it. Not with the Nobel Prize. |
| Q14 | But in some cases perhaps it may be different, in different fields. How much do you rate … I mean first there is experience, science has long tradition and lots of previous results and then you work hard and you have lots of collaborators but you also need that push, the creative environment and the creative realisation of yourself. How do you think first, what did you consider about that in your case and how can we promote it in general? |
|  | For me, I can tell you it was the love of science. Really that. The enormous pleasure, working in a lab, never knowing what you’ll get, getting extraordinary results that will prove wrong within a week, others that hold, it’s like reading a detective book, you try to follow some clues and try to build a story. I like the approach of making hypothesis and either trying to destroy them or to prove them and go this way, I like this approach. |
| Q35 | But most people have something they might wish to have changed, anything you would have changed? |
|  | No, when I went into science, I was at the conservatory in Geneva, playing the piano, and maybe there was some hesitation whether or not I should go into music. I would have never been able to become a concert pianist, you have to be a virtuoso at age 12, you know, like tennis players, and I was not, I didn’t have the virtue, but I would have probably become a conductor. I like music more than piano, but I don’t know, I felt that music, I should keep that for the garden, for the pleasure of it. |
| Q14 | Do you see any connection between the music and science because you had this connection. The previous person I interviewed here had the same, [Manfred Eigen](https://www.nobelprize.org/prizes/chemistry/1967/eigen/facts/), and my mentor [Hugo Theorell](https://www.nobelprize.org/prizes/medicine/1955/theorell/facts/) had the same. Do you see any reason for this? |
|  | Manfred Eigen is a super pianist and a good friend. I don’t know, I did a lot /- – -/ with [Jerry Edelman](https://www.nobelprize.org/prizes/medicine/1972/edelman/facts/) who is a very good violinist. I love chamber music, I love to accompany people who sings, lieder, but it sounded gross to me to make a living out of music, I view music as something that you don’t touch. |
| Q49 | If we should switch to support a little, how do you see the natural present-day support of science and the discussion that we just had in the lecture. |
|  | I have the same worries that were expressed. The fact that now more and more you go towards targeted research. There’s nothing basically wrong in targeted research, in fact many fundamental discoveries came through applied research as exemplified for instance by the work of Louis Pasteur. But nothing wrong as long as all the money doesn’t go towards targeted research. Unfortunately, many administrations have this erroneous feeling that you can solve a problem by throwing millions of dollar at it. They don’t understand what is creativity in science, they don’t understand that so many discoveries come from serendipity. Mendel didn’t know that he would find the laws of classical genetics by trying to solve why peas would grow white or pink or another colour. Or [Röntgen,](https://www.nobelprize.org/prizes/physics/1901/rontgen/facts/) who was interested simply in looking at the properties of electrons bouncing on the cathode. He didn’t know he would make maybe the largest discovery ever made in the field of medicine. If either Mendel or Röntgen would have applied to, let’s say NIH if it existed at that time, there’s not a chance in a million that their work would have been approved. |
| Q34 | Perhaps we can end up with a question about the future. I guess you must have got it several times before Now you have had a successful scientific life, full of science, for 50 years or more, if you now go 100 years ahead, what would you think happen and which of the present-day questions are not solved or are all solved. A difficult question. |
|  | If you ask me what percentage I would go zero upon zero, zero, zero, zero, etc. A tremendous problem will have to be solved. To predict, even in 10 years, you cannot do that. As a friend of mine once said it’s like asking a general of cavalry in 1880 to plan for World War III. He would tell you: Give me ten thousand cavaliers and I’ll protect Washington. You cannot predict, you cannot guess what you cannot imagine. The big problems that will be solved rapidly is genetic therapy, therapeutics, because we begin to understand a little bit the regulation of genes, the tremendous problems. To say: Oh, we’ll solve that in 10 years, it’s nonsense, I don’t know when, but it will. I’m certain we will be able to regenerate nerves when nerves are cut. I am sure that we will be able to grow stem cells, in all cases aplastic anaemias and things like, replace that, so many therapeutic problems will be solved. In my field which is cell signalling, there are many pathways, we begin to know those pathways, we know all the enzymes that are involved but enzymes are words, we know bits and pieces of phrases, but we don’t know the language, a cell has to speak among pathways to co-ordinate all those reactions, we don’t know that language. More importantly we don’t know the language that the cell has to speak with another cell to co-ordinate the development of multi-cellular organisms where messages have to be sent back and forth from one cell to the other. This communication has been crucial to the establishment of the very complex networks of communication we have in embryonic morphogenesis in the immune system, in the brain where you have some more than a thousand million cells speaking with one another through something like 10 million billion synapses, ultimately leading to generation of thought, memory, consciousness. That’s one of the huge challenges that faces the biologists. |
| Q66 | I think you gave a very good answer to this difficult question, and you did it so well you’ll have another difficult question after all, and that is there are many ways of treatment, one is the genetic therapy for the future like you just said, there’s also transplantation. I was recently at the lecture where we were told all the benefits from transplantation, and I saw this drug treatments like using inhibitors and receptor agonists and so on. How do you see the future between these three fields, do you think we will soon be overtaken with genetic therapy or soon overtaken with transplantation? |
|  | I don’t think so. I think that we developed all three and you know you’ll use the one which is the more advanced at one particular time and have taken over. What is remarkable now is that we begin to understand some of the mechanics that control each of these, for drugs we begin to know how to model the drug, so the opportunity, the potential for advances in those three fields is immense. I think that the young people today have a marvellous future ahead of them in those fields. |
| ID | 0576 |
| Biographical | I was born in Lansing, Iowa on June 6, 1918, the third of the four children of William Carl Krebs and Louise Helen (Stegeman) Krebs. My maternal grandmother, Bertha Stegeman, lived with us for most of her life. My father was a Presbyterian minister, who had started his ministry in the Moravian Church in Wisconsin. My mother taught school until she was married. (She must have been an excellent student because she could still help me with problems during my second course of algebra.) As was common in ministers’ families, we moved several times, first to Newton, Illinois and later, when I was age 6, to Greenville, Illinois. The family stayed in Greenville, which I always think of as my “home town”, until I was fifteen. Greenville is a small college town, has good schools, and is surrounded by pleasant countryside where I loved to go on walks with my older brothers – as soon as I became old enough that they didn’t mind having me tag along. In addition to hiking, other recreational pursuits included sand-lot sports, fishing, stamp collecting, and eventually ham radio. The last hobby was picked up not so much because of any strong scientific interests on my part in radio theory but rather from a desire to be able to talk to a grade school playmate who had moved to Chicago. I loved to read – mostly historical novels about the Civil War, the settling of the West, and related adventure stories. I worked hard at school in order to succeed, but I cannot claim to have been a highly intellectual child. I liked to make gun powder using materials purchased from the local drug store or taken from my older brother’s chemistry set, but I had no childhood aspirations of becoming a chemist. The closest that I came to expressing an interest in biology was the maintaining of a balanced aquarium.  At the end of my first year in high school my father died suddenly. I was fifteen and was strongly influenced by this unexpected event. Although I had never aspired to follow in his footsteps and become a minister, I had great affection for him and admired the skill that he had in some of his avocations such as carpentry and gardening. My mother was deeply affected by Dad’s death, but after recovering from the initial shock began making major decisions mostly centered around providing advanced educational opportunities for her children. It was determined that the family, which had very limited income (It was 1933.), would move to Urbana, Illinois, where my two older brothers were already enrolled at the University of Illinois. There we rented a large enough house so that we could rent out a room to help with expenses. Everyone got some kind of part-time job. The planning for these changes involved the entire family and without doubt had a maturing influence on both of my brothers and certainly had one on me.  In the period from 1933 to 1940 in Urbana I completed the last three years of high school and carried out undergraduate work at the University of Illinois. Urbana High School was an excellent institution with highly dedicated teachers and a broad range of extracurricular activities that were useful in helping me make up my mind as to what I wanted to do in life. This problem was one that was occupying my mind increasingly at this time. Because these were depression years, my thinking about various professions was colored by the question of whether or not a given choice of work was one in which I could earn a livelihood. I gravitated toward a scientific career, not because of deep interest in the challenges of the unknown, but because I felt that there was security in becoming a scientist. Science courses, more than the others, provided subject matter that I felt could actually be used. These feelings were strongly reinforced by the success of my older brother in obtaining an excellent position after obtaining a Ph.D. in chemical engineering in the mid 1930s. Medicine, as an applied science, was also appealing and offered the advantage of being directly concerned with people.  In 1936, I entered the University of Illinois with the idea of majoring in some branch of science related to chemistry, but I did not have a very clear idea of where I was headed. Taking advantage of an “individual curriculum” program that was available to those with reasonably good scholastic records – and for this reason presumably knew where they were going – I was relieved of the necessity of meeting many specific requirements and could pick and choose courses that I wanted. In this way I was able to take enough biology to meet premedical requirements but could also take the math, chemistry, and physics courses designed for professionals in these fields. By the beginning of my fourth year in college, I had narrowed my choices either to getting an advanced degree in organic chemistry or going to medical school. For the latter financial help would be required. This became available in the form of a scholarship to attend Washington University School of Medicine in St. Louis. At this point I assumed that the agony of indecision was over and my future was now defined. I would become a physician.  During my fourth year at the University of Illinois I carried out undergraduate research in organic chemistry and found it to be a fascinating experience. This was probably the first time that I had ever taken a “course” that seemed like fun. Because I was ahead in my credits, I was able to spend virtually unlimited time in the laboratory. My mentors were Harold Snyder and Charles Price, and to them I will always be grateful for having introduced me to research. Another influential teacher during this period was Carl S. Marvel. Had this research experience come earlier in my college career, I might well have opted for a Ph.D. in organic chemistry rather than going to medical school. But as it turned out, this introduction to research influenced my medical training and without doubt was a strong factor in my eventually becoming a research biochemist rather than a clinician.  Washington University School of Medicine proved to be an excellent choice as a place where I could receive classical medical training but at the same time learn to appreciate “medical research.” The basic science courses were the equivalent of graduate courses and there was no attempt to water down the curriculum based on the idea that physicians only need “core” knowledge in the various sciences. In addition to basic course work that took us to the fringes of knowledge in the various disciplines, students were encouraged to participate in laboratory projects. I personally undertook several projects, first under Dean Philip A. Schafer, who was also chairman of the Department of Biochemistry, and later under Arda A. Green, a faculty member associated with Dr. [Carl and Gerty Cori](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html). Ethel Ronzoni also offered me help and advice in some of the work that I carried out. During this period I first heard about the enzyme, phosphorylase, which was crystallized by Arda Green and the Coris and was found to exist in two interconvertible forms that they referred to as phosphorylase *b* and phosphorylase *a*. Phosphorylase *b* required 5′-AMP for enzymic activity whereas phosphorylase *a* was active without this nucleotide. This enzyme was later to play an important part in my life.  The medical school years, 1940-1943, were war years, and although I did some research as a medical student, my main preoccupation was with becoming a physician who could serve in the armed forces. Nobody knew how long the war would last and our immediate concerns were with being a part of the war effort. After graduation from medical school I had eighteen months of residency training in internal medicine at Barnes Hospital in St. Louis, and then went on active duty as a medical office in the navy. The war ended and so did the period of my life in which I actively used my medical training in any practical sense. I believe I would have been happy practicing medicine but this was not to be.  After being discharged from the Navy in 1946, I returned to St. Louis with the idea of continuing residency and becoming an academic internist. However, it immediately became apparent that I would have to wait my turn to get back into hospital work, and I was advised by my professor of medicine, Dr. W. B. Wood, to study in a basic science department during the interim. Because of my background in chemistry, I chose biochemistry for this and was fortunate in being accepted by Dr. Carl and Gerty Cori as a postdoctoral fellow. After two years in their laboratory, during which time I studied the interaction of protamine with rabbit muscle phosphorylase, I became so enamored with biochemistry that I decided to remain in that field rather than returning to internal medicine. Again, I had found laboratory experience to be very satisfying just as it had been when I was a senior in college.  While I was on active duty in the navy, my ship had put into Seattle, and I had been impressed by the beauty of the city. So in 1948, when I had an opportunity to go there as an assistant professor of biochemistry, I jumped at the chance. Because I was quite uncertain of my ability to succeed in biochemistry, however, I made certain that I was duly licensed and registered in the State of Washington, so that if worse came to worse I could always “hang out my shingle.” Happily, things seemed to go along reasonably well, and I did not find it necessary to use this insurance policy.  In 1950, Hans Neurath became the first permanent chairman of the Department of Biochemistry at the University of Washington and began to build what was to become one of the major departments in the country. The emphasis in the department was on protein chemistry and enzymology, and this provided an excellent environment in which to develop and pursue a research field. I had been in Seattle for five years when [Ed Fischer](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1992/index.html) joined the Department. Ed had had experience with potato phosphorylase during his graduate student days and, as indicated earlier, I had become acquainted with mammalian skeletal muscle phosphorylase in St. Louis. Together we decided to see whether or not we could determine the mechanism by which 5′-AMP served as an activator of phosphorylase *b*. We didn’t solve that problem, but in the course of trying we discovered the molecular mechanism by which interconversion of the two forms of phosphorylase takes place; namely, reversible protein phosphorylation. Similar work was being carried out on liver phosphorylase at approximately the same time in the laboratory of [Earl Sutherland](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1971/index.html) who discovered cyclic AMP, the second messenger of hormone action, which he showed was involved in phosphorylase *a* formation. A number of years were to elapse before it became apparent that reversible protein phosphorylation is a general process affecting countless cellular proteins.  During the early years of our work on protein phosphorylation, Ed Fischer and I worked together very closely even to the point that if one had to leave to give a lecture the other could carry on the experiment of the day. Later, as the field developed we each concentrated on our own specific areas related to the central problem. One of my own projects was concerned with the molecular mechanism of action of cyclic AMP in promoting the phosphorylase *b* to *a* reaction. This was eventually solved with the finding of the cyclic AMP-dependent protein kinase by one of my postdoctoral fellows, Donal A. Walsh. This discovery occurred just prior to my leaving the University of Washington in 1968.  In addition to the motivation provided by my research, I was also motivated by interests in teaching and various aspects of administration. These interests led to a desire on my part to become a departmental chairman, and I was attracted by the opportunity that presented itself at the University of California in Davis where a new medical school was taking shape in the late 1960’s. I went there in 1968 as the founding chairman of the Department of Biological Chemistry and stayed for a period of eight years. In 1977, however, I returned to the University of Washington as Chairman of the Department of Pharmacology. In each place, I viewed the principal role of the chairman to be the selection of good faculty members, and I feel proud of the results of my efforts in each place. Other aspects of these chairmanships were also rewarding, particularly the opportunity to interact with colleagues in the development of the respective institutions.  An important part of this autobiographical sketch, which I have saved for the end, concerns my family. During my residency years at Barnes Hospital I met my wife, Deedy, who was a student nurse at Washington University. We were married in 1945 shortly before I left to serve in the Navy. We had three children, Sally, Robert, and Martha and now have five grandchildren. After completing her degree in nursing my wife gave up her own career, but she has been a constant and important source of support for me in my own. We shared in the major decisions of our lives, and I feel that I owe her very much, not only for her constant help in my career but also in keeping me aware that there are other important aspects of life. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| ID | 0577 |
| Biographical | Buchloe is a small town in Bavaria, situated in a rolling countryside in view of the Alps, 70 km west from Munich. This is where I grew up and spent most of my life until 1963, when I entered university. I was born in Landsberg, another town close by on the 20th of March 1944. My father, Franz Xaver Neher, was involved in the administration of a dairy company. Fortunately, this was considered to be of importance for food supply during the wartime, such that he was spared from military service. My mother Elisabeth (née Pfeiffer), who had received an education as a teacher in the early 1930s, was caring for the family of five, which included my two older sisters. Thus, in spite of the difficulties of the postwar period, I had the privilege to grow up in an intact family. Our family home was situated in a big, park-like garden, in which I spent hours by myself, watching plants and animals, and where I knew almost every pebble.  At the age of 10, I entered the ‘Maristenkolleg’ at Mindelheim. Mindelheim is another nearby town, and the local ‘Gymnasium’ is operated by a catholic congregation, the ‘Maristenschulbrüder’. The big advantage of this school was that our teachers – both those belonging to the congregation and others – were very dedicated and were open not only to the subject matter but also to personal issues. During my years at the Gymnasium (1954 to 1963) I found out that, next to my interest in living things, I also could immerse myself in technical and analytical problems. In fact, pretty soon, physics and mathematics became my favourite subjects. At the same time, however, new concepts unifying these two areas had seeped into the literature, which was accessible to me. I eagerly read about cybernetics, which was a fashionable word at that time, and studied everything in my reach on the ‘Hodgkin-Huxley theory’ of nerve excitation. By the time of my Abitur – the examination providing access to university – it was clear to me that I should become a ‘biophysicist’. My plan was to study physics, and later on add biology.  In the fall of 1963, I took up the study of physics at the ‘Technische Hochschule’ in Munich. The Technische Hochschule, in some contrast to typical German universities had a pretty tight schedule with quite an amount of problem-oriented course work supplementing ordinary lectures. Such training was of great help for many aspects of my subsequent research work.  In 1966, I won a Fulbright Scholarship to study in the US. I had applied for this with the idea, that it might provide access to biophysics. This was, indeed, the case. During my year at the University of Wisconsin at Madison, I was fully integrated into a biophysics laboratory involved in low angle X-ray scattering. My own project, directed by Prof. W.W. Beeman, was an early attempt at producing molecular beams of macromolecules for mass spectrometry. In a little more than a year I earned a ‘Master of Science’ degree. With this formal conclusion of a physics education I felt ready for switching to biology. I returned to Munich in 1967 and looked around for some PhD project in biophysics, preferably related to nerve excitation. Fortunately, my search led me to the Max-Planck-Institut für Psychiatrie, where H.D. Lux was investigating synaptic mechanisms in motoneurones and ion currents in snail neurones. We readily agreed on a project on voltage-clamping snail neurones. To circumvent space-clamp problems Dieter Lux suggested to use suction pipettes for local measurement of current density.  During my years in Dr. Lux’s laboratory I met [Bert Sakmann](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1991/index.html), who did his PhD project in the same institute. Bert was very interested in the basic neuronal mechanisms that we were studying, we had many lively discussions, and became friends. Following his interests Bert decided to go to London to work in the biophysics laboratory of [Sir Bernhard Katz](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1970/index.html). We met again in Göttingen in 1973, where I had joined a physical chemistry laboratory to get experience with single channel recording in artificial membranes. Bert brought with him the experience on the neuromuscular junction and it required only little discussion to agree on a collaboration, aiming at the measurement of single channel currents. In 1976, we published the first single channel records while I spent a year in the laboratory of Charles F. Stevens at Yale University. Afterwards, our heads of department, Hans Kuhn and Otto D. Creutzfeldt, established independent ‘Young Investigator Laboratories’ for us. This was very helpful for close collaboration, and allowed us to attract a number of excellent postdoctoral fellows: Joseph P. Patlak, Fred Sigworth, Alain Marty and Owen P. Hamill. Together we perfected the technique, and developed the different recording configurations. I feel very much indebted to these collaborators as well as to colleagues who later joined the laboratory. After 1983, my interests shifted away from the channels themselves to processes they initiate inside cells, eventually leading to a cellular response-like secretion of hormones and neurotransmitters.  Just before starting to assemble my own laboratory I met my wife, Eva-Maria – in the laboratory, of course. We married in 1978, such that my family at home, and my ‘research family’ grew in parallel. We now have five children: Richard (12), Benjamin (11), Carola (10), Sigmund (7), and Margret (4). My wife has given up her own scientific career and given me constant support for the benefit of my research. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | 0557 |
| Interview |  |
| Q67 | Professor Erwin Neher, welcome. My first question would be about the lifestyle as a scientist. Is there a particular lifestyle? |
|  | During these days here in Lindau, I was asked several times by students: What do you do outside science and what other interests do you have? Of course I have other interests, but on the other hand, science is a lifestyle in the sense that it’s a combination of profession and hobby. What you like to do, I mean as a scientist you have the chance to combine these two things, you know, and I think in that way it’s a lifestyle. I mean you do what you like because you just follow your curiosity and you are happy when you find new things about nature, about how things work around us and inside us. |
| Q1 | How old were you when you decided that this is the way you wanted to go? |
|  | It was pretty clear even when I was a little child that I was very interested in nature, in all these things that I observed and later in school I would think I was pretty much determined to say at the age of 15, 16, 17, first of all that I would try to study basic sciences, physics, chemistry and then also by the time I graduated from high school it was pretty clear that I wanted to do what at this time just was a kind of wake discipline which was not really established yet, biophysics, you know an interdisciplinary field between physics and biology. |
| Q34 | What was the question you wanted to have answered? |
|  | Quite, quite specifically, I mean during my high school years I had a chance to read about the findings which were quite new at this time, the late 1950s, on the nerve conduction, on the generation of the nerve and pulses, electrical phenomenon which happens inside our bodies, in our nerve cells and I was fascinated by this fact because, I mean, I had this interest in biology on the one hand, on the other hand I knew from what I learnt at school that physics and chemistry about things which I understood well which was easy for me at school to cope with, you know, so to combine these two things in the form of biophysics was easy for me to do. |
| Q25 | You need to find like-minded people, I believe, as well you found friends and even I believe your wife in the field of science? |
|  | Yes, that was of course much later. I did meet my wife in the laboratory which is part of her lifestyle you know, and of course over the years I had many friendships which developed in the lab which were connected to our work of course and so part of this lifestyle of a scientist is that you do a lot of travelling that you have friends all over the world which you first learn to know by means of your work, but then they become friends and wherever you go you have friends and you don’t go as a tourist to some place but you have friends and these friends tell you much better than a tourist guide can do what the specialties of a given location are. |
| Q25 | Professor [Sakmann](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1991/sakmann-facts.html) of course is still a friend and a colleague that you eventually made this fantastic discovery with, how did it come about? |
|  | This is a story which comes in two steps: While I was doing my PhD in Munich at the Max-Planck-Institut for Psychiatrie, he also was doing his PhD in a different department on a different floor of the same building, but we met each other and we realised that we had joint interests. I came from the physics field, he came from medicine, he was a medical student at this time. He was very interested in this more physically oriented things which were going on in the laboratory where I was, which was run by Dr Lux, who also was a medical person but very deep into the quantitative description of things and quantitative methods. So when we met three years later at Göttingen again it was immediately clear that we would try to collaborate because he in between had been in London working with [Bernhard Katz](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1970/katz-facts.html).  I changed from Munich to Göttingen, doing a kind of detour for two years or so into more physical chemistry. Our Institute in Göttingen is called the Max-Planck Institute for Biophysical chemistry, which means a combination of all three of them, and so I went to Göttingen to learn about the currents of recordings of channel currents in artificial systems, more physicochemical approach to these things. We had already developed ideas in Munich about recordings in the channels in biological cells, you know, but this more or less were put back for some time so that I would have the chance to more or less practice with these less complicated physical or artificial systems.  … this combined was clear to the two of us that it should be a good start point for a collaboration …  Then when Bert Sakmann came from London joining the same institute where I was again in a different department, we got together again. He meanwhile had obtained tremendously valuable experience for that purpose of recordings in channels. Bernhard Katz lab where he learned how to isolate the cells of the neuromuscular junction, the muscle cells and the nerve cells which make this connection where he learned to enzyme treat these preparations so that they would have clean surfaces. With his expertise on the cells and my expertise on the recording currents and dealing with pipettes also, this combined was clear to the two of us that it should be a good start point for a collaboration and that should give us a good chance to tackle this problem which was one of the problems which was in the minds of quite a few researches at this time can one record discreet steps in current when single channels open and close. |
| Q37 | And you developed this little glass pipette |
|  | Yes. I had been dealing with little glass pipettes in my PhD project, I mean the little glass object is not very special in physiology. Microelectrodes, pipettes drawn out to very fine tips you know, were standard in electrophysiology since the late ’40s I think. The problem was that this and the techniques of this time which recorded currents or electric little signals in biologic tissue use these very fine microelectrodes to penetrate the cells. What we did differently was that we in fact made these pipettes a little bit larger, the openings were larger, not designed to penetrate but just designed to place them on top of the cells to isolate a small patch of membrane for the purpose of electric measurement without destroying it, you see. |
| Q37 | And when you did this and when you got the results, how did you react, the two of you, what did you do when you realised? |
|  | Of course we were quite happy but, this didn’t come as in all or nothing things suddenly a … it did take about two years or so you know, during which we step by step improved things. There are certain ways to record signals and to analyse them which doesn’t actually require the single individual steps to be seen, but also when you just do not have the resolution to do that, but have a situation where many such steps superimpose the responses from many channels are recorded together. You have a kind of characteristic fluctuations you see in the current and for years we just analysed these fluctuations which allowed us to infer from these how big these steps actually are supposed to be which we want to measure.  So having this done and made the pipettes smaller and smaller, we finally approached the situation where there was this noise, but now and then you could see some step-like thing which very much looked like the steps that we wanted to see. Then of course one day or other it was a little bit better, a little bit worse and there were certainties, some days where we thought that’s it, you know, and now we are convinced that we see these tiny signals and this was maybe ’74 or so. Then we gradually improved until we came to the point where we not only believed that the steps were there, but where we also dared to publish them. |
| Q38 | And then to me, not being a scientist at all, I understand that there must have been times when it was very difficult and maybe one of you wanted to give up and the other said no come on let’s go ahead … |
|  | Yes, yes, of course there were times when it seemed that we had done everything we could and we couldn’t do it better and still we wouldn’t see this dent, little things. And there were frustrations and as I said at one point we got a little bit frustrated and we took this other project with measuring these fluctuations just to assure ourselves that actually there is something which signified the presence of /- – -/ of these channels and this was it. But apart from that, it was pretty a step by step thing you know, without major frustrations. |
| Q15 | How important was it to be two then to sort of encourage each other |
|  | Oh I think it was important yes, I mean, first of all because we could put together our experiences which were in very different fields you know, and then also because maybe one might have been more easily distracted you know to … maybe the distraction might have lead to a fast response but maybe also it would have prevented the success, you never know. |
| Q15 | You have to be very open minded and very hard working I believe. |
|  | Hard working, yes, definitely and open minded in a sense that we dared to just try new approaches which nobody else does you know. |
| Q17 | When you now look at what you have achieved, are you happy in the way it has been used? |
|  | Very happy. In fact we think the way it has been used, the way it developed without our active participation actually was what won us a Nobel Prize you know. I mean on the one hand there is just the finding, well one can resolve these step-like changes which more or less prove the concept of ion channels, that there are ion channels, this by itself of course would have been a nice finding which would have been hailed by many of the colleagues. But what turned all this that given this new technique the improvement of ways how to look at channels that many colleagues took up this method you know, and so it was a powerful tool in the hands of hundreds and thousands of colleagues.  And through this work, all over the world, it turned out that channels are not only in these cells that we started, I mean when we started, started channels we thought they were a special thing which happened to nerve cells, which happens in muscle and maybe some gland cells.People tended to divide living cells into excitable cells and non-excitable cells and excitable cells are of course a minority in the body, and we definitely thought that channels were only important for excitable cells. But what turned out that you find these channels, I mean different types of channels in all kinds of cells, liver cells and the blood cells, and the white blood cells and the kidney cells, even in plants, you know. And they do the most diverse jobs, they could fill the most diverse functions in these different cell types and that’s a real impact that our discovery and this new method had in the science, and I think this is what won us the prize.  … it turned out that these channels are very important targets for drugs …  Another aspect which again is a quite unanticipated aspect is that it turned out that these channels are very important targets for drugs. This lies a little bit in the nature of channels I mean, channels have not so many in a given cell, there are maybe thousand molecules of this kind of this channels but their function is to control the cell you know, to regulate the function. And if you think about it, such a molecule then is a good target for a drug because you need only a few drug molecules to block these channels, and though you just influence the workings of the whole cell end. And due to this intrinsic property it turned out that channels are the targets of some of the drugs which have been used over the years to treat hypertension you know, diuretics, psycho-active drugs, all kinds of drugs turned out to be drugs which act on these channels. |
| Q17 | Which one didn’t know at the time, when one created. Having made this discovery, do you think scientists like you have some kind of moral responsibility in which way your discovery is used? |
|  | That’s a difficult question of course, I mean if we see potential harm, potential dangers, of course we have the responsibility to point this out you know, to warn against that. On the other hand one of course thinks that any new knowledge, any better understanding of the matter around us, in us, will give means to handle things and normally of course one would think that people use these things to handle things better of course a scientist can never safeguard against new knowledge to be used against other people you know. It used to be harmful I mean, this started with the invention of the hammer, now you can use the hammer to do useful things, to build a house and you can use a hammer to kill somebody else. |
| Q50 | Is that a debate that goes on though, among the scientists? |
|  | Yes, yes, this debates, and I mean that more or less this issue rests at the basis of the whole problem on whether what we are doing is good or wrong you know, if you, it’s morally a question on what do you think about mankind. Do you trust in your fellow citizens in a sense that whatever they will have in additional tools they will use in balance more to the good or more to the bad. If you think they will use it more to the bad, you shouldn’t do science you know. |
| Q7 | My last question Professor. We started off talking about lifestyle and you said it is really a lifestyle, but you also said you have other interests. What are you doing to relax and to just wind down probably from the lab work? |
|  | What I’m doing to relax, some reading, some music, just being at home with my family, many things but unfortunately time is always very limited because science not only is both a job and a hobby but it also consumes the time which usually spent on both of these issues.  Creative work, basically.  Erwin Neher: Hopefully. |
| ID | 0578 |
| Biographical | I was born during the second world war in Stuttgart, the capital of Swebia, as the first of two children. My father, Bertold Sakmann, was the director of a theatre, the third son of a physician whose family had lived in southern Germany for several generations. My mother, Annemarie Sakmann, was a physiotherapist and was born in Bangkok, the second child of a Prussian physician who served as doctor to the King of Siam and was the founder of the first hospital in Siam.  During the first half of my childhood I grew up in Lindau, on Lake Constance, in a completely rural environment. There I went to elementary school, before returning to Stuttgart where I completed my Abitur at the Wagenburg Gymnasium. My only real interests at school were the physics lessons. At home I spent most of my time designing and building model motor and sailing ships as well as remote control aeroplanes. It was generally assumed that I would become an engineer. In the final year of school however I learned about cybernetics and its possible application to biology. Cybernetics fascinated me, because it seemed to me that living organisms could be understood in engineering terms.  Since I could not make up my mind between physics and biology I enrolled at the medical faculty of Tübingen University. The first two years in medicine offered a broad spectrum in biochemistry and physiology and I decided to do my doctoral thesis in electrophysiology which seemed to be closest to engineering. At the time it was common practice to study at several different medical schools and I attended schools in Freiburg, Berlin and Paris. My decision to finish medical studies in Munich was largely dictated by a beautiful young lady whose attention I was desperate to catch in Tübingen, though without initial success. Today Christiane is my wife and we have two sons and a daughter. Christiane is a highly successful ophthalmologist specializing in pediatric ophthalmology. For most of the time since we have been married I have been known in Göttingen and Heidelberg as the “eye doctor’s husband”.  At that time ‘biological cybernetics’ was a field that fascinated many students of biology and physics. Werner Reichardt’s and Bernhard Hassenstein’s quantitative behavioural analysis of a beetle’s optomotor response promised to make brain functions understandable in terms of information theory. Otto Creutzfeldt in the Kraepelin Institute in Munich accepted me as a doctoral student to work on the electrophysiological basis of pattern recognition. Although small by today’s standards, the Kraepelin Institute encompassed almost all aspects of neurobiology at the time, ranging from voltage clamp current recordings from snail neurones in Dieter Lux’s department to quantitative analysis of monkey behaviour in Detlev Ploog’s department. In Otto Creutzfeldt’s department, great enthusiasm and optimism prevailed in trying to understand and build models of pattern recognition by the visual system, and there was close collaboration with electrical engineers and computer scientists from the Munich Technical University. After three years of experimental work on the neurophysiological basis of light adaptation in the cat’s visual system I realized that the central nervous system (CNS) was too difficult to comprehend without understanding the synaptic connections more clearly. I went to a course on basic mechanisms of vision in a summer school and I attended a lecture given by [Bernard Katz](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1970/index.html) on nerve, muscle and synapse, which convinced me that cellular physiology would be very helpful in trying to understand the functions of the central nervous system. To gain experience in voltage clamping I joined Dieter Lux’s laboratory and learned from [Erwin Neher](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1991/index.html) how to voltage clamp synaptic currents in snail neurones before moving to Bernard Katz’s department at University College, London.  There I worked with Bill Betz for one year, learning the basics of synaptic transmission and taking apart the neuromuscular synapse into its pre- and postsynaptic elements. During the following two years I learned, with Dale Purves, that the neuromuscular synapse is also a good model for studying long-term changes in chemical and electrical excitability. During this time Bernard Katz and Ricardo Miledi discovered ‘membrane noise’ and ‘elementary events’, and Linc Potter and Ricardo Miledi in the same department made the first attempts to count and isolate acetylcholine receptors. I was very lucky to be at University College at this particular time, when both the electrophysiology and the biochemistry of synaptic transmission became molecular. It seemed that a molecular understanding of the end-plate currents was within reach, and it became clear to me that I wanted to work on the molecular aspects of synaptic transmission, and on the development of synapses, which is what I have been doing since. The major experimental challenges were the direct recording of the elementary events that had been postulated from Katz and Miledi’s experiments, the biochemical and structural characterisation of the acetylcholine receptor molecule, and the relation between structure and function of ion channels and receptors.  When Otto Creutzfeldt offered me the opportunity to run a laboratory of my own in his department at the Max-Planck-Institute for Biophysical Chemistry in Göttingen, I gladly accepted because other physicochemical and biochemically orientated departments there seemed to provide the right background for molecular physiology. Erwin Neher had moved to Göttingen as well, and we agreed to characterize different subtypes of acetylcholine activated channels with biophysical methods. This project went rather well, and it suggested to us that ion channels in denervated muscle fibres might be a good choice to try out extracellular pipettes for the recording of elementary events. Some initial success was followed by many frustrations in attempts to improve the seal resistance by choice of different preparations and treatments of pipette tips. Finally, with the help of a group of very dedicated collaborators, Owen Hamill, Alain Marty and Fred Sigworth, we succeeded in establishing patch clamp recording configurations which allowed us to investigate almost any type of channel in almost every cell type. A practical course, and the book that resulted from this course, marked the end of our primary focus on methodological problems, and allowed me to concentrate my efforts on understanding the role of ion channels in synaptic signalling at the molecular level. The resulting work was carried out with David Colquhoun and Joachim Bormann in the following years.  The next methodological step was to apply molecular biology techniques to problems of ion channel physiology. It seemed that proper use of recombinant channels in Xenopus oocytes could only be made in combination with single channel conductance measurements. Together with Veit Witzemann we found a simple way to free mRNA-injected oocytes from their covering layers to perform the first single channel conductance measurements from heterogeneously-expressed acetylcholine receptors. Later, Shosaku Numa suggested we collaborate combining patch clamp and recombinant DNA techniques to establish structure-function relations of the acetylcholine receptor. This fruitful collaboration identified the structural basis of channel subtypes and localized domains important for ion transport. It also provided me with a strong incentive to learn recombinant DNA techniques myself. When I later established my own department, I made sure that the techniques of cellular biophysics and molecular biology were well represented. As a result, I was well equipped to follow my strong interest in structure-function relations of ion channels and in the synaptogenesis of the neuromuscular junction.  Another technical challenge, to develop new methods for recording postsynaptic currents from neurones in brain slices, was prompted by my ongoing interest in CNS synaptic physiology. Together with Tomoyuki Takahashi we developed a method to expose neurones in brain slices, so that patch clamp techniques could be applied to measure quantal synaptic currents and elementary events in the CNS. Understanding synaptic transmission in the CNS requires a close collaboration with molecular biologists, so I moved my laboratory from Göttingen, where I had been collaborating with Erwin Neher for sixteen years, to Heidelberg, one of the molecular biology centers in Germany. Here I am collaborating with Peter Seeburg to elucidate the functions and dysfunctions of CNS synapses at a molecular level, using an approach which combines the techniques of biophysics and molecular biology.  Looking back, I feel very fortunate that I began my career in two laboratories that guided me to important scientific issues that interested me for over twenty years. The scientists that influenced me most were Otto Creutzfeld, who made me decide to take up a scientific career in neurophysiology, and Bernard Katz, in whose department at University College, London I was trained in cellular biophysics, and who still remains my mentor. Later, I was fortunate to meet fellow scientists with whom I shared interests and who became good friends. With Erwin Neher I shared an exciting and wonderful sixteen years of scientific adventures and ‘basteln’ on new methods in the Max-Planck-Institute in Göttingen. In our collaboration it has always proven important to spend a good part of our time developing methods and instruments, and to share newly developed methods with fellow scientists.  I began my scientific career in the Max-Planck-Gesellschaft in 1966 and, with the exception of three postdoctoral years (1970-1973) at University College, London, I have remained affiliated with this organisation ever since. The ideal working conditions provided by this organisation have been invaluable. I am currently the Director of the Department of Cell Physiology at the Max-Planck-Institute for Medical Research in Heidelberg as well as, at present, the Acting Director of this Institute. Most of the major awards were given to me jointly with Erwin Neher, with whom I share also the Nobel Prize. These earlier awards were the Bunsen Prize, the Feldberg Prize, the Spencer Prize, the Leibniz Prize, the Gross-Horwitz Prize, the Louis Jeantet Prize and the Gairdner Prize. For me the most important awards, before I shared the Nobel Prize, were the Magnes Award of the Hebrew University (1982) and Harvey Prize of the Technion (1991). I am glad to be the first German scientist to receive these awards. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q20 | Why is that and what benefit has it given you? |
|  | We are talking about what happened over the many years after the Nobel Prize was awarded and many years after we did the initial work for which we got it so we are talking about the last maybe 6-7 years and it is the common interest, you know, in order to find out how a synapse, you probably know what a synapse is, how synapse works. We have been looking for a new preparation. We found it, we established the way how to look at it.  … there’s still a very close personal friendship, which is mostly driven by, you know, curiosity …  Erwin had other techniques available, like release of calcium from cage compound and it was only natural that we start to collaborate again on a topic that both of us find very interesting and which had basically nothing to do with what we did 20 years ago, or 30 years go. So I don’t know whether this answers your question, but what I want to say is there’s still a very close personal friendship, which is mostly driven by curiosity, find out how things work. |
| Q20 | Is it important to share your findings with other scientists and with students? |
|  | There is always a competition and one wants to share results once they’re published and this is good practice, it’s got to be and in our case it worked out very nicely because the results which you get have to be validated by as many laboratories as possible. In science very often they are singular achievements and it has been taken many years to validate them so other people could repeat them and the faster this happens the earlier you can proceed, you can proceed in looking into other questions and people will take you seriously.  So once it’s published you should do everything to make the result and all the techniques involved available to other people but as long as you’re in the process of following an idea, first of all you have to have an idea, then you follow it. You find out whether you can falsify it or whether it is true and then publish it. I wouldn’t share too many results with immediate competitors but in the case of Erwin and myself we are a team from the very beginning because we did experiments together. I mean sitting together at the experimental set up and taking shifts. |
| Q11 | Did you support each other during those years of working very hard, when somebody felt a little bit despair or down the other one could support the other person? |
|  | I must say in this respect Erwin is just unique because he never got excited or despaired. He has what we would call in Germany, ‘Bayerische bierruhe’. I’ve never seen Erwin, these 30 years, getting excited about things which are not related to science. I mean he gets very excited about science but not about external facts. So this had a very good influence on our comfortability or whatever you call it because he was so quiet and didn’t get excited by people, saying bad things or, you know, there are many things that happen in the lab. |
| Q4 | Because there could be many hiccups and people who don’t believe in the work that you’re doing as well. I’m thinking about young students today, what qualities do they have to have to be able to continue, particularly as funding is getting more scarce? |
|  | Well, you know, it’s easy to say this in retrospect but at the time when we started to collaborate in the 1970s you could still do quite elaborate experiments with a relatively little funding. Most of our money at the time was spent in developing tools, the tools which we developed in order to achieve our goal and verify the idea of ion channels elementary currents.  That’s a little glass …  … we had limited funding and this can be a benefit …  Bert Sakmann: Well, it’s not one of the glass pipette, it’s getting the right preparations that is frog muscles, you have to innovate a frog muscle you have to get the electronics, you have to have micro manipulators, you have to have a table that is almost completely free of vibrations. So in retrospect we had a relatively large investment in the beginning into, so to speak, our tools but then the consumables, the cost for the consumables were rather low, which is the opposite in many cases nowadays that you spend a lot of money on chemicals like restriction enzymes or things that are being sold by the industry and the industry wants to make money. So to summarize is we had limited funding and this can be a benefit even because you think of how you can solve a problem without spending too much money. |
| Q62 | A lot of discussions have been around the need for basic research. What is your opinion because it seems like a lot more research is now coming towards should be applied science? |
|  | I think this is a, I would say, European attitude because the European science politicians are not the most enlightened in the world.  Why not?  Bert Sakmann: This is what I was trying to ask Professor [Marcus](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1992/marcus-facts.html) today why is there this difference between the States and Europe and I would exclude England from Europe because they still have an Anglo-American tradition in investing into basic science. I mean I shouldn’t complain, in Germany we still have the Max-Planck-Gesellschaft but the Max-Planck-Gesellschaft is just the top of the whole science enterprise and it would be nice if basic science would be more funded at the universities because this is where the students are being educated and we cannot do research without well educated students. |
| Q59 | It seems like there’s then, as you say, this brain drain could lead to the scientific world here in Europe sort of becomes weaker and we don’t develop new methods. |
|  | That’s what’s happening. I mean despite what we hear from the politicians, especially from our present government, that they want to invest into science I think this is all, you know, hot air if I may say so, which I don’t know what the motives are but on the one side there is this appreciation of basic science, on the other side it’s been cut away in favour of applied science and my speculation is that politicians can’t think ahead more than two years this will have an effect in 5-10 years, it has already an effect. We will be completely dominated by American science has happened and this will happen. |
| Q23 | You have changed field partly and now looking more into the brain. Would you describe that in a way that we can understand? What are the issues that you really would like to get to at the moment by doing this research? |
|  | My goal, so to speak, is to understand how the brain, based on the change of experience, let’s say training or the lack of training, changes instructed such that the brain can perform a new task. Is this simple enough? You might say what are the mechanisms that underlie learning, ok. Now this can be described at a phenomenological logical level. Say you do this and this and then the brain will react like this, but the effect of all this is based on the change of the interaction of particular molecules and that’s what we want to find out; a change in brain structure induced by a difference in your external world that we can explain in molecular terms, and the structure that we have chosen is the cortex. This is sort of a mantle that covers the whole brain because there’s good evidence that most of these functions, the ability to learn, are located in the cells of the cortex and to be more specific there’s also good evidence that the changes in cortical organisation induced by change in experience are based on the change in the structure of particular contact points, which are referred to as synapses.  So my research at present is directed to understand the change in cortical structure at the level of synapses. What is happening when the brain has a new ability, how do the cells reconnect? How stable is this, is this happening for a period of days, for hours, for years? Does it come back? I mean the whole process of learning, if you may say so, or of development, is very well described at the phenomenological level but what we need to know is which molecules are involved in that. |
| Q23 | Now it’s also the discussion about genes and what is controlling, for example, different diseases. Partly through mass media, I think the public in general has got the impression that by the knowledge we now have about the gene set up that things would be more easy, for example treating certain diseases. Is that so or is the situation much more complex? |
|  | Maybe I’m a bit provocative but serious scientists never believed this sort of propaganda that came out of part of the molecular biology establishment. This was, you know, driven by too much publicity and I must say some of the molecular biology establishment has really overdone this, maybe in conjunction with the media but I think every serious scientist never thought it would be that simple. I only hope that the false promises that were made for gene therapy, the promises that were made for what we learn, I mean not what we learn academically, but what we will benefit from the genome and what we will benefit from stem cells are formulated a bit more cautiously so that the public does not get the impression science is driven too much by PR. I think it’s a bit of a problem and it also attracts the wrong people to science. |
| Q55 | And the risks that have been so much debated over the last number of years. Do you see that with the gene technology? Super humans or so on. |
|  | With respect to interfering in a rational way I think we are not 100 years, we are 500 years away. So this is completely overstated by people who have very different interests in, how do you say, hitting at molecular biology. I think these are scenarios which are so far away from reality that one doesn’t have to take them seriously but there are other more serious problems; who has access to information on your genome. In those cases there is indeed a single gene defect causing a disease, you know, I mean there are big successes in what you would call molecular medicine. So far this has been mostly on a rather limited fraction of diseases where you have one gene disease and there indeed I can see that rules have to be established but I think this can be done. I don’t think it’s going to be too difficult to establish proper rules. |
| Q16 | Your discovery certainly have made it more easy to find out about how the system works and how the diseases are part of this. What makes you most proud of your discovery if you look back at what you have achieved? |
|  | This was an unexpected benefit let’s say. There is a new class of diseases that came up in the last, yes I would say 10 years, they are called channelopathies. This means diseases related to defects in the function of ion channels and all of a sudden ion channels and electrical signals, which we’re not very popular for the general public because it’s somewhat difficult to understand how electrical signal comes about and that we all run on electrical signals but this development of finding channelopathies is quite, you know, rewarding I would say although I would have to say the major impact is not that we can look at ion channels, we can look at their defects but without the parallel development of molecular biology this would not have been possible. So you are now in a situation to be able to screen for defects in ion channels and you can, using our methods, find out what is really wrong with the function or what is not functioning properly. |
| Q7 | On a more personal level, both you and your wife are hardworking scientists. Have got any advice, I mean how is it possible to combine these two, you know, in a fast track life that so many people are living? Do you have time for leisure? Do you have time to structure your thoughts and go on? |
|  | The leisure for many, many years were our children . I mean we had two things which was work and family and nothing else . I mean you just have to take compromises and we felt that having children is so exciting that there’s no room for anything else. |
| ID | 0579 |
| Biographical | I was born, as were my father and his parents, in Milford, Massachusetts, a town 30 miles southwest of Boston. My father’s parents were of Southern Irish and English extraction. My mother was born in Providence, Rhode Island, soon after her parents had emigrated to the United States from Italy. Father was a lawyer and a District Court Judge, mother a school teacher. Both parents had benefited from and stressed the value of the educational opportunities this country offered. By example and precept they emphasized the need for service to others.  From earliest memory I wanted to be a surgeon, possibly influenced by the qualities of our family doctor who cared for our childhood ailments. As a second year high school chemistry student, I still have a vivid memory of my excitement when I first saw a chart of the periodic table of elements. The order in the universe seemed miraculous, and I wanted to study and learn as much as possible about the natural sciences.  I chose to attend a small liberal arts college, College of the Holy Cross, and concentrated on Latin, Greek, Philosophy and English. Assuming I’d receive ample science in medical school, I took the minimum of chemistry, physics and biology.  My four years at Harvard Medical School were all that I had dreamed they would be. The classmates and faculty were stimulating and friendly. The hospitals were filled with all varieties of patients. Although the hours of study and hospital duty were long, life was rich and full. Symphony Hall and the Gardner Museum were within walking distance, squash courts were available for daily exercise, our singing group met weekly, bicycle trips and club dances added to the variety. It was heaven.  During the final few months of medical school, while attending a Boston Symphony Orchestra concert with several classmates and their dates, I noticed a lovely young lady “far too nice” for the fellow she was with. At intermission I manipulated her towards the corridor and learned that she was Bobby Link, a music student concentrating on voice and piano. By the time the intermission had ended I realized that I had met the girl I would marry.  After intermittent dates during my internship and brief meetings during hectic wartime weekends while I was on active duty, Bobby and I were married in June 1945. We have six children, three boys and three girls. Each has contributed to society in her/his own way, in education, medicine, nursing, business and science. Bobby’s music, pursued professionally for 15 years after marriage, continually adds to the richness and beauty of our family and social life.  My only medical school activity bearing any resemblance to research was a study of the then new Papanicolau smear of epithelial cells. I presented a report before the student Boyleston Society with Dr. Arthur Hertig as my faculty sponsor. Later, while a surgical intern at the Peter Bent Brigham Hospital, I introduced this technique clinically.  My interest in the biology of tissue and organ transplantation arose from my military experience at Valley Forge General Hospital in Pennsylvania. As a First Lieutenant with only a nine-month surgical internship behind me, I was randomly assigned to VFGH to await overseas duty. World War II was still raging, the Rhine River had not been crossed, the Battle of the Bulge was ahead.  VFGH was a major plastic surgical center. While there, I spent all my available spare time on the plastic surgical wards which were jammed with hundreds of battle casualties. I enjoyed talking to the patients, helping with dressings, and observing the results of the imaginative reconstructive surgical operations.  I learned only years later that Colonel James Barrett Brown, the Chief of Plastic Surgery, had noticed my day and night presence on the wards and requested that Lt. Murray be kept at VFGH and not sent overseas like the rest of the “nine-month wonders.” Three years later, two years after the war ended, I finally was discharged in November 1947.  During my army service, we always had many burned patients to care for. Some were so extensively burned that donor sites for skin autografts were not available. As a life-saving measure for these patients, skin grafts were taken from other persons and used as a temporary surface cover.  The slow rejection of the foreign skin grafts fascinated me. How could the host distinguish another person’s skin from his own? Colonel Brown and I often discussed this while scrubbing. In civilian life Brown had treated many severely burned patients with temporary skin allografts and observed and written about the differential dissolution of skin allografts from various donors. He tentatively postulated that the closer the genetic relationship between the skin donor and the recipient, the slower the dissolution of the graft. In 1937, he had experimentally cross skin grafted a pair of identical twins and documented permanent graft survival in both twins. This was the impetus to my study of organ transplantation, which is the subject of my Nobel Lecture.  My life as a surgeon-scientist, combining humanity and science, has been fantastically rewarding. In our daily patients we witness human nature in the raw-fear, despair, courage, understanding, hope, resignation, heroism. If alert, we can detect new problems to solve, new paths to investigate.  Our laboratory work involved close contact with many non-clinical scientists. [Sir Peter Medawar](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1960/index.html), 1960 Nobel Laureate, was a frequent visitor to our lab and to the hospital. He once commented, after visiting an early renal transplant patient, that it was the first time he had been in a hospital ward. Dr. [George Hitchings](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1988/index.html) and Dr. [Trudy Elion](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1988/index.html), 1988 Nobel Laureates, were completely at home in our lab and knew many of the dogs by name. Sir Roy Calne, who worked in our laboratory at Harvard Medical School and Peter Bent Brigham in 1960-61 as a Surgical Research Fellow, and I frequently visited them in Tuckahoe, New York, to discuss prospective trial drugs. Billingham, Eichwald, Amos, van Rood – to mention only a few other basic investigators – also enriched the tapestry of our lives.  Medawar said it best, “This whole period was a golden age of immunology, an age abounding in synthetic discoveries all over the world, a time we all thought it was good to be alive. We, who were working on these problems, all knew each other and met as often as we could to exchange ideas and hot news from the laboratory.”  For recreation, I have always been a physical enthusiast. As a family we have camped, hiked, trekked, or backpacked over portions of five continents. Competitive tennis remains fun. Our extended family, with 11 grandchildren, gets together frequently during the year, and always every summer on Martha’s Vineyard Island in Massachusetts.  We have been blessed in our lives beyond my wildest dreams. My only wish would be to have ten more lives to live on this planet. If that were possible, I’d spend one lifetime each in embryology, genetics, physics, astronomy and geology. The other lifetimes would be as a pianist, backwoodsman, tennis player, or writer for the *National Geographic*. If anyone has bothered to read this far, you would note that I still have one future lifetime unaccounted for. That is because I’d like to keep open the option for another lifetime as a surgeon-scientist. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | 0579 |
| Interview |  |
| Q1 | I have the pleasure of sitting here with professor Joseph Murray, who won the Nobel Prize in 1990 for his work on organ transplantation. If I can start this little talk and say that from studying and from learning to know you it is quite clear that medicine was always a primary choice and that it was clear that you would become a physician from very early on. My first question is really when was it clear that you would be a researcher as well, what stimulated the early interest in research in you? |
|  | I think at Medical School the professors were doing interesting work. I remember one professor of pathology, he was really an instructor in pathology, was studying inflammation. I would look in the microscope with him and see different cells under different circumstances. I remember the trichina had ear centrefolds around it and an infection would have polymorphs. I wondered how the body attracted one, rather than another, and of course this is caused by xylocaine. We know now but this was back in 1941 and there was no knowledge of intercellular reactions. That interested me and then it was reinforced in my World War II experiences when we used skin from dead persons to cover burns in patients. We knew that the skin would last, survive, for maybe three weeks or four weeks but eventually it would melt away, whereas if his own skin had been used, the skin would have grown and then permanently survived and actually grown. I wondered how the body could be so smart as to distinguish between a piece of skin which to you and me would look the same, would treat one differently from another. Those were the two biological observations that were in the back of my mind. |
| Q68 | You came to the Valley Forge [Valley Forge General Hospital] shortly after you graduated from Harvard, I suppose, and got a lot of clinical experience I would say immediately. |
|  | Yes, we had battle casualties from all theatres, the European, African and the Pacific. We also cared for German prisoners of war, Italian and Italian prisoners of war as well in the same hospital and they received the exact same treatment. |
| Q68 | Problems associated with transplantation, the first one of those that you saw was the burns treatment and the difficulty in transplanting skin from unrelated individuals. I suppose a few years earlier there had been skin transplantation between identical twins. |
|  | Yes. that was 1934 or -35. A plastic surgeon in St Louis treating burns found that if skin came from relatives, it would survive longer than if it came from an unrelated person. He quite reasonably felt that if a related person has better survival, maybe an identical twin would have better survival and he found a pair of identical twins and cross skin grafted them and he got permanent survival. That was the only type of survival that we knew in the 1930s. |
| Q23 | What was the process between the burns treatment in the Valley Forge and the kidney transplantation? How did you focus on kidney and kidney transplantation? |
|  | It was quite logical. When I finally got out of the army and I finished my residency in the late 1940s I joined the kidney transplant team at the Brigham. It was already in operation. I joined them and rather than transplanting skin, it was more fun to transplant kidneys because you had the vascular anastomosis to do the ureter plantation and you could tell when the kidneys start functioning. It was a natural transition to use a kidney as a biological indicator rather than a piece of skin, but our research used both skin and kidneys throughout.  Was the animal experimentation, the transplantation in dogs, was that going on already when you arrived?  Joseph E. Murray: No, but I started a large series of dog transplants, also with mice, rabbits, all sorts of animals.  Based on that you performed the first transplantation between the identical twins.  Joseph E. Murray: Yes, in the course of operating on dogs, I figured if we didn’t have a good operation that would work in genetically similar persons, it would be no use and so I developed a surgical technique in dogs that was reproducible and could function normally. I had a whole group of dogs surviving on one transplanted kidney back to himself. It was an isogenic transplant but there was no genetic barrier.  Then of course a big jump or the major development was going from the identical twins to genetically unrelated people.  Joseph E. Murray: Yes, but before that we had to show that in man, the identical twin transplant would work.  Right.  Joseph E. Murray: We happened to get a set of identical twins, one of whom was dying of kidney disease, the other healthy. That took about two years to work it out against the ethics and the morals and the acceptance of the community. We went to doctors at other hospitals, we consulted clergymen of all denominations, we went to corporate executives to try to get a feeling for what the general public would feel about it because we were weak. We knew we were doing something experimental and we just wanted to inform as wide a variety of society as possible. |
| Q23 | When was the breakthrough coming, would you say, with immune suppression that would … |
|  | The real break came with the development of drug immunosuppression. However, we had had some success both in animals and in humans with total body radiation and we had one set of brothers with a permanent kidney survival with an allogeneic kidney, treated with x-ray therapy. We started to do a series of 12 humans and one did very well, several did well for a while but then they would, after five or six weeks, would reject the kidney. We needed something more predictable and fortunately at that time the drug 6-mercaptopurine and it’s derivative as the azathioprine came along. That was synthesised, as you know, by doctors [Hitchings](https://www.nobelprize.org/prizes/medicine/1988/hitchings/facts/) and [Elion](https://www.nobelprize.org/prizes/medicine/1988/elion/facts/) from Burroughs Wellcome and they were very helpful to us. They sat in with us, educated us about biochemistry, they saw our patients, they knew our dogs by names, and soon we had long term surviving dog kidneys /- – -/. |
| Q11 | It’s very interesting to hear because I’ve learned from you that you had regular visits, I think, by Medawar early and then you were long standing collaboration with Hitchings and Elion. My question is did you have to stimulate our colleagues, our immunology colleagues to come or was it obvious, did you have to recruit them so to say? |
|  | That’s a wonderful question because our local immunologists were not interested. They tolerated our interest they’d say: Joe you can’t do it, why don’t you wait until we solve the problem, but they did not attempt to discourage me, they just said, It won’t work. It wasn’t until [Peter Medawar](https://www.nobelprize.org/prizes/medicine/1960/medawar/facts/), who visited frequently, come to our lab, he would see some of our patients in the hospital and he was /- – -/ that a group of clinicians especially surgeons were interested in the biological problem. I think that he came to Harvard Medical School to give a series of lectures and he spent quite a bit of time in our lab and the immunologist wondered why.  I see.  Joseph E. Murray: A prophet is without honour in his own country. Once we got going and showed some good laboratory results our own immunology department became supportive. But an important thing was, we had the support of our chiefs of the clinical service. The chief of medicine was really behind it, Dr Thorn and Dr Moore achieved the surgery, supported us in every way including finances and so we developed a nice fine team. |
| Q34 | Coming back to the theme of today’s panel discussion which was extremely interesting, I would like to ask you, as we know that some people objected to the development of medicine and surgery at the time, did you experience much opposition, like people came up and told you that one shouldn’t do such things as transplant organs between different individuals? |
|  | Both yes and no. Some of my closest friends at the medical school faculty – I was young then just got out of the army – advised me not to get involved because they said it would ruin my career, but others were supportive and the ones that gave some warning didn’t forcefully stop me, they warned me in a friendly way. |
| Q34 | I guess, as you have said, it was very important that the first operation was successful. |
|  | Absolutely. We had done the operation in dogs many times successfully, but when the twins came, it had to work. We didn’t know whether the exact anatomy of the human was going to be receptive to a transplant kidney, so we went to the pathology department during a post mortem exam about a week or so before the operation and transplanted a kidney in the anatomy lab. All the way through from the beginning to the end, we wanted to be sure the blood vessels would work well, the ureter would fit into the bladder and so we prepared as well as we could. |
| Q20 | Your own career shows the importance very clearly in terms of the collaboration between clinical research and pre-clinical research and the fact that we can work together. I know that you have been a prophet for that ever since. I think a problem that exists in many medical universities and medical schools is to get enough collaboration between the pre-clinical scientists and the clinical scientists. |
|  | For today’s panel we had a breakfast meeting a few days ago and one of the persons in the panel, I won’t mention who, very fine person, said that a physician can never be a scientist. I didn’t say anything, but I don’t know how they define scientist unless it’s somebody who doesn’t work with patients. I hear that all the time and I have been a prophet of clinical investigation because people ask me why did we keep on when there were so many failures. It was the patients who were dying and most of them were young in their early twenties. The families knew that we were experimenting and even though they didn’t expect success, they said, It may not help us but it may help someone in the future. It gave me an indication of the wonderful generosity of human nature. |
| Q45 | That is really wonderful. Staying for a moment with pre-clinical and clinical medicine I would ask you something that relates to the Nobel Prize and some discussion which comes out now and then and which was obvious in some of the journeys last year. That is a question of pre-clinical prizes or prizes to basic science vs prizes to clinical science and to clinical medicine. I think that many of us have a feeling that it would be very nice to be able to give more prizes to clinical medicine. Do you think that clinical medicine is sometimes neglected in this respect? |
|  | Yes, I definitely do. I think Pasteur has a wonderful quotation that there is only one science, basic science and clinical, and they are locked together like the trunk of a tree to the branches. All forms of seeking knowledge, and I think that when a person feels that he or she must be in the laboratory to make scientific progress is stultifying their vision. I feel very strongly that we in the clinical side have certain advantages because we see patients, who have problems that need solving, that the bench scientist is never going to see. I feel very strongly that it would be a great loss to society if clinicians were not also research minded. |
| ID | **0580** |
| Biographical | My father, Dr. Edward E. Thomas was born in 1870 and moved to Texas with his family in a covered wagon in 1874. He grew up in frontier Texas and, with almost no formal schooling went to the University of Louisville, Kentucky, where he received his M. D. His first wife died of tuberculosis, and I was the only child of his second wife. He was 50 years old when I was born on March 15, 1920. He was a solo general practitioner in our small Texas village. Thus, together we span the time from horse and buggy house calls to modern high-tech medicine.  My high school class consisted of about 15 people. I was not an outstanding student even in this small group. I entered the University of Texas in Austin in 1937. In my first semester I made only B grades, but as time went on and the courses became more difficult and challenging I began to enjoy the studies, mainly in chemistry and chemical engineering. I received a B. A. in 1941 and an M. A. in 1943.  During my undergraduate years at the end of the depression money was almost non-existent so I worked at a number of odd jobs. One of the jobs was waiting tables at a girls’ dormitory. One January morning it snowed, a rare event in Texas. As I emerged from the girls’ dormitory, an attractive young woman hit me in the face with a snow ball. I naturally had to catch her and avenge the insult to my male ego. Thus, I meet Dorothy Martin, the Dottie who has participated in all my endeavors up to the present time. We have 3 children, Don Jr. who practices internal medicine in Montana, Jeffrey who is in business in Seattle and Elaine who is a Fellow in infectious diseases at the University of Washington. We have eight grandchildren.  I entered Harvard Medical School in 1943. During medical school Dottie abandoned her journalism work to enter training as a laboratory technician while working to help support us. Her training in writing, laboratory technology and library science has been invaluable in our work. I received the M. D. in 1946.  There followed an internship, a year of hematology training under my life-long friend Dr. Clement Finch, two years in the army, a year of postdoctoral work at Massachusetts Institute of Technology, two years of medical residency, the last as the chief medical resident at the Peter Bent Brigham Hospital in Boston. During that time Dr. [Joseph Murray](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1990/index.html) was a surgical resident and we have been friends and colleagues over the years because of our common interests in transplantation. I was on the wards of the Brigham and helped care for his first kidney transplant patient.  During medical school I became interested in the bone marrow and in leukemia. This interest was intensified by my early association with Dr. Sydney Farber who gave me my first laboratory in the new Jimmy Fund Building. I was fortunate to see the first child with acute lymphoblastic leukemia (ALL) whose remission was induced with an anti-folate drug. I became interested in factors that stimulate marrow function in part due to Allan Erslev’s attempt to demonstrate erythropoietin. During my year at M.I.T. I worked under Dr. John Loofborrow on stimulating factors released from irradiated yeast. I hoped to apply this knowledge to marrow stimulating factors. Fortunately I left the field of stimulating factors because it is only in recent years, with recombinant technology, that great strides have been made in this area.  I had been intrigued by the studies of Dr. Leon Jacobsen et al. who demonstrated that shielding the spleen would protect mice against otherwise lethal irradiation and the subsequent demonstration by Egon Lorenz et al. that a marrow infusion was also protective. These observations were initially thought to be the result of stimulating factors. In 1955, Main and Prehn published their paper showing that a mouse protected against lethal irradiation by a marrow infusion would accept a skin graft from the marrow donor. Their study and the demonstration by Ford et al. using cytogenetic technology of donor chromosomes in such mice made it suddenly clear that the irradiation protection effect was due to the survival of living bone marrow cells.  In 1955, at the invitation of Dr. Joseph Ferrebee I went to the Mary Imogene Basset Hospital in Cooperstown, N. Y., an affiliate of Columbia University. Immediately, we began to work on marrow transplantation in human patients and in the dog, as an outbred animal suitable for clinical care comparable to human patients. Except for an occasional patient with an identical twin, we quickly learned that allogeneic marrow transplants in man were going to be very difficult. Joe Ferrebee and I and our young colleagues concentrated on working with our dogs on many aspects of marrow transplantation. The long cold winters, absence of commuting problems and opportunity for long discussions were conducive to our work. Those years had a deep and abiding influence on subsequent work since most of the basic concepts were laid out during that time.  In 1963 I moved to Seattle at the invitation of Dr. Robert Williams, a famous endocrinologist and first chairman of the Department of Medicine at the University of Washington. Professor Williams recognized that our School of Medicine was in its infancy and rather isolated in the Pacific Northwest. He envisioned the affiliation of all the relevant institutions in the area with the School of Medicine in order to create the critical mass necessary for academic excellence. Within that concept I established my program in the Seattle Public Health Hospital.  The rest of the story seems short in retrospect. The recruitment of some brilliant young co-workers who still work with me, studies of immunology and irradiation biology in the dog, borrowing knowledge of human histocompatibility from Amos, Payne and [Dausset](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1980/index.html), the assembly and training of a critical care team of nurses, and, finally, the demonstration that some patients with advanced leukemia, aplastic anemia or genetic diseases could be cured by marrow transplantation.  Our team of physicians and nurses proved to be stable and dedicated. We did face problems that at times seemed almost insurmountable. In 1972, the Seattle Public Health Hospital was faced with closure by the federal government. After many conferences with the Dean of the School of Medicine, it was apparent that we could not move to the University of Washington. We found temporary space at Providence Hospital for a two year period. In 1975 our team moved into the Fred Hutchinson Cancer Research Center which provided superb facilities and the opportunity to expand the program with the cooperation of the Swedish Hospital Medical Center. While continuing laboratory and animal research, our team has now carried out more than 4,000 human marrow transplants.  It is always difficult to identify the many threads that make up the fabric of a life’s work. I know that my philosophy and ideas have been heavily influenced by more than 20 years of daily interaction with a small group of colleagues, all of whom are now distinguished scientists in their own right. Bob Epstein, Rainer Storb, Dean Buckner, Reg Clift, Paul Neiman and Alex Fefer were with me at the start of the Seattle adventure, and all except Bob are still my daily companions. Ted Graham moved with me from Cooperstown and has played an essential role in our animal research. Along the way we were joined by Joel Meyers, Fred Appelbaum, John Hansen and many others who made major contributions to the achievements honored by this award.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1990*, Editor Tore Frängsmyr, [Nobel Foundation], Stockholm, 1991  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1990 Addendum, June 2005 Dr. Thomas received the Nobel Prize in 1990 at age 70 only a few months after he had retired from patient care. For 10 years he continued local activity and traveled and lectured widely. In the past 5 years he goes in to work approximately 3 days per week in support of the Fred Hutchinson Cancer Research Center activities.  Most recently he has been active in support of stem cell research, a subject that has become a politically-dominated issue. Dr. Thomas has been active in scientific groups interested in clarifying the issues for both the public and legislators. He believes that stem cell research, with appropriate oversight, should be directed by scientists, not politicians. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| ID | 0581 |
| Biographical | My youth held little forecast of a career in biomedical research. I was born on February 22, 1936, in York, Pennsylvania, and spent my childhood in a rural area on the west bank of the Susquehanna River. Those years were pastoral in two regards: I saw little of metropolitan life until I was past the age of twenty-one; and my youth was permeated with the concerns of my father’s occupation as a Lutheran minister, tending to two small parishes. My most tangible legacy from then is a passion for music, sired by the liturgy of the church, fostered by my parents through piano, organ and vocal lessons. I am deeply grateful for the legacy, albeit apostate from the church.  I obtained eight years of elementary education in a two-room school, where I encountered a stern but engaging teacher who awakened my intellect with instruction that would seem rigorous today in many colleges. History figured large in the curriculum, exciting for me what was to become an enduring interest. But I heard little of science, and what I did hear was exemplified by the collection and pressing of wild flowers. My high school was also small: eighty students graduated with me, few of whom eventually completed college. Tests conducted before I graduated predicted a future for me in journalism, forestry or the teaching of music; persons who know me well could recognize some truth in those seemingly errant prognoses.  I had taken naturally to school and was an excellent student from the beginning. But my aspirations for the future were formed outside the classroom. During the summer months of my high-school years, I befriended Dr. Robert Kough, a physician who cared for members of my family. Although he was practicing general medicine in a rural community when I met him, he was well equipped to arouse in me an interest not only in the life of a physician but in the fundaments of human biology. His influence was to have a lasting impact.  I entered Gettysburg College intent on preparing for medical school. But my ambition was far from resolute. Every new subject that I encountered in college proved a siren song. I imagined myself an historian, a philosopher, a novelist, rarely a scientist. But I stayed the course, completing my major in chemistry with diffidence but academic laurels. I met the woman who was to become my only wife. I have never been happier before or since.  I graduated from college still knowing nothing of original research in science. I knew that I would be going to medical school, but I had little interest in practicing medicine. Instead, under the influence of my college faculty, I had formed a vague hope of becoming an educator – by what means and in what subject, I knew not. Learning of this hope, an associate dean at the University of Pennsylvania recommended that I decline my admission to medical school there and, instead, accept an offer from Harvard Medical School. I followed the advice. My pastoral years were at an end.  Boston was a revelation and a revel. I could for the first time sate my burgeoning appetite for the fine arts. Harvard, on the other hand, was a revelation and a trial. I discovered that the path to an academic career in the biomedical sciences lay through research, not through teaching, and that I was probably least among my peers at Harvard in my preparation to travel that path. During my first two years of medical school, I acquired a respect for research from new-found friends among my classmates, particularly John Menninger (now at the University of Iowa) and Howard Berg (now at Harvard University). I sought summer work in a neurobiology laboratory at Harvard but was rebuffed because of my inexperience. I became ambivalent about continuing in medical school, yet at a loss for an alternative.  Two pathologists rescued me. Benjamin Castleman offered me a year of independent study in his department at the Massachusetts General Hospital, and Edgar Taft of that department took me into his research laboratory. There was little hope that I could do any investigation of substance during that year, and I did not. But I became a practiced pathologist, which gave me an immense academic advantage in the ensuing years of medical school. I found the leisure to marry. And I was riotously free to read and think, which led me to a new passion: molecular biology. The passion was to remain an abstraction for another four years, but my course was now set.  I was slowly becoming shrewd. I recognized that the inner sanctum of molecular biology was not accessible to me, that I would have to find an outer chamber in which to pursue my passion. I found animal virology, in the form of an elective course taken when I returned to my third year of medical school, and in the person of Elmer Pfefferkorn. From the course, I learned that the viruses of animal cells were ripe for study with the tools of molecular biology, yet still accessible to the likes of me. From Elmer, I learned the inebriation of research, the practice of rigor, and the art of disappointment.  I began my work with Elmer in odd hours snatched from the days and nights of my formal curriculum. But an enlightened dean gave me a larger opportunity when he approved my outrageous proposal to ignore the curriculum of my final year in medical school, to spend most of my time in the research laboratory. In the end, I completed only one of the courses normally required of fourth year students. Flexibility of this sort in the affaires of a medical school is rare, even now, in this allegedly more liberal age.  My work with Elmer was sheer joy, but it produced nothing of substance. I remained uncredentialed for postdoctoral work in research. So on graduation from medical school, I entered an essential interregnum of two years as a house physician at the Massachusetts General Hospital. That magnificent hospital admitted me to its prestigious training despite my woeful inexperience at the bedside, and despite my admission to the chief of service that I had no intention of ever practicing medicine. I have no evidence that they ever regretted their decision. Indeed, years later, I was privileged to receive their Warren Triennial Prize, one of my most treasured recognitions. I cherish the memories of my time there: I learned much of medicine, society and myself.  Clinical training behind me, I began research in earnest as a postdoctoral fellow in the Research Associate Training Program at the National Institutes of Health in Bethesda, Maryland, a program designed to train mere physicians like myself in fundamental research. In its prime, the Program was a unique resource, providing U.S. medical schools with many of the most accomplished faculty. Without the Program, it is unlikely that I could have found my way into the community of science.  My mentor at N.I.H. was Leon Levintow, who has continued as my friend and alter ego throughout the ensuing years. My subject was the replication of poliovirus, which had a test case for the view that the study of animal viruses could tease out the secrets of the vertebrate cell. I managed my first publishable research: my feet were now thoroughly wet; I had become confident of a future in research.  Midway through my postdoctoral training, Levintow departed for the faculty at the University of California, San Francisco (known to its devotees as UCSF). In his stead came Gebhard Koch, who soon lured me to his home base in Hamburg, Germany, for a year. And again, I had an enlightened benefactor: Karl Habel, who agreed to have N.I.H. pay my salary in Germany, even though I would be in only the first year of a permanent appointment. I repaid the benefaction by never returning to Bethesda.  My year in Germany saw little success in the laboratory, but I learned the joys of Romanesque architecture and German Expressionism. As my year in Germany drew to a close, I had two offers of faculty positions in hand: one at a prestigious university on the East coast of the United States, the other from Levintow and his departmental chairman, Ernest Jawetz, at UCSF. I chose the latter, easily, because the opportunities seemed so much greater: I would have been a mere embellishment on the East Coast; I was genuinely needed in San Francisco. In February of 1968, my wife and I moved from Hamburg to San Francisco, where we remain ensconced to this day.  I continued my work on poliovirus. But new departures were also in the offing. In the laboratory adjoining mine, I found Warren Levinson, who had set up a program to study Rous Sarcoma Virus, an archetype for what we now know as retroviruses. At the time, the replication of retroviruses was one of the great puzzles of animal virology. Levinson, Levintow and I joined forces in the hope of solving that puzzle. We were hardly begun before [Howard Temin and David Baltimore](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html) announced that they had solved the puzzle with the discovery of reverse transcriptase.  The discovery of reverse transcriptase was sobering for me: a momentous secret of nature, mine for the taking, had eluded me. But I was also exhilarated because reverse transcriptase offered new handles on the replication of retroviruses, handles that I seized and deployed with a vengeance. I was joined in this work by a growing force of talented postdoctoral fellows and graduate students. Among our early achievements were a description of the mechanisms by which reverse transcriptase copies RNA into DNA, the characterization of viral RNA in infected cells, and the identification and description of viral DNA in both normal and infected cells.  The work on viral DNA was particularly notable because it was the handicraft of [Harold Varmus](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1989/index.html), who had joined me as a postdoctoral fellow in late 1970. Harold’s arrival changed my life and career. Our relationship evolved rapidly to one of coequals, and the result was surely greater than the sum of the two parts. Together we decided to extend our interests beyond the problems of retroviral replication, to address the mystery of how Rous Sarcoma Virus transforms cells to neoplastic growth.  Others had shown that transformation by Rous Sarcoma Virus could be attributed to a single gene (eventually dubbed *src*) located near the 3′ end of the viral genome. Two problems engaged us: what was the origin of *src*; and what was the protein product of the gene? It was not our lot to find an answer for the second question, although we later played a part in discerning the biochemical function of the *src* protein. But with experiments performed mainly by Dominique Stehelin and Deborah Spector, we found the answer to the first question: *src* is a wayward version of a normal cellular gene (which we would now call a proto-oncogene), pirated into the retroviral genome by recombination (in a sequence of events known as transduction), and converted to a cancer gene by mutation.  In the years that followed, we consolidated our evidence for retroviral transduction, generalized the finding to retroviral oncogenes other than *src*, helped elucidate the sorts of genetic damage that convert normal cellular genes into cancer genes, explored the contributions of proto-oncogenes to the genesis of human cancer, added to the repertoire of proto-oncogenes by several experimental strategies, pursued the physiological functions of proto-oncogenes in normal organisms, and shared in the discovery of the protein kinase encoded by *src*.  I began my career at UCSF as an Assistant Professor of Microbiology and Immunology. I am now a Professor in the same department and in the Department of Biochemistry and Biophysics. I serve as Director of the G. W. Hooper Research Foundation and of the Program in Biological Sciences – the latter, an effort to unify graduate education at UCSF. I am as devoted to teaching as to research: I find the two vocations equally gratifying.  I am a member of the National Academy of Sciences, U.S.A; the American Academy of Arts and Sciences; the American Association for the Advancement of Science (elected an Honorary Fellow); the American Society for Biological Chemistry and Molecular Biology; the American Society for Microbiology; the American Society for Cell Biology; the American Society for Virology; the Federation of American Scientists; Alpha Omega Alpha; and Phi Beta Kappa.  My honors include several awards for teaching from the students and faculty of UCSF; a Doctor of Science Honoris Causa from Gettysburg College; the American Association of Medical Colleges Award for Distinguished Research; the California Scientist of the Year; the Albert Lasker Award for Basic Medical Research; the Passano Foundation Award; the Warren Triennial Prize from the Massachusetts General Hospital; the Armand Hammer Cancer Prize; the Alfred P. Sloan, Jr. Prize from the General Motors Cancer Foundation; the Gairdner Foundation International Award; the American Cancer Society National Medal of Honor; the Lila Gruber Cancer Research Award from the American Academy of Dermatology; the Dickson Prize in Medicine from the University of Pittsburgh; the American College of Physicians Award for Basic Medical Research; and the Nobel Prize in Physiology or Medicine for 1989. Most of these have been shared with Harold Varmus.  I am married to Kathryn Ione Putman and have two sons with her, Dylan Michael Dwight and Eliot John Putman. These three have given me a gift of affection and forebearance that I cannot hope to repay. My mother and father have reached their eighth and ninth decades, respectively, and were able to join us for a joyful time at the Nobel ceremonies in Stockholm. My brother, Stephen, is a distinguished solid-state physicist and now Professor at the University of Illinois; my sister, Catharine, is arguably the finest elementary school teacher in Virginia.  If offered reincarnation, I would choose the career of a performing musician with exceptional talent, preferably, in a string quartet. One life-time as a scientist is enough – great fun, but enough. I am a self-confessed book addict, an inveterate reader of virtually anything that comes to hand (with the notable exceptions of science fiction and crime novels). I enjoy writing and abhor the dreadful prose that afflicts much of the contemporary scientific literature.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1989*, Editor Tore Frängsmyr, [Nobel Foundation], Stockholm, 1990  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1989 Addendum, January 2018 J. Michael Bishop is University Professor, Director Emeritus of the G.W. Hooper Research Foundation and Chancellor Emeritus at the University of California, San Francisco (UCSF).  Michael was born and raised in rural Pennsylvania, and educated at Gettysburg College, Harvard Medical School and the Massachusetts General Hospital. He began his research career working on the replication of poliovirus, before shifting his attention to the fundamental mechanisms of tumorigenesis. Together with Harold Varmus he directed the research that led to the discovery of proto-oncogenes – normal genes that can be converted to cancer genes by genetic damage. This work eventually led to the recognition that all cancer arises from the malfunction of genes, and has provided new strategies for the study and management of cancer. Michael and Harold shared the 1989 Nobel Prize for Physiology or Medicine for their work.  Michael continues to study proto-oncogenes – their functions in normal cells and their role in the genesis of cancer. He has served as chair of the National Cancer Advisory Board, as a trustee of the Salk Institute for Biological Studies, as member of the Board of Directors for the Burroughs Wellcome Foundation, and as scientific advisor to a variety of granting agencies, research institutes and biotechnology firms.  For more biographical information, see: Bishop, J. Michael, *How to Win a Nobel Prize. An Unexpected Life in Science*. Harvard University Press, London, 2003. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | **0582** |
| Biographical | I was born in the shadow of World War II, on December 18, 1939, on the south shore of Long Island, a product of the early twentieth century emigration of Eastern European Jewry to New York City and its environs. My father’s father, Jacob Varmus, left a village of uncertain name near Warsaw just after the turn of the century to become a farmer in Newburgh, New York, and later a hatter in Newark, New Jersey. His wife, Eleanor, was a victim of the influenza epidemic of 1918, when my father was eleven. My mother’s parents, Harry and Regina Barasch, came from farming villages around Linz, Austria, to found a children’s clothing store, still in existence, in Freeport, New York. As children of immigrants, my parents both had notable educations, my father (Frank) at Harvard College (until financial considerations required him to withdraw after two years) and at Tufts Medical School, and my mother (Beatrice) at Wellesley College and the New York School of Social Work.  Three years before my birth, my parents settled in Freeport, my mother’s home town, where my father established a general medical practice, while my mother commuted to a social services job in New York City. With the entry of the United States into the War, however, my father was assigned to an Air Force Hospital near Winter Park, Florida, and my first memories were to be of long beaches, and bass fishing on a lake with alligators. We remained in Florida, spared the pain of war, until early in 1946. In the interim, my only sibling, Ellen Jane, was born; she is now a genetic counselor and mother of three in Berkeley, California.  My growing-up in Freeport was undemanding and in many ways privileged. The public schools I attended were dominated by athletics and rarely inspiring intellectually, but I enjoyed a small circle of interesting friends, despite my ineptitude at team sports and my preference for reading. Life was enriched by frequent outings to Jones Beach State Park (where my father was the medical officer for many years), family skiing vacations to New England, and many outdoor adventures with the Boy Scouts and later the Putney Summer Work Camp.  The most decisive turn in my intellectual history came in the fall of 1957, when I entered Amherst College intending to prepare for medical school. The evident intensity and pleasure of academic life there challenged my presumptions about my future as a physician, and my course of study drifted from science to philosophy and finally to English literature. At the same time, I became active in politics and journalism, ultimately serving as the editor of the college newspaper. Following graduation from Amherst, a Woodrow Wilson Fellowship enabled me to test the depth of my interest in literary scholarship by beginning graduate studies at Harvard University. Within the year, I again felt the lure of medicine and entered Columbia College of Physicians and Surgeons. Although I began medical school with strong interests in psychiatry and international health, I was influenced towards basic medical sciences by the lectures of (among others) Elvin Kabat, Harry Rose, Herbert Rosenkrantz, Erwin Chargaff and Paul Marks. My desires to practice medicine abroad were also tempered by an apprenticeship in a mission hospital in Bareilly, India.  In preparation for a career in academic medicine, I worked as a medical house officer at Columbia-Presbyterian Hospital from 1966 to 1968, and then joined Ira Pastan’s laboratory at the National Institutes of Health as a Clinical Associate. This provided me with my first serious exposure to laboratory science and to the excitement of experimental success. Our studies of bacterial gene regulation by cyclic AMP (in collaboration with Bob Perlman and Benoit de Crombrugge) and the evening courses offered to incipient physician-scientists at NIH stimulated me to seek further postdoctoral training in molecular biology, specifically in tumor virology. This decision, combined with an interest in trying life in the San Francisco area, led me to [Mike Bishop’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1989/index.html) door in 1969. I joined him as a post-doctoral fellow at UC San Francisco in 1970, was appointed Lecturer shortly thereafter, and in 1972 became a regular member of the faculty in the Department of Microbiology and Immunology (led initially by Ernest Jawetz, later by Leon Levintow), ascending to the rank of Professor by 1979.  Throughout the nearly two decades I have been associated with UCSF, most of my research interests have been focused upon the behavior of retroviruses: various aspects of their unusual life cycle, the nature and origin of their transforming genes, and their potential to cause genetic change. Much of this work has been performed in collaboration with Mike Bishop, particularly in the years before 1984 when we shared facilities, personnel, and funds. Other faculty interactions during the 1970’s stimulated work on hemoglobinopathies (with Y.W. Kan) and on glucocorticoid action (with Gordon Tomkins and Keith Yamamoto). During the 1980’s, I also worked extensively on hepatitis B viruses in collaboration with Don Ganem (who was initially a post-doctoral fellow and later a faculty colleague). My career at UCSF has been greatly enhanced by the extraordinary collegiality of the faculty, the excellence of our graduate and medical students, an unremitting stream of first-rate post-doctoral fellows, and the loyalty of our staff research associates, especially Suzanne Ortiz, Nancy Quintrell, and Jean Jackson.  In 1969 I married Constance Louise Casey, then a reporter for *Congressional Quarterly* in Washington, D.C., her home town, and now the Book Critic for the *San Jose Mercury News*. Shortly after we moved to California, my parents died, my mother of breast cancer in 1971, my father of coronary artery disease in 1972. Our lives have been made more interesting by the births of Jacob Carey in 1973 and Christopher Isaac in 1978; the boys attend public schools in San Francisco, root for the Giants, and are musically-inclined (Jacob, especially, is a talented trumpeter). California weather has promoted my love of outdoor sports, particularly bicycling, running, backpacking, skiing, and fishing, but I also maintain strong interests in the arts – literature, theatre, music, and film. We have lived almost continuously since 1971 in a Victorian house in the Haight-Ashbury district of San Francisco, with the exception of 1978-79, when I was a sabbatic visitor in Mike Fried’s laboratory at the Imperial Cancer Research Fund in London, and 1988-89, when the award of a Nieman Fellowship to Connie brought her to Harvard and me to the laboratories of Bob Weinberg and [David Baltimore](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html) at the Whitehead Institute.  Most of the significant honors I have received have been awarded jointly to Mike Bishop, with whom I also share the Nobel Prize. The earlier awards include California Scientist of the Year (1982), the Albert Lasker Basic Medical Research Award (1982), the Passano Foundation Award (1983), the Armand Hammer Cancer Prize (1984), the Alfred P. Sloan Prize from the General Motors Cancer Foundation (1984), the Gairdner Foundation International Award (1984), and the American College of Physicians Award (1987). In addition, I was elected to the National Academy of Science (1984) and the American Academy of Arts and Sciences (1988). I received an honorary degree from Amherst College (1985) and the Alumni Gold Medal from the College of Physicians and Surgeons (1989), and I have been the American Cancer Society Professor of Molecular Virology since 1984. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0582** |
| Interview |  |
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| ID | **0583** |
| Biographical | I have never wanted to check out the family folklore that we could be traced back to a dominie at the hamlet of Balquhidder in the Scottish highlands. The romantic notion that I might have tenuous roots with two great traditions – with the political rebelliousness of Rob Roy McGregor and with the Scottish tradition of rural education, arguably one of the best anywhere – was too enjoyable to be seriously tested. The outcome, the fourth in an issue of five boys born into a staunch Baptist home, meant that from the beginning I was taught to be respectful of others no less than myself, influencing ever since both my political and administrative attitudes. My father, a mining engineer and colliery manager, gave his brood many advantages not least of which, for me, was his love of singing which gave music a central place in our lives.  Apart from two periods of intense study, of music between the ages of 12 and 14 and of mathematics between the ages of 14 and 16, I coasted, daydreaming, through most of my school years. The imprinting mathematical influence was Dr Waterson at Beath High School, a brilliant and rumbustious teacher, who more or less man-handled me into sitting the competitive entrance examination for St Andrews University. This led to an interview with the Vice-Chancellor, the redoubtable Sir James Irvine, flanked by elderly academic worthies, all poking into the mind of a nervous 15 year old boy. I was awarded the Patrick Hamilton Residential Scholarship, mercifully unaware at the time that the family budget couldn’t otherwise have stretched to yet another university student.  As a condition of the Patrick Hamilton Residential Scholarship I spent my undergraduate years in St Salvator’s Hall, a fine new building modelled on the Oxbridge colleges. The young aficionados of St Salvator’s Hall in my day were culled from every imaginable class and state from the United Kingdom and overseas. The few intimate years I spent in this company were an extraordinarily mind-broadening experience for the country boy from the coalfields of Fife, no doubt much as the scholarship architects had intended.  I chose to study Medicine mainly under the influence of an elder brother, William, a graduate in Medicine at St Andrews some years earlier. In the cold, forbidding, greyness of St Andrews – with its dedication to “causes purely spiritual and intellectual, to religion and learning” (Andrew Lang) – I learned, for the first time, the joys of substituting hard, disciplined study for the indulgence of day-dreaming. Undergraduate prizes seemed to confirm that I was working harder than my colleagues in a new-found love affair with knowledge. An important catalyst in my conversion to scholarship was my first year encounter with Professor D’Arcy Wentworth Thompson, last of the great Victorian polymaths, author inter alia of the classic allometric study “On Growth and Form”, and an intellectual giant if ever there was one.  I met Hilary Vaughan at a Student Ball in 1944 and we married in the summer of 1946, as soon as I graduated. I joined the Physiology Department under Professor R.C. Garry in October 1946 and Hilary, completing her degree in Biochemistry, was the best student I ever had. Had she chosen a sectarian approach to study she would have become a visible star but her eclectic pursuit of knowledge and her unwavering support for her family led her to study law and choose poetry as a distillate of her wisdom. Intellectually she was the most exciting person I have ever known and, quite simply, the mainspring of my life until she died in 1986.  My first year of research in Garry’s laboratory introduced me to some simple ideas which, in a variety of ways, have dominated my thinking ever since. Garry was trying to find out how the intestine was able to absorb sugars selectively. Na iodoacetate treatment eliminated selective absorption and Verzar had deduced that the selectivity was based on phosphorylation. Learning that Garry’s research student was showing that iodoacetate destroyed the intestinal epithelium, I wondered if iodoacetate was a general poison. What did it do to blood pressure, for example? When I developed the technology to show that, in rats, iodoacetate rapidly and irreversibly reduced the blood pressure to about 40 mm Hg, I was faced with the question which has influenced my thinking ever since: when and to what extent does local blood flow act as a metabolic throttle?  We went to Singapore at the end of 1947 – an inevitable result of marriage, debts accumulated to pay for the completion of my medical studies, and pitiful academic prospects. As a Lecturer at the King Edward VII College of Medicine I experimented with learning how to teach Physiology; and I learned that experimenting in Physiology was too difficult if the inspiration was no more than wishful thinking. Nevertheless, I made some progress in relating mucosal blood flow to rates of intestinal absorption to use in my carpet-bagging efforts later in London.  We paid off our debts, we learned some, made friends and returned in 1950 with a larger view of life. I had, however, no home, no income of any kind and no prospects whatsoever. I knocked on the doors of Physiology Departments all over London and met more sympathy than I expected; then a chance encounter with Professor Garry in Oxford Street led me to William Weipers, subsequently knighted, Director of the newly “nationalised” University of Glasgow Veterinary School. He gave me the opportunity to start a new Physiology Department, and during the next eight years I built a state-of-the-art physiology teaching laboratory based on my enduring belief that our brains work best when doing focuses our thinking. We had a daughter, Stephanie, born in 1951; I built a workshop-coupled research laboratory providing the most advanced cardiovascular technology I knew; and persuaded George Smith and Adam Smith, academic surgeons, to join me.  As I slowly learned, like a primitive painter, how to be an effective experimenter, ideas began to ferment. Work with Adam Smith on the effects of 5-hydroxytryptamine on gastric acid secretion was to surface again later on in my interest in the pharmacology of histamine-stimulated acid secretion. Work with George Smith, concerned with finding ways of increasing the supply of oxygen to the heart in patients with narrowed coronary arteries, led me to propose that reducing myocardial demand for oxygen by annulling cardiac sympathetic drive might be equally effective. By 1956, I had clearly formulated the aim, based on Ahlqvist’s dual adrenoceptor hypothesis, of finding a specific adrenaline receptor antagonist. Egged on by their local representative, I successfully approached I.C.I. Pharmaceuticals Division for help and ended up being employed by them at their exciting new laboratories at Alderley Park, Cheshire. During my six years with them Dr Garnet Davey (subsequently Research Director) constantly supported me and, I have no doubt, fought many battles on my behalf to keep the initially controversial programme going. All I ever promised was that I was sure I could develop a new pharmacological agent which might answer a physiological question. Any utility would be implicit in that answer.  My years at I.C.I., between 1958-1964, were some of the most exciting of my life. I was assigned a brilliant chemist, John Stephenson. He taught me about modern deductive organic chemistry; how to be more than merely curious about a molecule with an interesting biological effect: how to ask questions about it. He converted me to pharmacology. Indeed, my whole experience at I.C.I. was an educational tour de force. I had to learn how to collaborate across disciplines, how to change gears when changing from research to development, how to make industry work – in short, how to be both effective and productive.  Among the numerous people who were involved in bringing the first beta-receptor antagonist to the marketplace, three played crucial roles. Bert Crowther masterminded the medicinal chemistry development. Genial, enthusiastic and highly experienced he was a splendid colleague. Bill Duncan, biochemist, brilliantly controlled the linchpin between research and development. He illuminated the black box between drug delivery and effect, developing analytical methods for estimating the levels and tissue distribution of a drug and its metabolites which allowed us to monitor and control toxicity tests, human pharmacology and clinical trials. Duncan brings brio and bravura to everything he does; and he is reliably my severest critic. Without him I would have made many more mistakes than I did. Brian Pritchard, clinical pharmacologist at University College, London, spearheaded the clinical development of the beta-adrenoceptor antagonists and crusaded on their behalf – as well as revolutionising their use by his discovery of their antihypertensive effect.  By 1963, I faced opposing pressures. I saw that the success of the beta-receptor antagonist programme would suck me more and more into the role of giving the young propranolol technical support and promotion – just as I was itching to start a new programme. I was convinced that the histamine antagonists of the day were analogous to the alpha-receptor antagonists and that the equivalent of a beta-receptor antagonist was needed to block, for example, histamine-stimulated acid secretion. Then Edward Paget, Head of Pathology at I.C.I., who had accepted the Research Directorship at Smith, Kline & French Laboratories asked my advice about finding a pharmacologist to run the biological research there. Half-jokingly, I asked what was wrong with me. So we made a deal: I would run his biological research provided I had a free hand to run my new project. Bill Duncan joined me to run the Biochemistry Department, so maintaining a tremendously successful partnership which lasted 15 years.  The histamine project, modelled by analogy with the beta-adrenoceptor project, was also somewhat controversial at the beginning. It succeeded because of the faith of my managers and the scientific skill and devotion of my colleagues. When I was struggling at the front, Bill Duncan was defending the rear. Mike Parsons adopted the new pharmacology with rare enthusiasm and commitment and became one of the doughtiest colleagues I have ever had. I think we made a good team. Graham Durant made the initial breakthrough with a partial agonist, and Robin Ganellin exploited that lead by brilliant, deductive, medicinal chemistry. The years I spent working with Ganellin were the most sustained, intellectually exciting and productive period of medicinal chemistry I have ever experienced. John Wyllie, surgeon from University College London, contributed the last critical piece in a successful mission.  By 1972, the H2-receptor antagonist programme was launched, cimetidine was in development and I was looking for a new project. I was now totally committed to arranging marriages between bioassay and medicinal chemistry. Obvious candidates existed, such as 5-hydroxytryptamine, but other shadowy ideas were lurking about in my imagination.  The potential freedom from commercial constraints in academia was looking more and more attractive. Yet, when I was eventually offered the Chair in Pharmacology at University College, London, I was apprehensive about my ability to achieve my new goals. I had developed two ambitions. In research, I wanted to establish the medicinal chemistry/bioassay conjugation as an academic pursuit, as exciting to the imagination as astrophysics or molecular biology. In teaching, I wanted to offer a general pharmacology course based on chemical principles, biochemical classification and mathematical modelling. In the event I achieved neither of my ambitions. I failed to raise support for my medicinal chemistry project – by academic peerreview standards my proposals were altogether too wispy and expensive. My ideas about teaching based on a catechismal approach to drugs in general, rather than cataloguing drugs in particular, turned out to have too many curricular difficulties. I did help to set up an undergraduate course in medicinal chemistry and made progress in modelling and analysing pharmacological activity at the tissue level, my new passion. But after four years, I was suffering from withdrawal symptoms from lack of a chemical collaboration. Thus, I eagerly accepted [John Vane’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1982/index.html) invitation to join the Wellcome Foundation.  My years at the Foundation (from 1977 to 1984) were an emotional roller-coaster. I wanted to make use of ideas I had been chiselling out, over the years, about the differences between successful and failed industrial projects. The division I took over at Wellcome, however, was remarkable for its traditional, conservative, ways and feudal structures. Entrenched attitudes can absorb reformist efforts like a punch bag. Yet despite disappointment in my managerial role, I made great progress in my own research. Working with brilliant young investigators such as Paul Leff, I began to see analytical pharmacology as a viable discipline. I had found myself a new mission – and once more my recurring dilemma between corporate commercial needs and personal scientific ambitions was solved unexpectedly. The Wellcome Foundation offered me the chance to establish a small academic research unit, modestly funded, but with total independence. The real opportunity, however, came from King’s College, London. The College and Medical School between them have not only solved problems and smoothed diffficulties they have positively welcomed and supported my small unit. In intellectual terms the last five years at King’s have been the most productive in my life. Surrounded by talented researchers and PhD students, I feel I have found my niche at last. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0583** |
| Interview |  |
| Q19 | Professor Sir James Black, welcome to this Nobel interview. The Nobel Prize that you were awarded in 1988 was kind of unusual I would say, you got the prize for the discoveries in drug research, and this was the first prize in this area in 31 years. Were you very surprised when you got the news? |
|  | You bet that. Astonished. Yes, I didn’t think it was prize worthy frankly.  No? Do you think it was?  Sir James Black: I have no way of judging that. I mean I just played the cards that someone dealt me. |
| Q17 | But the drug that you have worked on is broadly spread today, it is beta-blockers from the beginning, everybody knows what it is. |
|  | Yes, but you see my notoriety is by an accident, the accident is that the drugs I developed made a lot of money. Now the science could have just been the same and the drugs might not have made much money and then I wouldn’t be here. I’m not here for the science; I’m here because of the notoriety of the widespread use. |
| Q16 | Why do you think so? Don’t you think that the development of drugs, there is commercial interests in it … |
|  | The citation was for a new method and that’s true in this sense that it so happened that when I got the idea for my first drug a discovery had been made and the discovery was that we have hundreds of messenger molecules that make our cells work together, we call them hormones. The discovery was that these messenger molecules have two properties, a property of, a cognition property, they recognise a cell which has a sight on it that they can, so there’s recognition and then they do some things to switch it on. The discovery was that these two properties, cognition and efficacy were separable. I wanted to stop the effects of adrenalin on the heart and so I reckoned maybe I can take adrenalin and get rid of its efficacy and leave behind the affinity which in essence was what happened. |
| Q16 | But don’t you think that most of the discoveries are kind of a surprise even for the discoverer? |
|  | It’s hard to go back, you know, we take memories and we smooth them like pebbles so we’re comfortable with them and I think memory isn’t about recollection, it’s about reconstruction and so I’m not at all sure now, at this stage, what I was actually thinking or planning or doing, all I know is outcomes and … But motives are very hard to be sure about. |
| Q69 | You have worked both for the university and for companies, industries … / How do you they compare? |
|  | About half my life in each. / I have worked as an employee for three drug companies and I have collaborated with a fourth and these companies are like people, they have quite different cultures, characters, but like people they have common diseases. I once thought I’d write a textbook of institutional pathology and the diseases are largely problems of magnitude, problems of communication. A technical company is very people intensive, it’s not something that you can scale up with the equipment and machinery, you have to have a lot of people and when you have a lot of people, you have the problems of communicating between them so that’s the industrial side. It’s very hard to make a general statement about companies because they’re all different. Universities on the other hand, the problem with universities is they have been changing continuously during my association with them … |
| Q69 | In what way? |
|  | … and I’m not too comfortable about the way we’re going, because more and more, the big universities, are becoming like companies, more and more they’re concerned mainly with the cash flow, more and more are they concerned with whether or not the intellectual output of the people can be turned into property and start-up companies, spin out companies, there’s huge obsession with making money and I don’t think this is compatible with the job of a university. The job of the university is to make discoveries, not to make inventions. Discoveries are about finding out something which, if you like, is already there but no one knew, whereas an invention … When I made a drug, that was an invention, there hadn’t been anything there before, but the invention was built on other people’s discoveries. If Ray Ahlquist and so on had not done their work, I couldn’t have done mine. So the job of academia is to make discoveries, it’s the job of business to make inventions I think and so I’m unhappy about this. One of the worrying things today is that scientists, because of pressure on them to raise money, either from grants or from private venture capital, are making promises, you know, once we get the protein, once we know it’s structure, once we get the gene, then we’ll get the drug. This is unwise because we’re leading the public, who ultimately are our paymasters, we’re leading them to have expectations. Now if … |
| Q69 | So you’re afraid of a blacklash … |
|  | I am afraid of this. If I was running a business and was making my shareholders promise like that they’d have me in prison, but scientists can get away with it. We’ll not get away with it forever, time will catch up with us because here’s the problem. The rate of accumulation of knowledge, the information, is so vast, none of us can take it in, but knowledge just adds, and you might think that all this knowledge will make progress but progress isn’t based on knowledge, it’s based on ideas, and whereas knowledge adds, ideas have to substitute. You have to replace the idea you already have with a new one and that’s painful and that’s slow and that is the rate limiting stamp. For example we’ve had now the human genome project, that has taken 125 years from the time when chemists were extracting material from spermatozoa, from the nucleus and getting out this gooey stuff and then showing there was four bases in there, that was in the 1870s, staying right through now to get a nearly complete map of the sequence of bases in the human genome but that’s, it’s just not even the beginning of the story because now the problems are conceptual. Suddenly we find there’s only about a third of the genes we expected, and we don’t know how they work. The big problem …  Why and what and …  Sir James Black: … and this is going to be the slow thing, our exploitation of the knowledge about the genome is going to require changes in our conceptions from what they are at the moment. At the moment we are still thinking that our gene does our job and so if you can find out the job the gene does, why you can control it, but it isn’t going to be like that.  No, it sounds too simple.  Sir James Black: It’s too simple.  So even if you get more money for thinking the process will take time anyhow …  Sir James Black: Yes.  … even if more people will do it?  Sir James Black: There are some problems you cannot solve just by throwing money at them. AIDS for example, we’ve been trying for what 25 years to get a vaccine for AIDS, so far we’ve failed. Now we’ve been making vaccines, you know, for a century. We want a vaccine, so we throw money at it and we’ve failed and we have to learn from these things that the wish is not enough, there has to be the understanding which is the platform for achieving what you want to do.  Yes, the creative process takes time.  Sir James Black: And the time, the slowness, is the thinking, the concept, that’s the hard bit. |
| Q6 | Has your life changed after winning the Nobel Prize? |
|  | There is a period when it’s hectic, yes.  And you become an official person …  Sir James Black: And the problems are we’re not trained, we don’t know how to handle it, we’re not film stars.  No. How did you manage?  Sir James Black: Badly.  And that means?  Sir James Black: It means I had to make a lot of rather messy compromises I suppose, compromises between doing what other people wanted me to do and doing what I wanted to do which was to get on with my work. One of the things people want you to do in this sort of ‘star business’ is give lectures, attend seminars and so on and I just happen not to like it. I have one thing I enjoy and that’s sitting in a room with maybe 10-15 young graduate scientists and just talking. Then I’m happy, but these stand-up lectures I don’t like. |
| Q3 | I understand. So what was the problem that you were working on that was known since 1905? |
|  | What I’ve been doing is I gave you the principle earlier and I just keep applying that principle, that’s why I’ve applied that to adrenalin, to histamine, to another small molecule called 5-hydroxytryptamine and then to a bigger molecule cholecystokinin and gastrin, but the principle is always the same. These molecules are messenger molecules, they do things, so I recognise each of them as being a messenger molecule because I have a piece of tissue or something which responds to them characteristically, that is I have an assay. I have the assay, I have the hormone, I expose one to the other and the system does something, it may secrete, contract or … I take this molecule and I walk around it, look at it and think, Well now, maybe if I take that piece off, maybe that will get rid, see. I make this new molecule and now I compete the hormone molecule with my new molecule and … First of all I try it on its own, does it do anything? Then I compete them. It’s an iterative process, it’s like Darwinian evolution only I synthesise, I test, I re-synthesise and on we go.  The one thing which is certain is it’s slow and this is why, in the drug industry today, this method which I have described and which everybody who’s tried it, it always works, you just don’t know how long it’s going to take. The beta-blockers was six years, histamine antagonist was nine years, 5-HTP was eight years, these are long periods. The drug industry has become inpatient, and it has now, if you like, got rid of this method which works and they’ve replaced it with a method which they don’t know yet if it’s going to work and this is now technological advances. We can now screen a hundred thousand molecules a day against proteins in one can or another, we have the technology to make hundreds of thousands of molecules, we have the technology to screen for them and what they’re looking for are leads, a molecule which does something. I never start a project without a lead and yet it still takes me these long periods of time. At the moment the drug industry has doubled its expenditure on research and development in the last ten years and the productivity as judged by newer drugs coming out has fallen by a fifth. This is not sustainable, and this is the thing, our earlier conversation about can you force drug discovery just by throwing money at it? The evidence is you can’t. There was a very well-known American philanthropist, but he was a psychiatrist, a scientist, he had trained as an artist, he became a great collector of paintings, gave them all to the Met eventually, but near the end of his life he summed his life up by saying that art is a passion pursued with discipline. Science is a discipline pursued with passion; passion is the engine of science and if you haven’t got that then give it up. |
| ID | 0584 |
| Biographical | I was born in New York City on a cold January night when the water pipes in our apartment froze and burst. Fortunately, my mother was in the hospital rather than at home at the time. My father emigrated from Lithuania to the United States at the age of 12. He received his higher education in New York City and graduated in 1914 from the New York University School of Dentistry. My mother came at the age of 14 from a part of Russia which, after the war, became Poland; she was only 19 when she was married to my father. My first seven years were spent in a large apartment in Manhattan where my father had his dental office, with our living quarters adjoining it.  My brother was born about six years after I was, and shortly thereafter we moved to the Bronx, which was then considered a suburb of New York City. There were still many open lots where children could play and large parks, including the Bronx Zoo, to which I was very much devoted. My brother and I had a happy childhood. We went to a public school within walking distance of our house. Our classrooms were generally quite crowded, but we received a good basic education.  I was a child with an insatiable thirst for knowledge and remember enjoying all of my courses almost equally. When it came time at the end of my high school career to choose a major in which to specialize I was in a quandary. One of the deciding factors may have been that my grandfather, whom I loved dearly, died of cancer when I was 15. I was highly motivated to do something that might eventually lead to a cure for this terrible disease. When I entered Hunter College in 1933, I decided to major in science and, in particular, chemistry.  By this time my father was not financially well-off since he, like many others, had invested heavily in the stock market, and in the crash of 1929 had gone into bankruptcy. Fortunately, he still had his profession and his loyal patients. Had it not been that Hunter College was a free college, and that my grades were good enough for me to enter it, I suspect I might never have received a higher education. My brother also was able to take advantage of a free higher education, going to the College of the City of New York where he studied physics and engineering.  I remember my school days as being very challenging and full of good comradery among the students. It was an all-girls school and I think many of our teachers were uncertain whether most of us would really go on with our careers. As a matter of fact, many of the girls went on to become teachers and some went into scientific research. Because of the depression, it was not possible for me to go on to graduate school, although I did apply to a number of universities with the hope of getting an assistantship or fellowship.  Jobs were scarce and the few positions that existed in laboratories were not available to women. I did get a three-month job teaching biochemistry to nurses in the New York Hospital School of Nursing. Unfortunately, because of the trimester system, the same job would not have been available again for nine months. By chance, I met a chemist who was looking for a laboratory assistant. Although he was unable to pay me any salary at that time, I decided that the experience would be worthwhile. I stayed there for a year and a half and was finally making the magnificent sum of $20 a week. By then I had saved some money and, with help from my parents, entered graduate school at New York University in the fall of 1939. I was the only female in my graduate chemistry class but no one seemed to mind, and I did not consider it at all strange.  After a year of graduate studies I had finished all the required courses but now needed to do the research work for my Master’s degree. During this period, I took a job as a teacher-in-training and then as a substitute teacher in the New York City secondary schools, teaching chemistry, physics and general science for two years. In the meantime, I did my research work at night and on week-ends at New York University, and obtained my Master of Science degree in chemistry in 1941.  By this time, World War II had begun and there was a shortage of chemists in industrial laboratories. Although I was finally able to get a job in a laboratory, it was not in research. I did analytical quality control work for a major food company. After a year and a half, during which I learned a good deal about instrumentation, I became restless because the work was so repetitive and I was no longer learning anything. I applied to employment agencies for a research job, and was chosen to go to a laboratory at Johnson and Johnson in New Jersey. Unfortunately, that laboratory was disbanded after about six months. At that time I was offered a number of positions in research laboratories but the one which intrigued me most was a position as assistant to [George Hitchings](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1988/index.html). My thirst for knowledge stood me in good stead in that laboratory, because Dr. Hitchings permitted me to learn as rapidly as I could and to take on more and more responsibility when I was ready for it. From being solely an organic chemist, I soon became very much involved in microbiology and in the biological activities of the compounds I was synthesizing. I never felt constrained to remain strictly in chemistry, but was able to broaden my horizons into biochemistry, pharmacology, immunology, and eventually virology.  At the same time, I was eager to get my doctorate degree and began to go to school at night at Brooklyn Polytechnic Institute. After several years of long range commuting, I was informed that I would no longer be able to continue my doctorate on a part-time basis, but would need to give up my job and go to school full-time. I made what was then a critical decision in my life, to stay with my job and give up the pursuit of a doctorate. Years later, when I received three honorary doctorate degrees from George Washington University, Brown University and the University of Michigan, I decided that perhaps that decision had been the right one after all. Unfortunately, neither of my parents lived to see this recognition.  The work became fascinating almost from the very beginning. We were exploring new frontiers, since very little was known about nucleic acid biosynthesis or the enzymes involved with it. I had been assigned quite early to work on the purines and, with the exception of a few deviations into the pteridines and into some other condensed pyrimidine systems, the remainder of my work concentrated almost completely on the purines. Each series of studies was like a mystery story in that we were constantly trying to deduce what the microbiological results meant, with little biochemical information to help us. Then, in the mid-1950’s came the work of Greenberg, Buchanan, [Kornberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1959/index.html) and others which elucidated the pathways for the biosynthesis and utilization of purines, and many of our findings began to fall into place. When we began to see the results of our efforts in the form of new drugs which filled real medical needs and benefited patients in very visible ways, our feeling of reward was immeasurable.  Over the years, my work became both my vocation and avocation. Since I enjoyed it so much, I never felt a great need to go outside for relaxation. Nevertheless, I became an avid photographer and traveler. Possibly my love for travel stems from the early years when my family seldom went away on vacation. Thus, my curiosity about the rest of the world did not begin to be satisfied until I began to travel. I have traveled fairly widely over the world, but there still remain many places for me to explore. Another major interest is music, not because I am musically talented, but because I love to listen to it. I am an opera lover and have been a subscriber to the Metropolitan Opera for over 40 years. I also enjoy concerts, ballet and theater.  Although I never married, my brother fortunately did, and I have had the pleasure of watching his three sons and daughter grow up. Several of them now have children of their own. We have been a close-knit family, although often separated by distance, and have shared each other’s happiness, sorrows, and aspirations.  In my professional career I was promoted frequently, and in 1967 I was appointed Head of the Department of Experimental Therapy, a position which I held until I retired in 1983. This department was sometimes termed by some of my colleagues a “mini-institute” since it contained sections of chemistry, enzymology, pharmacology, immunology and virology, as well as a tissue culture laboratory. This made it possible to coordinate our work and cooperate in a manner that was extremely useful for development of new drugs.  I have been associated with the National Cancer Institute in many capacities, from 1960 when I served on one of its study sections, to serving later on a number of its advisory committees and the Board of Scientific Counselors for the Division of Cancer Treatment, and most recently as a member of the National Cancer Advisory Board. I have taken an active part in the American Association for Cancer Research, serving on its Board of Directors, its program committees, and in 1983 – 84 as its President. In addition, I have served on Advisory Committees for the American Cancer Society, the Leukemia Society of America, and a number of committees for the Tropical Disease Research division of the World Health Organization, currently serving as Chairman of the Steering Committee on the Chemotherapy of Malaria. I am a member of the American Chemical Society, the Royal Society of Chemistry, the Transplantation Society, the American Society of Biological Chemists, the American Society of Pharmacology and Experimental Therapeutics, the American Association for Cancer Research, the American Society of Hematology, the American Association for the Advancement of Science, the American Association of Pharmaceutical Scientists, and am a Fellow of the New York Academy of Sciences.  After my official retirement as Department Head from Burroughs Wellcome, I have remained there as a Scientist Emeritus and Consultant, and have tried to take an active part in the discussions, seminars and staff meetings relating to research. In addition, I have become a Research Professor of Medicine and Pharmacology at Duke University and each year work with one third-year medical student who wishes to do research in the areas of tumor biochemistry and pharmacology. This has been a very stimulating experience and one that I hope to continue for some time to come. I serve on a number of editorial boards and continue to lecture and write. In a sense, my career appears to have come full circle from my early days of being a teacher to now sharing my experience in research with the new generations of scientists. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
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| ID | 0585 |
| Biographical | My forebears all came from the United Kingdom. On my father’s side, they migrated from London and County Derry in Northern Ireland to Londonderry, New Hampshire. When the American Revolution came, they, as loyalists, moved on to Canada. My father, grandfather and great-grandfather were born in St. Andrews, New Brunswick. In 1865, my grandfather, Andrew Hitchings, moved his family to Eureka, California. Andrew was a skilled craftsman in the building of wooden ships, and my father, George Herbert Hitchings, Sr., followed in his footsteps, eventually becoming a marine architect and master builder.  On my mother’s side, Scottish and English prevailed. The first American was one Thomas Littlejohn from near Edinburgh, who came to the New World about 1735. His descendants, including Shaws, Eldridges and Thomases, moved about in the Maritime Provinces and New England. My maternal grandfather and great-grandfather were descendants of the Matthews family that emigrated twenty-four strong from near Glasgow to Prince Edward Island about 1800. My grandfather, Peter Matthews, married Sara Elizabeth Eldridge, and my mother, Lillian Matthews, was born in Maine. In 1875, my grandfather moved his family across the United States. He, too, was a shipbuilder and settled in Eureka.  My mother and father met and were married in Eureka, and my two sisters were born there. About 1897, Peter Matthews established a shipyard in Hoquiam, Washington, to build lumber carriers for the E.K. Wood Lumber Company. The company built several schooners a year. When Peter Matthews died, my father succeeded to the management, which then became Hitchings and Joyce. Later, my father was master builder and supervisor in Bellingham, Washington, and Coos Bay, Oregon, and between times he engaged in marine architecture. He worked in the period between sail and steam and was especially noted for the design of the transition vessel, the steam schooner, which had a wooden hull and was steam propelled.  I was born in Hoquiam in 1905. Family wanderings put me in grade school in Berkeley and San Diego, California, as well as in Bellingham and Seattle, Washington. I enjoyed a warm and loving home environment. A high standard of ethics prevailed in our family, together with a thirst for knowledge and an urge to teach. In their schooling, my mother and father were limited to what was available in Eureka, but they were avid readers, especially my father. It is clear to me in retrospect that he would have been a scientist had opportunities been more easily attainable.  My father died after a prolonged illness when I was twelve years old. The deep impression made by this event turned my thoughts toward medicine. This objective shaped my selection of courses in high school and expressed itself when I was salutatorian at my class graduation. I chose the life of Pasteur as the subject for my oration. The blending of Pasteur’s basic research and practical results remained a goal throughout my career.  My experiences at Franklin High School in Seattle were notable for another reason. We had a most heterogeneous population, one that blended upper class and minorities including blacks, Filipinos, Japanese, Chinese and first generation Catanians. As a result I lost any self-consciousness I felt in dealing with people from different cultures and backgrounds.  I entered the University of Washington as a premedical student in 1923. The enthusiasm of faculty and students in the Chemistry Department was very infectious, however, and by the end of the first year I had become a chemistry major. I earned top grades, election to Phi Beta Kappa in my junior year, and a degree *cum laude* in 1927.  I stayed on to earn a master’s degree in 1928 with a thesis based on work carried out during the summer of 1927 at the Puget Sound Biological Station at Friday Harbor, Washington. This institution later became a branch of the Oceanographic Laboratories of the University of Washington, largely created and directed by Thomas C. Thompson, who had been my mentor for my master’s thesis. Thompson taught analytical chemistry and was notable for the keen wit and humorous twists that made his teaching memorable. Perhaps the most useful lessons I learned from him have to do with the mathematics of the precision of measurement.  For further graduate work I was offered fellowships at the Mayo Foundation and at Harvard. I chose Harvard, and after one year as a Teaching Fellow in the Department of Chemistry at Cambridge, I was accepted as a Teaching Fellow in the Department of Biological Chemistry at Harvard Medical School. I had intended to work with Otto Folin, but it was his habit to assign first-year Fellows to Cyrus Fiske for a year. By the end of the year, I was caught up in the Fiske-Subbarow program, and Folin very generously allowed me to continue there. After the discovery of phosphocreatine, this group had detected and isolated adenosine triphosphate. My assignment was to prepare for physiological studies by developing analytic methods (on a scale then viewed as ‘micro’ – 1 mg or less) for the purine bases. These methods constituted my dissertation and several early publications.  I earned my Ph.D. in 1933, a year memorable for another great event in my life – my marriage to Beverly Reimer. Her forebears were German, Austrian (Pennsylvania Dutch), Scottish and English. Her father, Azariah Reimer, was a Methodist-Episcopal minister who was pastor of a number of parishes in the Greater Boston area and superintendent of the city missionary society. Beverly had experience with many races and cultures and grew up having friends among all.  Beverly was highly artistic and intelligent. She was very accurate in her intuitive appraisals of people, almost always empathic, almost never disparaging. As she said, “The same quality is often exhibited in a person’s most liked and most disliked behavior.” Beverly expressed her talents in painting, jewelry making, writing and teaching. As my research career progressed, we traveled together and raised two children – Laramie Ruth and Thomas Eldridge.  Our marriage and my career began in the middle of the Great Depression. I experienced a nine-year period of impermanence, both financial and intellectual. I held temporary appointments at the C.P. Huntington Laboratories of Harvard in cancer research, at The Harvard School of Public Health in nutrition research, and at Western Reserve University, Department of Medicine, in electrolyte research.  My career really began in 1942 when I joined the Wellcome Research Laboratories in Tuckahoe, New York, as head and sole member of the Biochemistry Department. Support was limited, but I was free to develop my own program of research.  Elvira Falco was the first permanent member of my staff; [Gertrude Elion](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1988/index.html) joined in 1944, and Peter Russell in 1947. Additional help was added here and there, but our numbers were always small. Russell came from [Alex Todd’s](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1957/index.html) laboratory at Cambridge University and brought not only competence in organic chemistry but a sense of the workings of medicinal chemistry as well. Elion took part in most of the projects dealing with purines, and Falco participated in everything from bacteriology and animal feeding to organic chemistry. For several years our group was housed in one large laboratory. Under the leadership of Falco, a constant flow of banter developed covering a wide range of subjects and degrees of seriousness. We never had any obstacles to interpersonal communication.  In the mid-1940s we began a project that seemed like a digression at times, but one that had a notable reprise some 40 years later. This was the antiviral work carried out in collaboration with Randall L. Thompson, then at Western Reserve. It focused principally on vaccinia virus, and it produced some active compounds. It also convinced us that effective curative chemotherapy of viral infections would have to be applied early in the multiplication cycle.  In 1947, we began to send compounds to the Sloan Kettering Institute to be screened for activity. Among the first few compounds we submitted was 2,6-diaminopurine, which proved active and later produced several notable remissions in acute leukemia.  The association with Sloan Kettering was a major impetus for our growth. The director, C.P. Rhoads, offered us financial support to enable us to increase our search for antitumor agents. This rather unusual circumstance resulted from Rhoads’ realization that our compounds were of special interest, both intrinsically and because they were accompanied by a package of biological information. The external financial help allowed us to expand to about 15 persons. The arrangement continued for a number of years. By that time Burroughs Wellcome Co. was able to furnish our support completely. The arrangement with Sloan Kettering was productive and very satisfying for the contacts it provided, especially with C.P. Rhoads, C.C. Stock, J.H. Burchenal, F. Philips, D. Hutchison and others.  In 1948, we began to divide responsibilities with respect to developing purine and pyrimidine analogs. In 1947, Falco had synthesized *p*-chlorophenoxy-2,4-diaminopyrimidine, and it was apparent at once that we had a new kind of antifolic acid in hand. This line was pursued vigorously by Falco and Russell, and within a short time yielded a very exciting line of investigation – the end of which is not yet in sight.  The decision to refer the “thiation” of hypoxanthine to Elion was based on her developing expertise in the field of purine metabolism. Elion participated in much of the subsequent work with the compound and the agents that followed, including azathioprine and allopurinol.  It was always stimulating to work with Elion. She is intelligent, hard working and ambitious. She became my first assistant, and as I was promoted she succeeded to the position just left. She became head of the Department of Experimental Therapy, a large segment of the Chemotherapy Division. There she elucidated the mode of action of acyclovir, a study which is described as a major part of her Nobel address.  In 1967, I was offered the position of Vice President in Charge of Research of Burroughs Wellcome Co. It was not a post I had sought, but my experience had suggested that a scientist was much better able to support the interests of working scientists than were administrators who got science second hand. I owe much to D.W. Adamson, Wellcome’s Group Research and Development Director, for his support and encouragement.  By 1968, Burroughs Wellcome Co. had outgrown its facilities at Tuckahoe, and we were plunged into a new set of administrative problems by the decision to move the company to a new site. In the end we chose North Carolina and, acceding to my strong representations, selected a site in the new Research Triangle Park. The move provided *Lebensraum*, a good environment and excellent relationships with the three local universities – Duke, the University of North Carolina at Chapel Hill, and North Carolina State. The move to North Carolina was a monumental undertaking, but the company soon took root and today has grown fourfold.  I left my position as Vice President with its heavy administrative duties to become Scientist Emeritus in 1976. This allowed more time for my own research and for travel. By 1971, Beverly was handicapped by strange afflictions classed as “collagen disease” that required close monitoring and constant medication. She exhibited remarkable courage and continued to be a joy as a companion. During our last 10 years together we traveled nearly 400,000 miles, much of it on lecture tours. Beverly’s disease ended in her death in December 1985.  For the past 20 years I have pursued my growing interests in philanthropy. I became Director of The Burroughs Wellcome Fund in 1968 and its President in 1971. The Fund is a nonprofit foundation dedicated to the support of biomedical research. The Fund is supported solely by Burroughs Wellcome Co. and is a relatively small foundation. We have focused The Fund’s resources on underfunded areas of medical research with competitive grants in fields including clinical pharmacology and innovative methods in drug design. It has been very rewarding to guide this enterprise and see it grow.  In 1983, I founded what is now the Greater Triangle Community Foundation. It has been remarkably successful in fulfilling needs in the Triangle area. I am designated as Founder and Director for Life.  I have been involved also with a number of volunteer civic activities. These were undertaken partly to provide for activity in the retirement that has not yet come. They include United Way (Director and Vice President), American Red Cross (Director and Committee Chairman), Foundation for Better Health of Durham (Director, President and Chairman), N.C. Board of Science and Technology, Carolina Consulting Scientists and Engineers (Director); Royal Society of Medicine Foundation (Director); The Life Sciences Research Foundation.  Somehow these activities have found a place in my scientific career with no more cliffficulty than my former administrative duties. Today I devote one-third of my time to philanthropy and two-thirds to science.  I am vitally interested in current developments in innovative methods in drug design, and I look back with pride at our contributions to this field. Our research was untargeted, and the line of inquiry we had begun in the 1940s yielded new drug therapies for malaria (pyrimethamine), leukemia (6-mercaptopurine and thioguanine), gout (allopurinol), organ transplantation (azathioprine) and bacterial infections (cotrimoxazole (trimethoprimA). The new knowledge contributed by our studies pointed the way for investigations that led to major antiviral drugs for herpes infections (acyclovir) and AIDS (zidovudine).  My greatest satisfaction has come from knowing that our efforts helped to save lives and relieve suffering. When I was baptised, my father held me up and dedicated my life to the service of mankind. I am very proud that, in some measure, I have been able to fulfill his hopes. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
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| ID | 0586 |
| Biographical | I was born in Nagoya, Japan on September 5th, 1939, the second of three sons. I have also a younger sister. My father was an engineer working for a textile company that had several factories scattered in rural towns in the southern part of Japan. The company policy made it necessary for my father to move from one factory to another every few years. I and my brothers and sister spent most of our childhood in these small provincial towns, enjoying the space and freedom of the countryside. As my elder brother and I reached adolescence, however, my parents decided to send us to Tokyo so that we could receive a better education.  I commuted to the prestigious Hibiya high school from my Uncle’s home in Tokyo. During the high school years I developed an interest in chemistry, so upon graduation, I chose to take an entrance examination for the Department of Chemistry of the University of Kyoto, the old capital of Japan. After having failed once, I was admitted to this University in 1959. This happened to be one year before the first ten-year term of the defence treaty between Japan and the United States expired and the governments of both countries were preparing for a second ten-year term.  The nation was deeply divided between the pragmatic pro-American conservatives and the idealistic anti-military leftists. Being the home of the most radical leftist student groups, classes at Kyoto University were often cancelled due to frequent political discussions and demonstrations on the streets. I was only a passive participant, withdrawn from the turmoil, but could not help having a feeling of defeat shared with many of my classmates when the treaty was finally extended for the next ten-year term. I believe that this experience might have been a major factor in making me give up the original goal of becoming a chemical engineer to pursue the academic life.  I became fascinated by the then blossoming science of molecular biology when in my senior year I happened to read the papers by [François Jacob and Jacques Monod](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html) on the operon theory. I decided to pursue graduate study in molecular biology and was accepted by Professor Itaru Watanabe’s laboratory at the Institute for Virus Research at the University of Kyoto, one of a few laboratories in Japan where U.S.-trained molecular biologists were actively engaged in research. However, only two months after I started my work in his laboratory, Professor Watanabe called me into his office and suggested that I carry out my graduate study in the United States. He explained how inadequate the graduate training programs in molecular biology laboratories were in Japan, including his own, and offered to help in my application to some major universities in the United States, if I would seriously consider studying abroad.  At that time, it was a common career development for a Japanese molecular biologist to go to the United States for a few years of postdoctoral study after obtaining the Ph.D. in Japan. I already had a vague wish to follow that pattern. Professor Watanabe’s advice to enroll in an American graduate school therefore came to me as a bit of a surprise, but I was excited by the idea and accepted his help immediately. I cannot thank Professor Watanabe enough for this critical suggestion in the early phase of my scientific career.  With the additional help of Dr. Takashi Yura, then an assistant professor in Watanabe’s laboratory, I was admitted to the graduate school of the Department of Biology of the University of California at San Diego that had recently been established by Professor David Bonner in La Jolla, the beautiful southern Californian town near the Mexican border.  At UCSD I studied in the laboratory of Professor Masaki Hayashi, carrying out a thesis project on the transcriptional control of phage lambda and received my Ph.D. in molecular biology in 1968. I remained in Professor Hayashi’s laboratory as a postdoctoral fellow working on the morphogenesis of a phage, ØX174, until early 1969. Then I moved, also as a postdoctoral fellow, across the street to the laboratory of Dr. [Renato Dulbecco](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html) at the Salk Institute.  Like many others, I believed that the golden age of prokaryotic molecular biology was coming to an end and that the great excitement would be in higher organisms. However, the complexity of high organisms was baffling and the necessary tools seemed hopelessly insufficient. Small tumor viruses like polyoma and simian virus 40, the biological material primarily dealt with in Dulbecco’s laboratory, seemed to offer a bridge for the gap between prokaryotes and eukaryotes. Indeed Dulbecco’s laboratory was filled with first-class postdoctoral fellows from around the world, who were trained in prokaryotic molecular biology and who came there intending to expand their research into eukaryotic molecular biology.  My project was to define the transcripts of SV40 during lytic infection and in transformed cells. Since this was the pre-restriction enzyme and pre-recombinant DNA age, the information I could obtain was very limited. However, being a member of the best laboratory in the field I glimpsed the excitement of the cutting edge of scientific research. Furthermore, I very much enjoyed the free and stimulating atmosphere of the laboratory. Unfortunately, as an awardee of a Fulbright travel grant, my U.S. visa was to expire by the end of 1970 and I had to leave the country for at least two years before I was eligible for another U.S. visa.  I had two or three job possibilities outside of the United States, but none were particularly interesting. In the autumn of 1970, only a few months before my visa was to expire I received a letter from Renato Dulbecco who was travelling in Europe. Renato mentioned the newly established Basel Institute for Immunology in Basel, Switzerland, and suggested that the time might be ripe for a molecular biologist to tackle immunological problems. I had very little knowledge of immunology, but decided to take Dr. Dulbecco’s advice and sent an application letter to the Director of the Institute, Professor [Niels Kaj Jerne](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1984/index.html), who offered me a two-year contract.  In the winter of 1971, I thus found myself surrounded by immunologists in this small town located in the middle of Europe. I must admit that the first year in the Institute was not easy for me. I had a continuing interest in work on SV40, but I was also keenly aware that I would not be able to take much advantage of the circumstances if I isolated myself by pursuing that subject. I therefore decided to study immunology in the hope of finding an interesting project.  An immunologist, Dr. Ita Askonas, and a geneticist, Charles Steinberg, were very helpful to me on my entering the new field. By the end of 1971, I was introduced to the great debate on the genetic origins of antibody diversity. I felt from the beginning that I could contribute to resolving this question by applying the recently invented techniques of molecular biology, namely, restriction enzymes and recombinant DNA. Initially I worked only with my skillful technicians, Monica Shöld and Rita Schuller, but was soon joined by Drs. Nobumichi Hozumi, Minoru Hirama, and Christine Brack. Later, as my research group expanded, I had the good fortune to work with many capable postdoctoral fellows and devoted technical assistants. In addition, Charles Steinberg was a very important collaborator and consultant, particularly in the initial phase of the research.  Looking back, the research progressed with amazing speed from 1974 to 1981, the year I left Basel. We all worked hard and had had a great deal of fun. Our work resolved the long held debate on the genetic origin of antibody diversity. It turned out that this diversity is generated by somatic recombination of the inherited gene segments and by somatic mutation. To our very good fortune, Director Niels Jerne was quick to understand the importance of our approach and became a staunch supporter of the research in its early phase.  In the beginning of the 1980’s I began to feel that the great mystery of antibody diversity had been solved, at least in its outlines. I thought that it might be good to change my environment to launch into a new project. I also recalled that I had initially come to Switzerland with the intention of staying for two years and then returning to the United States. Fortunately, I received a few offers from the United States and decided in 1981 to take a professorship at the Center for Cancer Research at M.I.T. Professor [Salvador E. Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html), Director of the Cancer Center, was extremely helpful, not only in bringing me to M.I.T., but also in providing me with a beautiful laboratory.  The research projects on which I had decided concerned two major problems. One was to investigate the role of somatic rearrangement in the activation of the rearranged antibody gene, and the second was to extend the research in Basel to “the other half” of the immune system, namely, to the antigen receptor of T cells. Fortunately, we could contribute to the understanding of both problems by discovering a tissue-specific transcriptional enhancer in the immunoglobulin heavy chain gene and by identifying, cloning, and sequencing genes coding for the polypeptide subunits of the T cell receptor. A particularly intriguing development made during the latter study was the identification of a gene that led to the discovery of a new T cell receptor, gamma delta. While the function of the T cells bearing this receptor is currently unknown, data accumulated during the past year in our laboratory as well as many other laboratories suggest that these T cells may be involved in an entirely new aspect of immunity.  When I look back on my scientific career to-date, I am amazed at my good fortune. At every major turn, I met scientists who were not only at the very top in their own fields, but who also gave me insightful advice and generous help. I am most grateful to Professors Itaru Watanabe, Renato Dulbecco, Niels Kaj Jerne, Charles Steinberg, and Salvadore Luria. I also wish to extend my unending gratitude to many colleagues and technical assistants.  My parents were firm believers that education is the best asset that parents can give to their children. I am deeply grateful to them for their outstanding support of my study and professional career. I am extremely grateful to my wife, Mayumi, whom I married in September 1985 for her devotion, interest, encouragement and criticism. I also wish to express my sincere thanks to my first wife, Kyoko, for her limitless devotion during my days in La Jolla and Basel.  I have been fortunate enough to receive many professional honors which include: The Cloetta Prize of Foundation Professor Dr. Max Cloetta, Switzerland (1978), Warren Triennial Prize of the Massachusetts General Hospital, U.S.A. (1980), Genetics Grand Prize of Genetics Promotion Foundation, Japan (1981), Avery Landsteiner Prize of the Gesselshat für Immunologie, West Germany (1981), Asahi Prize of Asahi-Shimbun (Asahi Press), Tokyo, Japan (1982), Louisa Gross Horwitz Prize of Columbia University, New York, U.S.A. (1982), The V.D. Mattia Award of the Roch Institute of Molecular Biology, Nutley, U.S.A. (1983), Gairdner Foundation International Awards of the Gairdner Foundation, Toronto, Canada (1983), Person of Cultural Merit “Bunkakorosha” of the Japanese Government (1983), Order of Culture “Bunkakunsho” from the Emperor of Japan (1984), Bristol-Myers Award for Distinguished Achievement in Cancer Research (1986), Robert Koch Prize of the Robert Koch Foundation, West Germany (1986). Albert and Mary Lasker Award, New York City (1987) and NOBEL PRIZE in Physiology or Medicine, Stockholm, Sweden (1987). |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
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| ID | **0587** |
| Biographical | I was born in Brooklyn in 1922. Both my mother and father were Russian Jewish emigrants who came to America in the early 1900’s. My father was a tailor and my mother, a housewife. Though of limited education themselves, they instilled in me the values of intellectual achievement and the use of whatever talents I possessed.  I was educated in the public school system of New York City and was bright enough to be accepted at Brooklyn College. Fortunately for me, my college education was most thorough (I majored in both Biology and Chemistry). Perhaps equally important was the fact that Brooklyn College was a city school and had a policy of no tuition; the cost of an education would have been prohibitive for my parents.  My scientific interests throughout my undergraduate days were directed to cell biology and especially the mysteries of embryonic development. I think my one insight into these problems was the recognition that much could be learned by the application of chemistry to biology.  After working for a short period as a bacteriologist in a milk processing plant to save enough money to go to graduate school, fellowships enabled me to continue my education, first at Oberlin College, where I received an M.A. in Zoology in 1945, and then in the Biochemistry Department at the University of Michigan where I received a Ph.D. in 1948. My Ph.D. thesis concerned the metabolic mechanism by which the end product of nitrogen metabolism in the earthworm is switched from ammonia to urea during starvation. I remember spending my nights collecting over 5,000 worms from the University campus green.  I believe it was my ability to stomach-tube earthworms that convinced Dr. Harry Gordon to offer me my first job in the Pediatrics and Biochemistry Departments of the University of Colorado, where I was involved in metabolic studies of premature infants.  Feeling the need to gain experience with the then emerging application of radioisotope methodology to biological research, I left Colorado and went to Washington University in 1952 to work with Martin Kamen in the Department of Radiology at Washington University as a postdoctoral fellow of the American Cancer Society. I learned isotope methodology while studying carbon dioxide fixation in frog eggs and embryos, and also derived a priceless education participating in the journal club administered by Dr. [Arthur Kornberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1959/index.html) who had just arrived at Washington University.  In 1953 I became associated with the Department of Zoology under the leadership of Viktor Hamburger at Washington University with a two-fold purpose in mind. I joined with [Rita Levi-Montalcini](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1986/index.html) to isolate a Nerve Growth Factor (NGF) that Dr. Levi-Montalcini had discovered in certain mouse tumors and to become educated in the field of experimental embryology. I leave it to Dr. Levi-Montalcini, with whom I am honored to share this Nobel Award, to recount the results of our early collaboration.  I came to Vanderbilt University in 1959 as an Assistant Professor in the Biochemistry Department where I have been ever since, exploring the chemistry and biology of epidermal growth factor (EGF) that is the subject of this lecture.  In 1976 I was appointed an American Cancer Society Research Professor and in 1986 Distinguished Professor. The works recognized by this Nobel Prize are clearly a group effort of achievement as may be seen from the names associated with our publications on EGF. They share in this honor. I have received much recognition during my research career and I am most grateful. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | **0588** |
| Biographical | My twin sister Paola and I were born in Turin on April 22, 1909, the youngest of four children. Our parents were Adamo Levi, an electrical engineer and gifted mathematician, and Adele Montalcini, a talented painter and an exquisite human being. Our older brother Gino, who died twelve years ago of a heart attack, was one of the most well known Italian architects and a professor at the University of Turin. Our sister Anna, five years older than Paola and myself, lives in Turin with her children and grandchildren. Ever since adolescence, she has been an enthusiastic admirer of the great Swedish writer, the Nobel Laureate [Selma Lagerlöf](https://www.nobelprize.org/nobel_prizes/literature/laureates/1909/index.html), and she infected me so much with her enthusiasm that I decided to become a writer and describe Italian saga “à la Lagerlöf”. But things were to take a different turn.  The four of us enjoyed a most wonderful family atmosphere, filled with love and reciprocal devotion. Both parents were highly cultured and instilled in us their high appreciation of intellectual pursuit. It was, however, a typical Victorian style of life, all decisions being taken by the head of the family, the husband and father. He loved us dearly and had a great respect for women, but he believed that a professional career would interfere with the duties of a wife and mother. He therefore decided that the three of us – Anna, Paola and I – would not engage in studies which open the way to a professional career and that we would not enroll in the University.  Ever since childhood, Paola had shown an extraordinary artistic talent and father’s decision did not prevent her full-time dedication to painting. She became one of the most outstanding women painters in Italy and is at present still in full activity. I had a more difficult time. At twenty, I realized that I could not possibly adjust to a feminine role as conceived by my father, and asked him permission to engage in a professional career. In eight months I filled my gaps in Latin, Greek and mathematics, graduated from high school, and entered medical school in Turin. Two of my university colleagues and close friends, [Salvador Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) and [Renato Dulbecco](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html), were to receive the Nobel Prize in Physiology or Medicine, respectively, seventeen and eleven years before I would receive the same most prestigious award. All three of us were students of the famous Italian histologist, Giuseppe Levi. We are indebted to him for a superb training in biological science, and for having learned to approach scientific problems in a most rigorous way at a time when such an approach was still unusual.  In 1936 I graduated from medical school with a summa cum laude degree in Medicine and Surgery, and enrolled in the three year specialization in neurology and psychiatry, still uncertain whether I should devote myself fully to the medical profession or pursue at the same time basic research in neurology. My perplexity was not to last too long.  In 1936 Mussolini issued the “Manifesto per la Difesa della Razza”, signed by ten Italian ‘scientists’. The manifesto was soon followed by the promulgation of laws barring academic and professional careers to non-Aryan Italian citizens. After a short period spent in Brussels as a guest of a neurological institute, I returned to Turin on the verge of the invasion of Belgium by the German army, Spring 1940, to join my family. The two alternatives left then to us were either to emigrate to the United States, or to pursue some activity that needed neither support nor connection with the outside Aryan world where we lived. My family chose this second alternative. I then decided to build a small research unit at home and installed it in my bedroom. My inspiration was a 1934 article by Viktor Hamburger reporting on the effects of limb extirpation in chick embryos. My project had barely started when Giuseppe Levi, who had escaped from Belgium invaded by Nazis, returned to Turin and joined me, thus becoming, to my great pride, my first and only assistant.  The heavy bombing of Turin by Anglo-American air forces in 1941 made it imperative to abandon Turin and move to a country cottage where I rebuilt my mini-laboratory and resumed my experiments. In the Fall of 1943, the invasion of Italy by the German army forced us to abandon our now dangerous refuge in Piemonte and flee to Florence, where we lived underground until the end of the war.  In Florence I was in daily contact with many close, dear friends and courageous partisans of the “Partito di Azione”. In August of 1944, the advancing Anglo-American armies forced the German invaders to leave Florence. At the Anglo-American Headquarters, I was hired as a medical doctor and assigned to a camp of war refugees who were brought to Florence by the hundreds from the North where the war was still raging. Epidemics of infectious diseases and of abdominal typhus spread death among the refugees, where I was in charge as nurse and medical doctor, sharing with them their suffering and the daily danger of death.  The war in Italy ended in May 1945. I returned with my family to Turin where I resumed my academic positions at the University. In the Fall of 1947, an invitation from Professor Viktor Hamburger to join him and repeat the experiments which we had performed many years earlier in the chick embryo, was to change the course of my life.  Although I had planned to remain in St. Louis for only ten to twelve months, the excellent results of our research made it imperative for me to postpone my return to Italy. In 1956 I was offered the position of Associate Professor and in 1958 that of Full Professor, a position which I held until retirement in 1977. In 1962 I established a research unit in Rome, dividing my time between this city and St. Louis. From 1969 to 1978 I also held the position of Director of the Institute of Cell Biology of the Italian National Council of Research, in Rome. Upon retirement in 1979, I became Guest Professor of this same institute. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | **0589** |
| Biographical | Michael S. Brown was born on April 13, 1941, in Brooklyn, New York, the eldest child of Harvey Brown, a textile salesman, and Evelyn Brown, a housewife. His sister Susan was born three years later. When Brown was 11 years old the family moved to Elkins Park, Pennsylvania, a suburb of Philadelphia, where Brown attended Cheltenham High School. An amateur radio operating license obtained at age 13 led to a life-long fascination with science. A serious interest in journalism also developed early. These two passions, science and writing, have remained paramount ever since.  Brown graduated in 1962 from the College of Arts and Sciences of the University of Pennsylvania, with chemistry as his major subject. He spent most of his time at the headquarters of the student newspaper, the Daily Pennsylvanian, where he served as features editor and briefly as editor-in-chief. In 1966 Brown received his M.D. degree from the University of Pennsylvania School of Medicine. In 1964 he married Alice Lapin, a companion from childhood. The next two years were spent as intern and resident in Internal Medicine at the Massachusetts General Hospital in Boston. Here Brown met [Joseph L. Goldstein](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/index.html), a fellow intern, and the two established the friendship and mutual respect that led to their long-term scientific collaboration.  The years 1968-1971 were spent at the National Institutes of Health where Brown served initially as Clinical Associate in gastroenterology and hereditary disease. He then joined the Laboratory of Biochemistry, headed by Earl R. Stadtman, a pioneer in the disclosure of the mechanisms by which enzymes are regulated. Here Brown learned the techniques of enzymology and the fundamental principles of metabolic regulation. Brown made an important contribution to the Stadtman effort when he and a colleague discovered that a regulatory enzyme in the glutamine synthetic pathway was controlled by covalent attachment of a nucleotide, uridine.  In 1971 Brown joined the division of Gastroenterology in the Department of Internal Medicine at the University of Texas Southwestern Medical School in Dallas. His selection of Dallas was strongly motivated by his friendship with Goldstein, who had graduated from the Southwestern Medical School. In Dallas, Brown came under the influence of Donald W. Seldin, Chairman of the Department of Internal Medicine, an inspirational figure whose passion for medical science shaped the lives of a generation of Texas students.  Soon after his arrival in Dallas, Brown succeeded in solubilizing and partially purifying 3-hydroxy-3-methylglutaryl coenzyme A reductase, a previously enigmatic enzyme that catalyzes the rate-controlling enzyme in cholesterol biosynthesis. He and Goldstein had developed the hypothesis that abnormalities in the regulation of this enzyme were the cause of familial hypercholesterolemia, a genetic disease in which excess cholesterol accumulates in blood and tissues. The formal scientific collaboration with Goldstein began one year later, in 1972, just after Goldstein returned to Dallas from a postdoctoral fellowship in Seattle. The two young physicians initially maintained separate laboratories, but by 1974 the laboratories had been formally joined.  Throughout the decade of the 1970’s, when their scientific work was most intensive, Brown and Goldstein continued to function as academic physicians, each performing clinical attending rounds on the general medicine wards of Parkland Memorial Hospital for six to twelve weeks per year. They also conducted frequent teaching rounds in medical genetics. Their research efforts were aided by a number of talented senior collaborators and junior associates, as well as by frequent interchange with interested members of the Department of Internal Medicine.  In 1974, Brown was promoted to the rank of Associate Professor of Internal Medicine at the University of Texas Southwestern Medical School. He became a Professor in 1976. In 1977 he was appointed Paul J. Thomas Professor of Medicine and Genetics, and Director of the Center for Genetic Disease at the same institution. In 1985, Brown was appointed Regental Professor of the University of Texas.  Brown was elected to membership in the National Academy of Sciences of the United States in 1980. He is a member of the American Academy of Arts and Sciences, the American Society for Clinical Investigation, the Association of American Physicians, the American Society of Biological Chemists, and the American Society for Cell Biology. He is a Diplomate of the American Board of Internal Medicine and a Fellow of the American College of Physicians.  Brown received several student awards at the University of Pennsylvania, including a Proctor and Gamble Scholarship (1958-1962), the David L. Drabkin Prize in Biochemistry (1962), and the Frederick L. Packard Prize in Internal Medicine (1966). He was elected to Phi Beta Kappa and Alpha Omega Alpha. From 1974 to 1977 he was an Established Investigator of the American Heart Association. He has served on several review boards including the Molecular Cytology Study Section of the National Institutes of Health (1974-77) and the editorial boards of the *Journal of Lipid Research*, the *Journal of Cell Biology*, *Arteriosclerosis* and *Science*. He has been a member of the Board of Scientific Advisors of the Jane Coffin Childs Fund since 1980.  Brown received the honorary degree of Doctor of Science from the University of Chicago (1982) and Rensselaer Polytechnic Institute (1982). With his colleague, Goldstein, Brown has shared the following awards: Heinrich Wieland Prize for Research in Lipid Metabolism (1974); Pfizer Award for Enzyme Chemistry of the American Chemical Society (1976); Albion O. Bernstein Award of the New York State Medical Society (1977); Passano Award (1978); Lounsbery Award of the U.S. National Academy of Sciences (1979); Gairdner Foundation International Award (1981); New York Academy of Sciences Award in Biological and Medical Sciences (1981); Lita Annenberg Hazen Award (1982); V.D. Mattia Award of the Roche Institute of Molecular Biology (1984); Distinguished Research Award of the Association of American Medical Colleges (1984); Research Achievement Award of the American Heart Association (1984); Louisa Gross Horwitz Award (1984); 3M Life Sciences Award of the Federation of American Societies for Experimental Biology (1985); William Allan Award of the American Society of Human Genetics (1985); and the Albert D. Lasker Award in Basic Medical Research (1985).  Brown and Goldstein jointly delivered the following lectures: Harvey Lecture (1977); Christian A. Herter Lectures at Johns Hopkins University (1979); Harry Steenboch Lectures at the University of Wisconsin at Madison (1980); Smith, Kline, and French Lectures at the University of California, Berkeley (1981); Duff Memorial Lecture of the American Heart Association (1981); Doisy Lectures at the University of Illinois at Urbana-Champaign (1983); the first Pfizer Lecture in Honor of Konrad Bloch at Harvard University (1985); and the Berzelius Lecture at the Karolinska Institutet, Stockholm (1985).  Brown and his wife, Alice, have two daughters: Elizabeth (born in 1973) and Sara (born in 1977). |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0589** |
| Interview |  |
| Q1 | I’d like to start, if I may, by exploring your scientific beginnings a little and I don’t know where they began so I don’t know where to start, but perhaps at University of Pennsylvania where you read chemistry and then did an MD. Did you know at that time that you were set to become a serious scientist? |
|  | It’s an interesting story, it goes back even before that. I trace my interest in science to when I was 13 years old and a friend convinced me to get my license to do amateur radio operating, and I got my license when I was 13. He and I would build transmitters and receivers and obviously we didn’t design them, but we’d follow instructions and go out and buy the parts and put them together and solder all these wires. I remember very clearly that you’d work for days or weeks on something and you’d usually finish building it sometime around 2 or 3 in the morning and then I’d plug it in, and it would blow every fuse in the house. I wasn’t popular with my parents either but that’s when the science began because you had to go back and troubleshoot and try to figure out what was wrong, what had you done wrong, what was soldered wrong or what resistor was put in backwards or whatever. I think that that experience of troubleshooting and problem solving was really very important in my thinking about being a scientist.  I also always wanted to be a physician and when I got the Nobel Prize actually the *New York post*, the newspaper went to my father’s apartment in New York to interview him and he produced a baby picture of me, and they ran this thing in the newspaper and the caption said “He wanted to be a doctor ever since he was two years old” and actually I think it’s true. So I knew I wanted to be in medicine and I really liked this problem solving. I went back recently and looked at some papers I had from high school and when I was applying to college I sent out a little resume for people who were going to write letters of recommendation on my behalf and it said “Career interest” and I only listed one thing and it said “Medical research” so I guess I was interested in research. I remember very clearly, in fact I found a book report that I had written on *Arrowsmith* by [Sinclair Lewis](https://www.nobelprize.org/prizes/literature/1930/lewis/facts/), which you know had a major influence on almost everybody of my generation, who went into medical science. I knew I wanted to be a physician and a scientist and so at university I majored in chemistry although I spent most of my time as editor of the *Daily Pennsylvanian*, this daily student newspaper.  Then in medical school I had an experience in a summer in elective rotation with a very impressive scientist who managed to be imaginative but critical at the same time, highly critical and it was that combination of being a critic of your own work along with imagination trying to drive yourself forward that really aroused my interest in science. And I did a residency in medicine and there I met Joe Goldstein and he and I immediately … We were in the same residency group and although our job was to take care of patients, what attracted us to each other was our common interest in the scientific basis of the diseases that we were seeing. |
| Q11 | I want to explore that relationship in greater detail later. |
|  | But at any rate and then I went to the National Institutes of Health after my residency and was exposed to a very inspirational scientist, a man named Earl Stadtman, whose other student, [Stanley Prusiner](https://www.nobelprize.org/prizes/medicine/1997/prusiner/facts/), also received the Nobel Prize and he produced a lot of very successful scientists and was a very inspirational character. |
| Q5 | You’ve spoken of how he taught you the principles of enzymology. What was it that particularly made him a good teacher, what did he have? |
|  | Again, I think it was integrity. As I recall, if you made a novel observation and that lead to a new theory, his attitude wasn’t ok let’s design as many experiments as we can to prove that this new idea is right, his approach was let’s design as many experiments as we can to shoot down the idea and only if we can’t shoot it down do we then begin to accept it. Of course that’s straight out of scientific philosophy but watching it in practice by somebody whose sole devotion was the truth rather than self-promotion or any ulterior motive for doing science, I think that’s the characteristic, his characteristic that washed off on so many of his students. |
| Q11 | Yes, I imagine a very rare characteristic to find. |
|  | Yes, especially in medical research where people have a variety of motivations. |
| Q83 | The fact that you read chemistry and then did medicine, I guess that’s a fairly standard path here but do you think that contributed a lot to your approach to medicine, doing basic science prior to clinical science? |
|  | I always liked basic science and you know, I enjoyed chemistry, but I must say I wouldn’t have considered a career in pure basic science, I never thought about going to graduate school for a PhD in chemistry. I always had the over-riding motivation to become a physician. In fact, even after I came to Dallas and started my own laboratory and was also doing clinical work. Every time I spoke to my father, my father would say “Well, how many patients have you seen today?” I’d say “Dad, today I worked in the lab”, and he would say “Well, that’s not a very good thing”. It wasn’t until after Joe and I began to receive the prizes, the first one was in San Francisco, he lived in New York and we invited him to San Francisco to see us receive this prize and he came up to me afterwards and said “Well, maybe there is something about this research”. |
| Q3 | But in a way you were very blessed to have such an unswerving determination to follow that path. |
|  | I did and there were obstacles in the way. In the summers when I was in medical school, I had to earn money because we didn’t have very much money and so I worked for a pharmaceutical company in their lab, in fact Smith Kline now, you know, eventually became Smith-Kline Beacham and then Glaxo Smith Kline, but they were then called Smith, Kline & French in Philadelphia. I worked in their laboratories every summer and I had a very trivial kind of job injecting things into rats and all my friends who didn’t need the money were working in the summers in much more exciting labs at the medical school and I was quite jealous of that. So, I had a real eager desire to do serious science. |
| Q5 | I daresay the job gave you an insight into something that other people weren’t seeing anyway, which paid off later. So, after NIH and Earl Stadtman you then had these three choices that came together, it seems to me that you 1) decided that you were going to move to Dallas, 2) you decided that you were going to work on hypercholesterolemia … |
|  | Cholesterolemia.  Cholesterolemia. Let’s call it FH for ease of pronunciation and the third thing was that you decided to work with Joe Goldstein, very close collaboration. Those these things inter-related …  Michael Brown: Oh, yes  … and they all paid off to a great degree and they’re all important, so I’d like to investigate each one.  Michael Brown: And they were all not very obvious. Let’s discuss Dallas first. I had grown up in the Northeast. I had gone to the world’s oldest medical school, sorry, the oldest school in the United States, which is University of Pennsylvania. Then I met Joe as residents at the Mass General in Boston and Joe kept telling me what a wonderful place this medical school was in Dallas and I had never heard of it. In fact, I remember when I first saw that they had accepted Joe Goldstein for a residency and it listed his institution as Southwestern Medical School in Dallas, Texas, I thought it was a bible school. You have to recall it, Kennedy was shot here in 1963, I was a second-year medical student at that time. Dallas had this terrible reputation of being sort of a far right wing city and it would have been the last place that I would have ever dreamed that I would have ended up. But Joe kept telling me what a wonderful place it was, not the city but the medical school, how exciting.  We had a chairman of medicine named Donald Seldin who was trained in medicine but had this strong belief in science and had recruited and inspired a whole generation of scientists, Joe among them. I came here for a visit and I was tremendously impressed, again by the intellectual rigour of the science that was going on in a clinical department of medicine. I decided to come here after the NIH, but the problem was my wife and I give her enormous, enormous credit because she too had grown up in the Northeast and certainly had no desire … I mean we lived outside of Washington DC at NIH, we thought that was the deep south and my other offer after the NIH, the other thing that I considered was going to San Francisco at the University of California, San Francisco, that was her favourite city and I will always give her tremendous credit for agreeing to come with me to Dallas. The promise was it was only going to be for a year, that was 36 years ago …  Never trust that sort of promise.  Michael Brown: … and we’re still here. But she fell in love with the city and we raised our children here and she’s never never wanted to go anywhere else but … |
| Q29 | I guess it’s an easy place to live? |
|  | Yes it is, it’s a wonderful place to do science because it is such an easy place to live. But at any rate, I did come here for a year and then I was so inspired by the place, it happens that Joe Goldstein was not here when I arrived. We were both at NIH together but he did an additional fellowship in Seattle, so when I came I was working alone on a sort of a cholesterol related project, not FH but a biochemical project. Fortunately I achieved some success so by the time he came, I had already at least established a certain reputation locally and so it made it easier for the two of us to work together. |
| Q11 | Was the fact that you were here instrumental in the fact that he came back? Had you already made a pact? |
|  | An informal pact. His story is that he was a student here and he was recognised as being literally a genius, while he was a medical student and doctor Seldin, Donald Seldin who is this great inspirational man who built this school, called him in as a student and said – and Joe at that time wanted to be a neurosurgeon – I hope you get him to tell the story, but he was like a second-year medical student and he was fascinated with neurosurgery. Seldin said “No, you’re not a neurosurgeon, you’re a geneticist” and Joe said “You know what’s genetics?” This is back in 1963 and there was no such thing as clinical genetics. Anyway, they arranged this training programme so Joe went to the Mass General where we met, then he went to NIH, and then he went to Seattle. The promise was that he would then come back to Dallas and start a genetics unit, so he had already promised to come back to Dallas and he basically wouldn’t let me rest until I agreed to come also.  But while we were at NIH we had seen these children – this gets now into the second part of your question of FH. We had both clinical duties and research duties when we were at the National Institute of Health and so we’re taking care of patients with rare diseases who had been referred there because their diseases were so rare that doctors of the community didn’t really know how to take care of them. We saw two children who had enormously high blood cholesterol levels, in the US units we talked about it in milligrams per desolator and their blood levels were over 1,000 milligrams per desolator, 10 times above the normal value for a child. Because of these very high cholesterol levels they were getting cholesterol deposits in their arteries and they were having heart attacks, very severe heart attacks and their hearts were failing. This was in 1969 and there was very little you could do for them. Coronary bypass surgery hadn’t been invented and certainly no-one was doing heart transplants. We put them on a zero-cholesterol diet hoping that their blood cholesterol would go down and they just ate rice for six months and didn’t budge.  So, we knew they had a genetic problem and it wasn’t due to anything in the diet and we decided that, we talked about various hypothesis what might account for this and we decided that if we were both ever to be united in Dallas that we would collaborate and try to work this out. So we actually had a plan but it was nowhere near. The idea was always that each of us would have our own separate interests but we would do this one project jointly. I think as I remember it, this was not going to be the central focus for either one of us, in fact I was working on an enzyme in cholesterol biosynthesis at the time, trying to understand it’s bio-chemistry and to isolate the enzyme and Joe, when he came here, was working on roosters, you have to ask Joe about his rooster days, but in administering oestrogen hormones to roosters which would raise their blood cholesterol levels enormously and try to figure out how that was working. |
| Q11 | Should annoy them as well, I imagine. |
|  | It was, not only annoying them, but they would run around and the image I have of Joe running down the hall chasing a rooster, I’ll never forget. But anyway, we both had separate laboratories but we decided to do this one project together in trying to figure out what was wrong with these children and the important approach we took – it was different than what people had done before – was not to study the children directly but rather to take cells from the children, grow them in tissue culture. Tissue culture was just coming in as sort of an experimental tool for human genetics. It had been used by few other people to study genetic defects prior to us and we realised that this was the only way, if whatever was wrong with the children was also manifested by the behaviour of their cells in tissue culture, then we’d be able to figure it out. I think that’s where our basic science training came in because as we mentioned I trained with a very basic enzymologist.  Joe trained with [Marshall Nirenberg](https://www.nobelprize.org/prizes/medicine/1968/nirenberg/facts/) who was a molecular biologist, a Nobel Prize winner and the person who figured out, deciphered the genetic code. So both of us had been exposed to the most rigorous science at the most reductionist levels and we realised that if we’re going to solve a complicated problem like this high cholesterol, we had to reduce it down to something where you could really do experiments. Our whole goal was to be able to do an experiment each day and get the result before we went home that night and if we couldn’t have done that we wouldn’t have done the project. The idea was having these tissue culture cells, we could study what was wrong with them and fortunately the defect was manifest in these tissue culture cells so we were able to work out the defect. What happened then was that work expanded, the joint work, we both abandoned our separate work and just decided to work together to solve this problem. |
| Q23 | Things went so terribly fast, didn’t they, because you got together on that project in 1972 and by -73 you had the LDL receptor concept and then in -74 you merged your labs, you just said this is working**.** |
|  | Right. And I, at that time I gave up my clinical specialty so I hadn’t been trained in gastroenterology which is a technically demanding field. When I started it wasn’t. When I started it was a very nice sort of cerebral thing, people came with abdominal pain, or some problem with absorbing things and they had ulcers and it was all sort of a rational feel. That’s what I like about it, but over that time these endoscopes were invented, these flexible scopes where you could look into somebody’s stomach or intestines and that required a lot of technical dexterity. I was very good at it but I realised that if I were going to keep doing that, it would require that I spend many hours every week just to stay competent in it technically and so I didn’t want to do that so I gave up that specialty. |
| Q23 | So that was becoming a technician rather than a problem solver right. |
|  | Exactly, and so, even though I enjoyed it, I enjoyed interacting with patients, and it is problem solving to figure out what’s wrong with somebody and figure out how to fix, it but at any rate, that was a very big step for me to sort of give up my independent lab, give up my specialty and I remember agonising about it for a very long time. It was not easy for the two of us to establish this working relationship because both of us were sort of super-achievers. Both of us had been at the top of our classes throughout education including medical school, that’s how we got to the Mass General, you had to be at the top of your class to get to the Mass General, and we both had a lot of ego invested in science. We realised that if we were going to work together we would have to share the credit. It wouldn’t be possible for me to say oh, I thought of this experiment, and if you go back through our entire 36 years that we’ve been collaborating, we’ve never made the public statement or the private statement even between the two of us. To say oh that was your idea, this was my idea. We’ve actually worked it out in a lot of conversations as we were starting to collaborate and what we said was if I say something brilliant on a Wednesday it’s probably because he’d said something that just as brilliant on Tuesday that planted the seed. We we’re just not going to try to distinguish it’s going to be Goldstein and Brown or Brown and Goldstein and not the genius of Michael Brown or Joseph Goldstein. That was not easy to do. |
| Q38 | No, and particular when you’re still trying to establish yourself, there must have been the thought in the back of both your minds that what may happen is that one of us gets ahead on the back of this work. |
|  | We actually, and you can ask Joe his recollection, but I remember clearly there were issues like that because Joe actually was more recognised than I was in the beginning, because when he was in Seattle he had done a monumental clinical study of high blood cholesterol and delineated several diseases of which one was FH. He was recognised as an expert in the cholesterol field already and I had no standing in the cholesterol field. I had done this work with Stadtman on bacterial enzymes, so the natural tendency would have been to have given him the credit for what was going on, but we agreed that we would split invitation. If one person got invited to give a lecture somewhere then the next person would do the other one. We alternated senior authorships on the papers, if you go back to the early papers I’m always the last author on one paper and then, or the first author. I think the most important thing that made it possible was that our university recognised this as a joint effort. It’s extremely hard … For example, there are many many universities where this couldn’t happen because when it comes to making decisions about tenure, when you’re promoted to tenure, they want to know that you did x otherwise you’ll never get to be a tenure professor. In our case, that was not possible and so the school promoted us equally at every step. We were both treated almost as a single entity. |
| Q3 | That’s amazing on so many levels. It’s amazing that you two had the maturity to adopt this approach at such a young age, it’s amazing that the university had the confidence in you. Was this driven by Don Seldin? |
|  | It was driven by Seldin, yes. It was his vision that made it possible, but the only reason that it worked was that both of us had enormous amounts of respect for each other. It wouldn’t work in the slightest, if for a minute I thought he was just wrong about things and just not up to the task, not shouldering his load and vice versa. I think the idea that we both respect tremendously … Not that we agree all the time or even most of the time, I mean we disagree on all kinds of minor things, how much calcium to put in the buffer or whether to do a pH curve or a salt curve or something like that. The students who work with us know that and you know, the smart ones, when one of us suggest one thing and the other suggest another, the smart ones do both. The fact is that on the major issues we’ve always agreed and on the major steps and the directions that we take because in a long career like ours there are a lot of turns and twists that you have. Sometimes you have to abandon projects because the technology just isn’t there to get you to the next step. Other times you have to just take a leap of faith and try something new, then and we’ve always agreed on those and those kinds of questions. Sometimes one of us has to convince the other one but it works. |
| Q11 | Forgive me for dwelling on it, but it’s such a rare thing to find such a productive and long-lived collaboration. How does it work in practice, you share the same office space pretty much, your labs are completely inter-changeable if you like or inter-twined and your students come to one or the other or both? |
|  | No, we don’t take separate students. Every student basically has a do-all mentor, the labs are as you mentioned our offices are immediately adjoining with an open door in between so we’re rarely out of earshot of each other. We have joint lab meetings, we’re always present, we have lab meetings with different groups every day during the week and the two of us are always there and there’s a tremendous give and take during these meetings between the two of us, that the students get to participate in and watch. There have been long-term collaborations, the [Coris](https://www.nobelprize.org/prizes/medicine/1947/summary/) are classic, they were married to each other, but to have one so close as ours is maybe almost unique. |
| Q11 | Are you aware of anybody who has actually modelled themselves on you? |
|  | No, we’ve tried, we’ve written articles extolling the benefits of it. I remember times when crucial experiments, back in the early days before we even had students it was just the two of us and a couple of technicians working in the laboratory. We would do really important experiments and the results would come off and usually in those days we were doing things with radioactivity so there would be a liquid simulation counter and the counts, it would printed out on a tape and you’d be looking at this tape as it emerged from the machine and looking at these numbers. When we saw something really dramatic … The kinds of discoveries you really like in the laboratory are ones that open new areas that you know that you know my goodness now that x is true, we can do y, z, a, b and c and d and you just see the next six months of your work right laid out before you and everything you’re going to find during that six months is going to be new. Those are rare moments but they happen and when you share that moment, when the two of you look at each other and the sense of excitement … We never had a press conference in the whole 35 years working on cholesterol which is certainly a topic of great interest, we’ve never had to brag about our work, we’ve never had to go out and give talks, pointing at ourselves as being important and the reason is because the two of us. For me the most important critic is him and vice versa and if both of us realise hey, this is really spectacular, we don’t need to tell anybody else. |
| Q11 | I realise that you don’t want to apportion credit individually, but can you identify at least what it is that is complimentary, what each of you brings to this relationship? |
|  | It’ll be interesting to see how Joe answers this, but I always think about it this way. In the beginning, when we used to look through a microscope at tissue culture cells or of sections of tissues from animals, we would go to the microscope and Joe would always immediately switch the lenses to the lowest power so he could see this broad field. I would instinctively always go to the highest power, so I could see the most intimate detail and Joe has the kind of a mind that can connect things that no-one else can connect. He’s got this very very eclectic kind of a mind and makes connections between concepts that other people just wouldn’t see connection. I’m probably more analytical in trying to really focus on how does this actually work, what are the nuts and bolts of it. But it doesn’t always work that way, it changes, sometimes I’m the guy who connects two crazy things and he’s the one who says no we’ve really got to understand how this little detail works. |
| Q26 | And broadening it to the students who work in the lab, I imagine that in some ways it’s quite an intense relationship for them to break in on. Obviously the practices of sharing credit and things must be very appealing but at the same time it’s a bit like being the gooseberry when you’re out with a couple. Do you think that’s something that you’ve addressed? |
|  | That’s an interesting point, I haven’t been that sensitive to that. One thing that I have noticed, it’s been very very rare that a student will try to play one of us off against the other. I’ve always been worried that you might have a student who would come to me and say that Dr Goldstein just told me to do this, but I think it’s a stupid idea, that kind of thing. Somehow the students learn that you don’t do something like that, so they really always try to get the approval of both us and I really think that they enjoy having two opinions, kind of like having two parents, I think they like having both of us. Very frequently a student will have a conversation with Joe about something and then come in and say to me, here’s what Joe and I decided what do you think about this and vice versa. It’s funny, one or the other things that distinguishes ourselves is Joe tends to like to stay in his office and call the students in for confidences. I on the other hand, like to walk around the lab.  Could be taken as a sign of broad picture versus /- – -/ again.  Michael Brown: I guess it could be, maybe it’s related but you know, just walking up to a student and saying what’s new, what’s wrong, what’s the problem, anything I can help you with? I think that helps. |
| Q11 | Incidentally that was Paul Janssen’s way of working, he founded Janssen Pharmaceutical, he walked round the lab every day and said what’s new to everybody. |
|  | Exactly, I think you learn so much just by asking that one question because you get them sort of unexpectedly and instead of having some prepared presentation the student will tell you oh gosh, I just did this and it didn’t work and then you can sit down and go through it and figure it out. Anybody, any scientist who runs a big lab will tell you that a huge part of it is just trouble shooting, just helping the students figure out why an experiment hasn’t worked or what technique to use, or which way to go. Both of us do that and the students seem to react very well. We’ve never had a student that couldn’t adjust to this system. |
| Q34 | We should move on, but last question on this shared lab topic, there’s a current trend for shared first authorship to try and get away from the problem of distributing experiments among individuals when they were actually done by more than one person. Do you have a view on the way to proceed there, because it sounds as if you should. |
|  | Yes, we’ve done it with some of our students. It’s a little sad that the reason that you have to have shared first authorship is because everyone just assumes that the first author is the real driving force. I like the idea that some journals are doing now, which is very extreme where they actually have a footnote and say this author did x, y and z, this one wrote the paper and this one designed figure 3, 7 and 9. That’s really telling it like it is and I think that would be ok. But I just hate the whole ego thing in science. I think it’s one reason why we lose a lot of young students who don’t go into science because they’re sort of afraid, they see is as a competition and that there are winners and losers and it’s really a shame that they can’t see the excitement of actually doing the experiments. |
| Q20 | That’s just a toe in the water, but often the award of a Nobel Prize can at least knock people for six for a while but you seemed not to have suffered from that. Do you think the fact that you were together allowed you in some ways to share the load that comes? |
|  | Definitely, it’s a tremendous benefit of having a partnership because as you know, all the hoopla that goes on around the Nobel Prize and the lot of distractions that happen immediately afterwards, being invited to dinner parties and be trotted out for donors. I always say that Joe Goldstein and I have been so /- – -/ more often than the Brooklyn Bridge. The fact is you have a lot of those distractions and then invitations, speaking invitations, and you know, joining boards and advisory committees and things like that, but Joe and I helped each other to keep our feet on the ground. We literary said to each other, what do we really like to do, what’s the thing that I like the most, coming in to work in the morning. What I like the most coming into work in the morning is to have some excited graduate student or post doctor fellow having been there all night and run up with some result that they’re so excited about where you can sit down with them and really talk about the implications and what it all means and where it’s going. We both decided that we wanted all these other things to interfere as little as possible and we made a certain rule. For example, if somebody calls up and asks you to speak somewhere a year from now, the tendency is always to say yes ok, but we had this rule that you always imagine that it’s tomorrow. Ok. And would you want to get on an aero plane this afternoon and fly to this far off city, no matter how enticing if it had to be tomorrow. As a result of that we’ve been able to avoid a lot of temptations.  In the last few years though, we both have developed more outside interests and we’re less intensely involved in the lab and we’re more dependent on our students and we’ve always run … People who run laboratories run them in very different ways. We’ve always had a very strong … Some people let students develop their own projects, and a lot of people think that’s the right way to teach sciences, where the students come in, give them a good environment but let them develop their own project. Our view has always been we’re committed to understanding certain things, if a student wants to come and join us and help work on that, then that’s wonderful. I’m not saying students don’t make suggestions and aren’t helpful and active participants, but it’s all along the themes that we’ve established in the lab, the things that we’re fundamentally interested in, so again that helps keep us more firmly involved in the laboratory because the goals are goals that we ourselves set. We were young, I was 44 years old and Joe was 45, we always kid each other because he’s a year older, there are five days every year, my birthday’s April 13th and his is April 18th and there are five days every year where we’re the same age and then he jumps ahead. |
| Q70 | I know there was a positive slant on the way you said it and I’m glad to hear it. When you gave your banquet speech in Stockholm, you mentioned that there were two attributes you saw were essential to good clinical research, one is basic science and basic science training and you’ve touched on that. The other was a technical courage, the ability to go out and try new things and you mentioned that for instance with cell culture in your approach to FH but how do you go about making sure that these two attributes are taught to the medical students here? |
|  | It’s very very difficult. I’m actually helping to direct what we do the MD PhD programme here where students get both an MD and PhD degree and the whole goal of that programme is to expose the students to a basic scientist working on a basic science problem, not to have a student work in a lab that’s working on a clinical problem. What I say to the students is listen, if you want to solve cancer and you go train with the best cancer researcher, in the end the best you can be is a copy of that person, you’re not bringing anything new to cancer research. But if you go out and you train in something else, genomics or biochemistry or some molecular biology and then you start working on cancer now you’re coming to a fresh approach. The MD PhD programmes are designed so that the students work with a basic science and basic scientists learn, view the world differently.  I’ve given talks to the students about this and what I say is that physicians are trained to have an enormous amount of knowledge because when you see a patient who is sick, you don’t have time to look things up in books you don’t even have time to look it up on your Palm Pilot. You’ve got to react and you have to have reflexes and you have to react and you have to be totally sensitive to all the attributes of a disease you have to know all about the disease and what fits and what doesn’t fit and medical students don’t like memorisation but in fact there’s a reason why medical students have to remember a lot because that’s what you do. You really don’t have time to think about where the gaps are in knowledge whereas scientists, a good scientist … The stuff that’s already known is not of much interest, what you want to know is what’s unknown and I would say it’s kind of like looking at a Henry Moore sculpture, the physician looks at the solid bronze and sees the facts of the thing. The scientist looks at the air spaces between the bronze and a good physician scientist is able to do both, to deal with patients and disease through this factual knowledge base and then to somewhat switch your brain in your spare time and think about what the real unknowns are and how really weak the knowledge is. Doctors have to do so many things which are really not based on the knowledge that rigorous scientists would accept but just because you have to do something, and this is the way Doctors do x, you have to learn to do that. Anyway, for Joe and me I think the fact that both of us had training in basic science labs, things that had absolutely nothing to do with human disease, really helped us enormously, and there’s no way that we could have done anything. |
| Q70 | I imagine that the MD PhD programme forces people to take the time to take the other approach because otherwise you are just so pressured by the need to get through your exams and get onto the next stage that you just can’t afford to step away from great learning. |
|  | Exactly, exactly, so they take a three or four year period out and do a thesis and really do a full PhD programme.  Is it easy to get people to sign up for that?  Michael Brown: It’s not that easy, we have a medical school class of about 200 students of whom 15 are doing this dual degree. But I think it’s the future of medicine, I think that you, when we talk about technical courage, that’s what we’re talking about, we’re talking about people who are trained enough so that they’re not afraid to reach into this tool bag of tricks that the basic scientists have given us and use those to solve a problem related to disease. |
| Q17 | I’d like to turn to turn to a related, but slightly different topic which is your involvement in the world of drug discovery in pharmaceutical research. You’re on the board of Pfizer and I imagine given the history of your research and the fact that your research has been partly to the development of statins that you have a very strong belief in the need for basic research within the drug discovery field and I wondered how you feel drug discovery does generally in bringing basic research into the environment of industry. |
|  | My view is that the pharmaceutical industry is essential in bringing basic discoveries to the bedside. There’s been a notion circulating around the United States in the last couple of years that universities should do more in developing drugs and then National Institutes of Health have something called a road map which is trying to produce funds for universities to set up drug screening laboratories and produce drugs. I personally think that’s a wasted misguided effort. It’s really really difficult to produce a drug and the hurdles are getting higher and higher because the drugs that we already have are safe and effective for many many conditions so that if you want to have the next drug it’s got to be even more safe and more effective or it has to treat a disease for which no previous drug has ever been developed, all of which are very very high hurdles. I think it requires the intense focus of pharmaceutical companies to do this but pharmaceutical companies are under their own pressures from their shareholders because it’s the lead times in the industry are so long. Between the time a discovery is made and the time it becomes a commercial product is a minimum of 10 years. From the same point of investors who are funding the pharmaceutical effort, that’s an enormous amount of time. So we have this problem.  I personally think that the system, in the US anyway, is actually working very well, because a company that finds a new drug and they have a period of exclusivity to sell that drug under patent protection and again because all the time that it takes to get the drug to market, they usually have only about 8–10 years of exclusivity before it becomes generically available and other companies can make versions of it and give it away for nothing. That means that the big pharma companies have to keep reinventing themselves every 10 years or so they can’t rest on their laurels. The pressure in these big companies to develop new drugs is just enormous. That guarantees that there’s either going to be new productivity or these companies are going to go out of business and they’ll be replaced by other companies that are more productive. The cost to society is the founding, for the first 10 years when that drug is under patent, patients and society has to pay for it as long as they believe that the benefits of the drug are worth the cost. But then after the 8–10 years it becomes generic and basically society gets it for free. I can’t think of a better system to incentivise people to discover and develop and yet force them to have to keep doing it over and over again. The question is can the companies really keep doing this and a company like Pfizer develop Lipator, the statin that lowers cholesterol, their market right now for laboratories are approximately 13 billion dollars a year. Lipator will go off patent in 2011 that’s only four years from now. They will lose 13 billion dollars worth of income. 13 billion dollars is more than the total sales of any other pharmaceutical company or close to it anyway, so the company will probably not be able to replace that drug and the company will have to downsize and will have to find new inspiration and new discoveries.  I think that the system’s actually working now, people say oh, but the number of new drug approvals hasn’t gone up. We have the genome sequence now, we have 30,000 drug targets and why don’t we have all these drugs. I think that’s what happened is that the genes have gone ahead of the physiology and we know all these genes but we really really don’t know what the proteins actually do and we don’t know where the Achilles heal of a given disease is. We’re almost in a time of trial and error, companies select the target, some receptor or some enzyme, they develop an inhibitor, they get it into human testing and then 19 times out of 20 it doesn’t do what they think and they have to abandon it. The success rate at that level is only 5% once you get even to the stage of humans. But each time we hit a try target and it doesn’t work we discard that target, we go onto the next target and actually we’re going to have a lot of great drugs but we’re in the period now where there’s a lot of trial and error, that’s basically what’s going on. |
| Q71 | But the need for, as you say, pharma to reinvent itself on a regular cycle means that they need a discovery engine which creates new possibilities although that very phrase discovery engine is rather worrying because it indicates that it should happen in some kind of processed way and discovery probably I suppose doesn’t happen like that. But is there, therefore, a need to take basic drug research from wherever one can possibly find it and to broaden the base of research that’s feeding into the pharma pipeline. |
|  | I think that’s certainly true and I think the other side of it, at least the big pharma companies have always been dominated by chemists. These companies were all built on chemistry and the ability to make new molecules that can do impressive things. They’ve been actually weak on biology. These big companies generally, generally I mean, obviously there are exceptions, but they don’t have a deep understanding of the diseases that they’re trying to cure. I think one thing that’s necessary is to bring more basic biology into the companies to complement their basic chemistry. The biotech industry has grown up and has the image of being more creative and they certainly try more things, but there are 2,000 bio tech companies and less than 20 actually earn a profit so I’m not sure they have any special way of doing drugs.  There’s another interesting thing about drug development and discovery. We went back at Pfizer and looked at, this was done a couple of years ago, and they looked at all of their drugs that were selling over a billion dollars and at that time I think there were 10 of them, and they went back and said who were the inventors of these drugs and in all 10 cases the inventors were chemists. All of the chemists were young, they were in their early 30s when they did this discovery. The drugs had been discovered about 15 years earlier because of this time lag and get on the market and then work up to a billion dollars so these chemists had an additional 15 years to make a second discovery and not a single one of them had ever made a second discovery. And it’s very very rare in the industry to have somebody who can actually discover two drugs. Once somebody discovers one drug you might as well retire them. And so my interpretation of that is that it’s not brilliance, whereas if these people were so brilliant they made one drug, then why don’t they make a second and third and a fourth. I think there’s definitely a certain randomness here, a certain stochastic chance that any given drug will turn out to be hugely important. The story of the statins, some day when we have time, I’ll go over that story, it’s a fascinating fascinating story, but the actual discovery of the first stand was made in Japan.  Joe and I had been working on these human fibroblast tissue culture cells and studying their cholesterol synthesis and discovered the LDL receptor and realised that the receptor was regulated so that when cells had too much cholesterol in them they actually down regulated the gene for the receptor and they made fewer receptors so if you could ever deplete a cell of cholesterol it would make more receptors. If you could do this in the body, especially in the liver, if you could deplete the liver of cholesterol so that the liver would make more receptors it would take more of this cholesterol particle out of the blood and the LDL and the level would be low. Just at that moment this guy in Japan, named Akira Endo at the Sankyo drug company, discovered the first statin. He was screening moulds, extracts of penicillin type moulds, and he found this compound and it blocked this enzyme HMG-CoA reductase and stopped cholesterol synthesis. We immediately wrote to him and said please send us some of this. because we wanted to see whether it would cause the cell to make more LDL receptors in this tissue culture system and he actually came to the United States to a meeting on drugs affecting lipid metabolism and gave a talk. The meeting was in Philadelphia and we invited him to stop in Dallas on his way back to Tokyo and when he stopped in Dallas on his way home and we met him he was really dejected and we said why, he said no-one came to my – his English isn’t perfect but in translation – you know, no-one came to my talk. Why is that, nobody seems to think it’s important that you can stop cholesterol production. At that time the whole field was interested in these resins that actually bind bile acids in the intestine and remove them from the body. But we were very interested and so we arranged a collaboration and we worked together and showed basically that when you trigger this regulatory response that leads to an increase in LDL receptors.  That was the first paper published outside of Japan on this class of drugs and we knew it was very important. And it just happened that Roy Vagelos was the head of science at Merck. Vagelos is a scientist. He was a member of the National Academy, he was chairman of biochemistry at Washington University at St Louis but then he’d gone to Merck as their head of drug discovery, but he had worked in the field of lipids. He had studied fatty acids and we studied cholesterol, so we knew him and we worked with him and helped him and his colleagues to develop this drug because we really thought it was important. Then, ten years later in 1987, it gets approved by the FDA and by that time the clinical trials had shown that it was very effective in lowering cholesterol, but the question of safety was really, because you can only test these drugs … At that time it would have been tested on maybe 5,000 people before.  I remember just for the first year after it came on the market … Every time the phone rang I was afraid of somebody saying oh we just found this horrible side effect and everybody was just very fortunate that the drugs are remarkably safe. But there was no way to predict that in advance. How do you know that you wouldn’t have had liver failure? A lot of our friends said oh this is terrible because cholesterol production is so important in the body and if you block that pathway you’re going to definitely have some terrible side effect and we certainly didn’t know that it wouldn’t happen, but we were hoping it wouldn’t. |
| Q71 | The story illustrates at least two things, one is that the importance of biology and the importance of understanding the relevance of the target and also the ability to take risks, the ability to have enough programmes going at once that if you do find that it was a mistake to block cholesterol production you can abandon that approach. |
|  | You’re very perceptive. That risk thing is exactly right, and I’ve noticed, I’ve known this man Roy Vagelos for years and I have always noticed that whenever he takes a risk he has an alternative strategy. It’s never the final risk that will bury the company. I think risk taking is part of the business and I personally think that people who run these big pharma companies are pretty courageous folks even though the actual reputation of the pharma companies now is very very low. Why they’re considered to be profit mongers and inventing diseases … |
| Q71 | They face an enormous public relations challenge these days. |
|  | Enormous. But in the end, I think society’s going to have a lot of new medicines that do things that we can only dream, even now certain kinds of leukaemia that we had thought were incurable are now converted at least into a chronic disease. Anybody old enough to remember AIDS in the 1980s knows what a death sentence it was and the fact that the industry has produced drugs that now convert it into a manageable chronic disease. We get very little credit from the public but these are not easy things to do and science has done it. |
| Q77 | One last question on the pharma, there’s a large growth in the field that is called experimental medicine, these days, but experimental medicine is basically what you’ve been talking about all the time isn’t it? |
|  | Yes, they’re calling it experimental medicine or translation or research. One of my pet peeves is that people talk about translational research and they’re always talking about taking basic discoveries and translating them to the bedside. But I think that real medical research always starts at the bedside. Starts at the bedside and then it goes to the basic scientist and then it goes back to the bedside. I point out that all these basic scientists, a lot of them are trying to cure three diseases of the brain, Alzheimer’s disease, Parkinson’s disease, Huntington’s disease. Why do we know about those diseases? Because there were three doctors named Parkinson, Alzheimer and Huntington who discovered them. There would be no way that a basic scientist would even know what a disease was unless there are perceptive physicians out there, describing them and trying to figure out where the actual real central defect lies. I think this interaction between people that understand medicine and people that understand basic science, that interface is the real place where the action happens. Joe Goldstein and I were lucky to have been able to stay in that interface for 35 years and it’s been a great interface to be in. |
| Q56 | Yes indeed. So to close, just the question of what will happen to the Brown Goldstein environment as time marches on. It sounds like it’s not possible to conceive of bringing in two new people to take over those roles. |
|  | I don’t think so. First of all, we hope to continue to do this for as long as we are both mentally competent. As you can imagine we’ve both had lots of offers to do other things, but again we’re still getting kicks out of doing it. Now we’re seeing something else because some of the junior people who started out as post doctor fellows with us have now become independent and some of them have actually stayed on our faculty in our department. They’re working on their own, we’re not authors of their papers and yet they have enough confidence to confide in us and tell us their results and ask for guidance. I’m getting a tremendous kick out of just /- – -/ and guiding these young people and so maybe that’s how we’ll fade out and give me grandfatherly advice. |
| ID | 0590 |
| Biographical | Joseph L. Goldstein was born on April 18, 1940, in Sumter, South Carolina, the only son of Isadore E. and Fannie Alpert Goldstein. The family owned and operated a clothing store in Kingstree, South Carolina, a town of 5000 people. After his education in the primary and secondary public schools of Kingstree, Goldstein attended Washington and Lee University in Lexington, Virginia, and received the B.S. degree in chemistry, *summa cum laude*, in 1962. He then attended Southwestern Medical School of the University of Texas Health Science Center in Dallas where he was inspired to pursue a career in academic medicine by Donald W. Seldin, then and now Chairman of the Department of Internal Medicine. During his last year in medical school, Seldin offered Goldstein a future faculty position if he would become trained in genetics and return to Dallas to establish a division of medical genetics in the Department of Internal Medicine. After receiving the M.D. degree in 1966, Goldstein moved to Boston where he was an Intern and Resident in Medicine at the Massachusetts General Hospital (1966-68).It was at the Massachusetts General Hospital that Goldstein first met and developed a friendship with [Michael S. Brown](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1985/index.html), his long-term scientific collaborator.  After completion of his medical training, Goldstein spent two years (1968-70) at the National Institutes of Health, where he worked in the laboratory of [Marshall W. Nirenberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1968/index.html) and also served as a clinical associate at the National Heart Institute. The opportunity to work in a first-rate basic science laboratory while at the same time carrying a limited clinical responsibility proved highly influential in shaping Goldstein’s career. In Nirenberg’s laboratory, Goldstein and his colleague C. Thomas Caskey isolated, purified, and worked out the mechanism of action of several proteins required for termination of protein synthesis. Here he acquired scientific skills and taste, experienced the thrill of discovery and the excitement of science, and appreciated the power of a molecular biology approach to human disease. As a clinical associate, Goldstein served as physician to the patients of Donald S. Fredrickson, then Clinical Director of the National Heart Institute and an expert on disorders of lipid metabolism. His curiosity about hypercholesterolemia was aroused when he cared for patients with the striking clinical syndrome of homozygous familial hypercholesterolemia. These patients were intensively discussed with Brown. In view of his and Brown’s common interest in metabolic disease, Goldstein convinced his colleague to join him as a faculty member at the University of Texas Health Science Center at Dallas, where they would work collaboratively on the genetic regulation of cholesterol metabolism. While at the National Institutes of Health, Goldstein and Brown became avid duplicate bridge players. Their successful bridge partnership proved to be a valid testing ground for their future scientific partnership.  Before returning to Dallas, Goldstein spent two years (1970-72) as a Special NIH Fellow in Medical Genetics with Arno G. Motulsky at the University of Washington in Seattle. Motulsky was one of the creators of human genetics as a medical specialty. In Seattle, Goldstein initiated and completed a population genetic study to determine the frequency of the various hereditary lipid disorders in an unselected population of heart attack survivors. He and his colleagues discovered that 20% of all heart attack survivors have one of three single-gene determined types of hereditary hyperlipidemia. One of these disorders was the heterozygous form of familial hypercholesterolemia, which was found to affect 1 out of every 500 persons in the general population and 1 out of every 25 heart attack victims. During his fellowship in Seattle, he became conversant with tissue culture techniques, which proved to be invaluable in the subsequent studies with Brown.  In 1972, Goldstein returned to the University of Texas Health Science Center at Dallas, where he was appointed Assistant Professor in Seldin’s Department of Internal Medicine and head of the medical school’s first Division of Medical Genetics. He became Associate Professor of Internal Medicine in 1974 and Professor in 1976. In 1977, he was made Chairman of the Department of Molecular Genetics at the University of Texas Health Science Center at Dallas and Paul J. Thomas Professor of Medicine and Genetics, a position that he currently holds. In 1985, he was named Regental Professor of the University of Texas.  Goldstein was elected to membership in the National Academy of Sciences in 1980. He is also a member of the American Academy of Arts and Sciences, Association of American Physicians, American Society for Clinical Investigation (President, 1985-86), American Society of Biological Chemists, American Society of Human Genetics, American Society for Cell Biology, and the American Federation for Clinical Research (National Council, 1979-82). He is also a Fellow of the American College of Physicians and is a Diplomate of the American Board of Internal Medicine. Goldstein has served on study sections for the American Heart Association (1975-78) and the National Institutes of Health (1975-78). He served on the Scientific Review Board of the Howard Hughes Medical Research Institute (1978-84) and is presently a member of its Medical Advisory Board (1985-present). In 1983 he became a Non-resident Fellow of The Salk Institute for Biological Sciences. He is, or has been, a member of the Editorial Board of the following journals: *Annual Review of Genetics* (1979-84), *Arteriosclerosis* (1981-present), *Cell* (1982-present), *Journal of Biological Chemistry* (1980-85), *Journal of Clinical Investigation* (1977-82), and *Science* (1985-present).  He has received honorary Doctor of Science degrees from the University of Chicago (1982) and Rensselaer Polytechnic Institute (1982). His other academic honors include membership in Phi Beta Kappa and Alpha Omega Alpha. He was also the recipient of the Ho Din Award for Outstanding Medical School Graduate of the University of Texas Southwestern Medical School (1966) and of a Research Career Development Award from the National Institutes of Health (1972-77).  In addition to the 1985 Nobel Prize for Physiology or Medicine, Goldstein and his colleague Brown have been jointly honored for their research with the following awards: Heinrich Wieland Prize for Research in Lipid Metabolism (1974); Pfizer Award for Enzyme Chemistry of the American Chemical Society (1976); Albion O. Bernstein Award of the New York State Medical Society (1977); Passano Award (1978); Lounsbery Award of the U.S. National Academy of Sciences (1979); Gairdner Foundation International Award (1981); New York Academy of Sciences Award in Biological and Medical Sciences (1981); Lita Annenberg Hazen Award (1982); V.D. Mattia Award of the Roche Institute of Molecular Biology (1984); Distinguished Research Award of the Association of American Medical Colleges (1984); Research Achievement Award of the American Heart Association (1984); Louisa Gross Horwitz Award (1984); 3M Life Sciences Award of the Federation of American Societies for Experimental Biology (1985); William Allan Award of the American Society for Human Genetics (1985); and the Albert D. Lasker Award in Basic Medical Research (1985).  Goldstein and his colleague Brown have shared the podium for a number of distinguished lectureships, including the Harvey Lecture (1977), Christian A. Herter Lectures at Johns Hopkins University (1979), Harry Steenboch Lectures at the University of Wisconsin at Madison (1980); Smith, Kline, and French Lectures at the University of California, Berkeley (1981); Duff Memorial Lecture of the American Heart Association (1981); Doisy Lectures at the University of Illinois at Urbana-Champaign (1983); the first Pfizer Lecture in Honor of Konrad Bloch at Harvard University (1985); and the Berzelius Lecture at the Karolinska Institute, Stockholm (1985).  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1985*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1986  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1985 Addendum, October 2012 Since receiving the Nobel Prize in 1985, I have continued hands-on involvement with research, electing to pass up opportunities for positions in scientific administration. Michael Brown and I continue to work together, and our most significant discovery in the post-Nobel era has been the purification and molecular identification in 1993 of a family of membrane-bound transcription factors called SREBPs (Sterol Regulatory-element Binding Proteins). Since 1993, we and our students and postdoctoral fellows have delineated the complex machinery that proteolytically releases the SREBPs from membranes, thus allowing their migration to the nucleus where they activate all the genes involved in the synthesis of cholesterol and fatty acids. The machinery for generating active SREBPs is tightly regulated by a negative feedback mechanism, which explains how human and animal cells maintain the necessary levels of cholesterol and fats in the face of varying environmental conditions.  The SREBP feedback system also explains the mechanism of action of the statin drugs, the LDL-cholesterol lowering compounds that are taken by millions of people for reducing the risk of coronary heart disease and stroke. Inhibition of cholesterol synthesis in the liver by a statin drug leads sequentially to feedback activation of the SREBP pathway, increased expression of LDL receptors in liver, and reduction of LDL-cholesterol in the blood.  For our research on the SREBP pathway, Michael Brown and I have been honored with several awards, including the Warren Alpert Foundation Prize, Harvard Medical School (2000); the Albany Medical Center Prize in Medicine and Biomedical Research (2003); and the Stadtman Distinguished Scientist Award, American Society for Biochemistry and Molecular Biology (2011). In 1991, we were elected as Foreign Members of The Royal Society of London.  Michael Brown and I have worked together as scientific partners since 1972. Our 40-year collaboration is now the longest such scientific partnership in Nobel history. Other long-term Nobel partnerships include those of [Cori and Cori](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/) (34 years, Nobel Prize in 1947); [Stein and Moore](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1972/) (33 years, 1972); [Cournand and Richards](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/) (30 years, 1956); [Hubel and Wiesel](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1981/) (20 years, 1981); and [Bishop and Varmus](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1989/) (19 years, 1989).  Brown and I have recently written three articles that summarize the highlights of our 40-research scientific partnership. One article deals with the discovery of the LDL receptor ([http://atvb.ahajournals.org/content/29/4/431.full.pdf+html](https://www.ahajournals.org/doi/epub/10.1161/ATVBAHA.108.179564)). A second article describes how we discovered the SREBP pathway (http://www.jlr.org/content/50/Supplement/S15.full.pdf+html). And a third article reflects on six scientific side trips that we have made over the last 40 years, telling about our research excursions off the beaten path of the LDL receptor and the SREBP pathway (http://www.jbc.org/content/287/27/22418.full.pdf+html).  In addition to my research activities, I am currently a member of the Boards of Trustees of the Howard Hughes Medical Institute and The Rockefeller University. Since 1996, I have served as Chairman of the Albert Lasker Medical Research Awards Jury. In this role, I have written a series of essays connecting creativity in science with creativity in the arts. These essays, which deal with questions such as “How does a series of scientific experiments come to be regarded as ‘elegant’ or a body of research deemed as ‘beautiful’?”, have been published in *Nature* *Medicine* (beginning in 2001) and are collected on the Lasker Foundation web site (http://www.laskerfoundation.org/awards/artofscience.htm). |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0591 |
| Biographical | Niels K. Jerne, born 23rd December 1911, London  My parents, Hans Jessen Jerne and Else Marie Lindberg, and their ancestors (back to the seventeenth century and earlier) all lived on the island Fanø and in a small adjacent area of western Jutland in Denmark. My family moved to London in 1910, and then to Holland during the first world war. I received my Baccalaureate in Rotterdam in 1928.  After two years of studying physics at the University of Leiden, I switched to medicine at the University of Copenhagen where I presented my thesis on the avidity of antibodies in 1951.  My wife Alexandra and I married in 1964, and now live in our house near Avignon. Further details of my curriculum vitae:   |  | | --- | | Research worker at the Danish State Serum Institute (1943-1956) | | Research fellow at the California Institute of Technology, Pasadena (1954-1955) | | Head of the Sections of Biological Standards and of Immunology at the World Health Organization, Geneva (1956-1962) | | Professor of Biophysics at the University of Geneva (1960 – 1962) | | Professor of Microbiology and Chairman of the Department, University of Pittsburgh (1962-1966) | | Professor of Experimental Therapy at the Johann-Wolfgang-Goethe-Universität, Frankfurt, and Director of the Paul-Ehrlich-Institut, Frankfurt (1966-1969) | | Director of the Basel Institute for Immunology, Basel (1969-1980) | | Special Immunology Adviser to the Director of the Institut Pasteur, Paris (1981-1982) | | Member emeritus and Honorary Chairman of the Advisory Board of the Basel Institute for Immunology (from 1981) | | Member of the WHO Advisory Committee on Medical Research (1949-1968) | | Member of the Advisory Committee on Medical Research of the Panamerican Health Organization (1963-1966) | | Member of the Expert Advisory Panel of Immunology of the WHO since 1962 | | Honorary Member of the Robert-Koch-Institut, Berlin (1966) | | Foreign Honorary Member of the American Academy of Arts and Sciences (1967) | | Member of the Royal Danish Academy of Sciences (1969) | | Chairman, Council of the European Molecular Biology Organization (1971-1975) | | Gairdner Foundation International Award, Toronto (1970) | | Doctor of Science, h.c., University of Chicago (1972) | | Honorary Member of the American Association of Immunologists (1973) | | Foreign Associate of the National Academy of Sciences (USA) (1975) | | Waterford Bio-Medical Science Award, La Jolla (1978) | | Doctor of Science, h.c., Columbia University, New York (1978) | | Foreign Member of the American Philosophical Society (1979) | | Doctor of Science, h.c., University of Copenhagen (1979) | | Marcel Benoist Prize, Bern (1979) | | Fellow of the Royal Society (1980) | | Doctor of Science, h.c., University of Basel (1981) | | Member of the Académie des Sciences de l’Institut de France (1981) | | Paul Ehrlich Prize, Frankfurt (1982) | | Honorary Member of the British Society for Immunology (1983) | | Doctor of Medicine, h.c., Erasmus University, Rotterdam (1983) | |  | | The work referred to in the citation for the award of the Nobel Prize is mainly included in the following papers: | | “The natural selection theory of antibody formation”  Proc. Nat. Acad. Sci. USA *41*, 849-857, 1955 | | “Immunological speculations”  Ann. Rev. Microbiol. *14*, 341-358, 1960 | | “Plaque formation in agar by single antibody-producing cells”  (with Albert A. Nordin), Science *140*, 405, 1963 | | “The natural selection theory of antibody formation: ten years later”  in “Phage and the origins of molecular biology” Cold Spring Harbor Lab. of Quant. Biology 301-312, 1966 | | “Antibodies and learning”  in “The Nerurosciences”, The Rockefeller University Press 200-205, 1967 | | “Waiting for the End”  Cold Spring Harbor Symp. on Quant. Biology *32*, 591-603, 1967 | | “The somatic generation of immune recognition”  Eur. J. Immunol. *1*, 1-9, 1971 | | “What precedes clonal selection?”  in “The ontogeny of Acquired Immunity”, Ciba Foundation Symposium, Elsevier, Amsterdam 1-15, 1972 | | “Towards a network theory of the immune system”  Ann. Immunol. (Inst. Pasteur) 125C, 373-389, 1974 | | “The immune system: a web of v-domains”  Academic Press, New York, Harvey Lectures *70*, 93-110, 1976 | | “Idiotypic networks and other preconceived ideas”, Immunological Reviews *79*, 5-24, 1984 | |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0592 |
| Biographical | *Education and research experience*   |  |  | | --- | --- | | April 1965 | Abitur in Kehl, beginning of studies in Biology at the University of Freiburg. | | January 1971 | Diploma in Biology, work on repair-deficient strains of Escherichia coli and computer assisted instruction. | | April 1974 | Ph.D., University of Freiburg. Thesis work on immunological studies of the enzyme ß-galactosidase, carried out at the Institute for Immunology, Basel, Switzerland, under the supervision of Professor Fritz Melchers. | | April 1974 to March 1976 | Postdoctoral work in cell biology (lymphocyte fusion) in Dr. [C. Milstein’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1984/index.html) laboratorium at the Medical Research Council, Laboratory of Molecular Biology. Work supported by an EMBO long-term fellowship. Publication: G. Köhler and C. Milstein (1975) “Continuous cultures of fused cells secreting antibody of predefined specificity”. Nature 256:495-497. | | April 1976 to present | Member of the Basel Institute for Immunology; Molecular and cellular work on lymphocyte hybrids. |   Member of the European Organization of Molecular Biology (EMBO), Honory Lecturer at the University of Basel, Switzerland, Doctor honoris causa of the University of Centre Limburg, Belgium, numerous awards, becoming director of the Max-Planck-Institut für Immunbiologie in Freiburg, |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0593 |
| Biographical | My father was a Jewish immigrant who settled in Argentina, and was left to his own devices at the age of 15. My mother was a teacher, herself the daughter of a poor immigrant family. For both my mother and my father, no sacrifice was too hard to make sure that their three sons (I was the middle one) would go to university. I wasn’t a particularly brilliant student, but on the other hand I was very active in Student Union affairs and in student politics. It was in this way that I met my wife, Celia. After graduation, we married, and took a full year off in a most unusual and romantic honeymoon, hitch-hiking our way through most countries in Europe, including a couple of months working in Israel kibbutzim. As we returned to Argentina, I started seriously to work towards a doctoral degree under the direction of Professor Stoppani, the Professor of Biochemistry at the Medical School. My PhD thesis work was done with no economic support. Both Celia and I worked part-time doing clinical biochemistry, between us earning just enough to keep us going. My thesis was on kinetics studies with the enzyme aldehyde dehydrogenase. When that was finished, I was granted a British Council Fellowship to work under the supervision of Malcolm Dixon. There, in the Department of Biochemistry at the University of Cambridge, I started a project on the mechanism of metal activation of the enzyme phosphoglucomutase. It was through that enzyme that I started to collaborate with [Fred Sanger](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1958/index.html). I have described this collaboration in some detail previously (Lynen Lecture; Miami Winter Symp. Proc., In: “From gene to protein: translation into biotechnology”; Ed. W. Whelan, Academic Press, 1982). It was after completing my PhD thesis that I took a short-term appointment with the Medical Research Council in Sanger’s group, and then returned to Argentina for a period of two years. During that period I extended my studies of mechanisms of enzyme action to the enzymes phosphoglyceromutase and alkaline phosphatase. It was then that I had my first experience at directing other people’s work, including my first research student. The political persecution of liberal intellectuals and scientists manifested itself as a vendetta against the director of the institute where I was working. This forced my resignation and return to Cambridge to rejoin Fred Sanger, who by then had been appointed Head of the Division of Protein Chemistry in the newly-formed Laboratory of Molecular Biology of the Medical Research Council. Following his suggestion, I shifted my interests from enzymology to immunology. The evolution of my research in this area is described in the Lynen Lecture as mentioned above and in the Nobel Lecture.  Born 8 October 1927, in Bahía Blanca, Argentina. Married in 1953, to Celia (née Prilleltensky). No children.   |  |  | | --- | --- | | 1939-1944 | Colegio Nacional, Bahía Blanca (Bachiller) | | 1945-1952 | Facultad de Ciencias, Universidad de Buenos Aires (Licenciado en Ciencias Químicas) | | 1950-1956 | Part-time clinical analyst at Laboratorios Liebeschutz | | 1952-1957 | Research Student at the Instituto de Química Biológica, Facultad de Ciencias Médicas, Universidad de Buenos Aires | | 1957 | *Doctor en Química* (Universidad de Buenos Aires) | | 1957-1963 | Staff of Instituto Nacional de Microbiología, Buenos Aires (Leave of absence 1958-1961) | | 1958-1960 | British Council Fellowship at the Department of Biochemistry, University of Cambridge | | 1960 | *Ph.D. degree* (University of Cambridge) | | 1960-1961 | Scientific staff of Medical Research Council at the Department of Biochemistry, University of Cambridge | | 1961-1963 | Head of División de Biología Molecular, Instituto Nacional de Microbiología, Buenos Aires | | 1963- | Scientific Staff of Medical Research Council Laboratory of Molecular Biology, Cambridge | | 1983 | Head, Protein and Nucleic Acid Chemistry Division, Cambridge |   Honorary member, Scandinavian Immunological Societies (1970); Member, European Molecular Biology Organization (1974); Fellow of the Royal Society (1975); Honorary member, American Association of Immunologists (1979); Fellow of Darwin College, Cambridge (1980); Honorary Fellow of Fitzwilliam College, Cambridge (1982); Foreign Associate, National Academy of Sciences, USA (1981); Honorary Fellow, Royal College of Physicians (1983); Foreign Honorary Member, American Academy of Art and Sciences (1983); Member of the Deutsche Akademie der Naturforscher Leopoldina (1983); Académico Correspondiente Extranjero of the Real Academia de Ciencias Exactas, Fisicas y Naturales, Madrid (1984).  Prizes and Awards  Prize Herrero Doucloux of the Asociación Química Argentina (1957); CIBA Medal and Prize (1978); Lewis S. Rosenstiel Award, Brandeis University (1979); Avery-Landsteiner Prize, Society for Immunology (1979); V. D. Mattia Lectureship Award, Roche Institute (1979); Adolph Rosenberg Award, University of Miami (1980); Wolf Prize in Medicine, Wolf Foundation, Israel (1980); Louisa Gross Horwitz Prize, Columbia University (1980); Robert Koch Prize and Medal, Germany (1980); Royal Society Wellcome Foundation Prize (1980); Madonnina Award, Fondazione Carlo Erba, Milano (1981); William Bate Hardy Prize, Cambridge Philosophical Society (1981); Jimenéz Díaz Memorial Award, Fundación Conchita Rabago de Jimenéz Díaz, Spain (1981); General Motors Cancer Research Foundation Sloan Prize, USA (1981); The Gairdner Foundation Annual Award, Canada (1981); Krebs Medal, Federation of European Biochemical Societies (1981); Brown-Hazen Memorial Award, Albany, New York (1982); Lynen Medal, Miami Winter Symposium (1982); Gerónimo Forteza Medal, Valencia, Spain (1982); David Pressman Memorial Award, U.S.A. (1982); Biochemical Analysis Prize 1982, German Society for Clinical Chemistry (1982); Karl Landsteiner Award, American Association of Blood Banks (1982); Royal Medal, Royal Society (1982); XI International Congress of Allergology and Clinical Immunology Award (1982); Rabbi Shai Shacknai Memorial Prize, Hebrew University, Jerusalem (1982); Philip Levine Award, American Society of Clinical Pathologists (1983); Franklin Medal, Franklin Institute, U.S.A. (1983); Mallinkrodt Award for Investigative Research, Clinical Ligand Assay Society, U.S.A. (1983); Carlos J. Finlay Prize for Meritorious Work in Microbiology, UNESCO (1983); Common Wealth Award in Science, Sigma XI Scientific Research Society, U.S.A. (1983); Dale Medal, Society for Endocrinology (1984); Albert Lasker Basic Medical Research Award, Albert and Mary Lasker Foundation (1984); John Scott Award, Board of Directors of City Trusts, Philadelphia, U.S.A. (1984). |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0594 |
| Biographical | In the fall of 1921 I attended the only course in genetics open to undergraduate students at Cornell University. It was conducted by C. B. Hutchison, then a professor in the Department of Plant Breeding, College of Agriculture, who soon left Cornell to become Chancellor of the University of California at Davis, California. Relatively few students took this course and most of them were interested in pursuing agriculture as a profession. Genetics as a discipline had not yet received general acceptance. Only twenty-one years had passed since the rediscovery of Mendel’s principles of heredity. Genetic experiments, guided by these principles, expanded rapidly in the years between 1900 and 1921. The results of these studies provided a solid conceptual framework into which subsequent results could be fitted. Nevertheless, there was reluctance on the part of some professional biologists to accept the revolutionary concepts that were surfacing. This reluctance was soon dispelled as the logic underlying genetic investigations became increasingly evident.  When the undergraduate genetics course was completed in January 1922, I received a telephone call from Dr. Hutchison. He must have sensed my intense interest in the content of his course because the purpose of his call was to invite me to participate in the only other genetics course given at Cornell. It was scheduled for graduate students. His invitation was accepted with pleasure and great anticipations. Obviously, this telephone call cast the die for my future. I remained with genetics thereafter.  At the time I was taking the undergraduate genetics course, I was enrolled in a cytology course given by Lester W. Sharp of the Department of Botany. His interests focused on the structure of chromosomes and their behaviors at mitosis and meiosis. Chromosomes then became a source of fascination as they were known to be the bearers of “heritable factors”. By the time of graduation, I had no doubts about the direction I wished to follow for an advanced degree. It would involve chromosomes and their genetic content and expressions, in short, cytogenetics. This field had just begun to reveal its potentials. I have pursued it ever since and with as much pleasure over the years as I had experienced in my undergraduate days.  After completing requirements for the Ph.D. degree in the spring of 1927, I remained at Cornell to initiate studies aimed at associating each of the ten chromosomes comprising the maize complement with the genes each carries. With the participation of others, particularly that of Dr. Charles R. Burnham, this task was finally accomplished. In the meantime, however, a sequence of events occurred of great significance to me. It began with the appearance in the fall of 1927 of [George W. Beadle](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html) (a Nobel Laureate) at the Department of Plant Breeding to start studies for his Ph.D. degree with Professor Rollins A. Emerson. Emerson was an eminent geneticist whose conduct of the affairs of graduate students was notably successful, thus attracting many of the brightest minds. In the following fall, Marcus M. Rhoades arrived at the Department of Plant Breeding to continue his graduate studies for a Ph.D. degree, also with Professor Emerson. Rhoades had taken a Masters degree at the California Institute of Technology and was well versed in the newest findings of members of the [Morgan](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1933/index.html) group working with Drosophila. Both Beadle and Rhoades recognized the need and the significance of exploring the relation between chromosomes and genes as well as other aspects of cytogenetics. The initial association of the three of us, followed subsequently by inclusion of any interested graduate student, formed a close-knit group eager to discuss all phases of genetics, including those being revealed or suggested by our own efforts. The group was self-sustaining in all ways. For each of us this was an extraordinary period. Credit for its success rests with Professor Emerson who quietly ignored some of our seemingly strange behaviors.  Over the years, members of this group have retained the warm personal relationship that our early association generated. The communal experience profoundly affected each one of us.  The events recounted above were, by far, the most influential in directing my scientific life.   |  | | --- | | Born | | Hartford, Connecticut, U.S.A, 16 June, 1902 | |  | | Secondary Education | | Erasmus Hall High School, Brooklyn, New York. | |  | | Earned Degrees | | B.S. Cornell University, Ithaca, New York, 1923 | | M.A. Cornell University, Ithaca, New York, 1925 | | Ph.D. Cornell University, Ithaca, New York, 1927 | |  | | Positions held | | Instructor in botany, Cornell University, 1927-1931 | | Fellow, National Research Council, 1931-1933 | | Fellow, Guggenheim Foundation, 1933-1934 | | Research Associate, Cornell University, 1934-1936 | | Assistant Professor, University of Missouri, Columbia, Missouri, 1936-1941 | | Staff Member, Carnegie Institution of Washington, Cold Spring Harbor, New York, 1942-1967 | | Distinguished Service Member, Carnegie Institution of Washington, Cold Spring Harbor, New York, 1967 to Present Visiting Professor, California Institute of Technology, 1954 | | Consultant, Agricultural Science Program, The Rockefeller Foundation, 1963-1969 | | Andrew D. White Professor-at-Large, Cornell University, 1965-1974 | |  | | Honorary Doctor of Science | | University of Rochester, 1947 | | Western College for Women, 1949 | | Smith College, 1957 | | University of Missouri, 1968 | | Williams College, 1972 | | The Rockefeller University, 1979 | | Harvard University, 1979 | | Yale University, 1982 | | University of Cambridge, 1982 | | Bard College, 1983 | | State University of New York, 1983 | | New York University, 1983 | |  | | Honorary Doctor of Humane Letters | | Georgetown University, 1981 | |  | | Awards | | Achievement Award, Association of University Women, 1947 | | Merit Award, Botanical Society of America, 1957 | | Kimber Genetics Award, National Academy of Sciences, 1967 | | National Medal of Science, 1970 | | Lewis S. Rosenstiel Award for Distinguished Work in Basic Medical Research, 1978 | | The Louis and Bert Freedman Foundation Award for Research in Biochemistry, 1978 | | Salute from the Genetics Society of America, August 18, 1980 | | Thomas Hunt Morgan Medal, Genetics Society of America, June, 1981 | | Honorary Member, The Society for Developmental Biology, June, 1981 | | Wolf Prize in Medicine, 1981 | | Albert Lasker Basic Medical Research Award, 1981 | | MacArthur Prize Fellow Laureate, 1981 | | Honorary Member, The Genetical Society, Great Britain, April, 1982 | | Louisa Gross Horwitz Prize for Biology or Biochemistry, 1982 | | Charles Leopold Mayer Prize, Académie des Sciences, Institut de France, 1982 | |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0595 |
| Biographical | I was born January 10th, 1916 in Stockholm, Sweden.  Degrees  1944D. Med. Sci., Biochemistry, [Karolinska Institutet](http://www.ki.se/), Stockholm  1944  M. D., Karolinska Institutet, Stockholm  1944Docent of Physiological Chemistry, Karolinska Institutet, Stockholm   |  |  | | --- | --- | | Appointments | | | 1938 | Research Fellowship, London University, London | | 1940 – 41 | Research Fellowship, Columbia University, New York | | 1941 – 42 | Squibb Institute for Medical Research, New Brunswick, N.J. | | 1944 – 47 | Assistant at the Biochemical Department, The Medical Nobel Institute, Karolinska Institutet, Stockholm | | 1946 – 47 | Research Fellowship, Basel University, Basel | | 1947 – 58 | Professor of Physiological Chemistry, The University of Lund, Lund | | 1958 – 80 | Professor of Chemistry, Karolinska Institutet, Stockholm | | 1963 – 66 | Dean of the Medical Faculty, Karolinska Institutet, Stockholm | | 1969 – 77 | Rector of Karolinska Institutet, Stockholm | | 1975 – | Chairman of the Board of Directors, [The Nobel Foundation](https://www.nobelprize.org/nobel_organizations/nobelfoundation/index.html), Stockholm | | 1977 – 82 | Chairman of the WHO Global Advisory Committee on Medical Research, Geneva | | 1983 | President of the [Royal Swedish Academy of Sciences](http://www.kva.se/) | |  |  | | Memberships and Honorary Memberships | | | 1952 – 58 | Swedish Medical Research Council, Stockholm | | 1964 – 70 | Swedish Medical Research Council, Stockholm | | 1955 – 62 | Swedish Natural Science Research Council, Stockholm | | 1965 | Royal Swedish Academy of Sciences, Stockholm | | 1965 | Swedish Academy of Engineering Sciences, Stockholm | | 1965 | American Academy of Arts and Sciences, Boston | | 1973 | National Academy of Sciences, Washington, D. C. | | 1973 | American Society of Biological Chemists | | 1976 | Academy of Sciences USSR, Moscow | | 1977 | Academia Leopoldina, Halle, DDR | | 1978 | Institute of Medicine, NAS, Washington, D. C. | | 1980 | Royal Society of Edinburgh, Edinburgh | | 1982 | Medical Academy USSR, Moscow | | 1982 | Finska Vetenskaps-Societeten, Helsingfors | | 1982 | Swedish Society of Medical Sciences, Stockholm | |  |  | | Honors and Awards | | | Doctor h. c., University of Basel, Basel, 1960 | | | Doctor h. c., University of Chicago, Chicago, 1960 | | | “La Madonnina”, Lectureship, Milan, 1972 | | | Dunham Lecturer, Harvard University, Boston, 1972 | | | Anders Jahre Medical Prize, Oslo, 1972 | | | The Gairdner Award, University of Toronto, Toronto, 1972 | | | Dohme Lecturer, Johns Hopkins University, Baltimore, 1972 – 73 | | | Merrimon Lecturer, University of North Carolina, Chapel Hill, 1973 | | | The V. D. Mattia Lectureship of the Roche Institute, USA, 1974 | | | Harvey Lecture, The Harvey Society, New York, 1974 | | | The Louisa Gross Horwitz Prize, Columbia University, New York, 1975 | | | The Francis Amory Prize, American Academy of Arts and Sciences, 1975 | | | Doctor h. c., Harvard University, Boston, 1976 | | | Doctor h. c., Mount Sinai Medical School, New York, 1976 | | | Doctor h. c., Medical Academy of Wroclaw, Poland, 1976 | | | The Albert Laser Basic Medical Research Award, New York, 1977 | | | General Amir Chand Oration, All India Institute, New Delhi, 1978 | | | Cairlton Lecture, University of Texas Health Science Centre, Dallas, 1979 | | | The Robert A. Welch Award in Chemistry, Houston, 1980 | | | Nobel Laureate in Physiology or Medicine, Stockholm 1982 | | |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0596 |
| Biographical | I was born in Halmstad, Sweden, on May 21, 1934 to Anders and Kristina Samuelsson. After attending public schools I studied medicine at the University of Lund where I met my wife Karin (Bergstein). We have one son (Bo) and two daughters (Elisabet and Astrid).  After a few years in Lund I moved to [Karolinska Institutet](http://www.ki.se/) in Stockholm in order to do graduate work in biochemistry in parallel with medical studies. In 1960 I finished my dissertation and became docent in medical chemistry. A year later I also obtained my MD degree from Karolinska Institutet. After a year as research fellow in the Department of Chemistry at Harvard University, Cambridge, Mass., U.S.A., I returned to Karolinska Institutet. In 1967 I was appointed professor of medical chemistry at the Royal Veterinary College in Stockholm, and after a few years I moved back to Karolinska Institutet to become professor and chairman of the department of physiological chemistry. Concurrently with my research positions I have also held administrative posts. I was dean of the medical faculty from 1978 to 1983, and is presently rector of Karolinska Institutet.  My research interests were originally in cholesterol metabolism with emphasis on reaction mechanisms. After the structural work on prostaglandins with [Sune Bergström](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1982/index.html) in 1959-1962 I have mainly been interested in transformation products of arachidonic acid. This has led to the discovery of endoperoxides, thromboxanes and the leukotrienes, and my group has mainly been involved in studying the chemistry, biochemistry and biology of these compounds and their role in biological control system. The research has implications in several clinical areas, particularly in thrombosis, inflammation and allergy.   |  | | --- | | Appointments | | Assistant professor of medical chemistry, Karolinska Institutet 1961-1966 | | Research fellow, Department of Chemistry, Harvard University, Cambridge, Mass., U.S.A., 1961-1962 | | Professor of medical chemistry, Royal Veterinary College, Stockholm, Sweden, 1967-1972 | | Professor of medical and physiological chemistry, Karolinska Institutet, Stockholm, Sweden, 1973- | | Chairman of the Department of Chemistry, Karolinska Institutet, Stockholm, Sweden, 1973- | | Visiting professor in chemistry, Harvard University, Cambridge, Mass., U.S.A., spring term 1976 | | Dean of the Medical Faculty, Karolinska Institutet, Stockholm, Sweden, July 1, 1978 – June 30, 1983 | | Rector of Karolinska Institutet, July 1, 1983 – Jun 30, 1995 | |  | | Memberships, Awards and Honors | | Swedish Medical Association’s Jubilee Award, Stockholm, Sweden (1968) | | Anders Jahres Award, Oslo University, Oslo, Norway (1970) | | Louisa Gross Horwitz Award, Columbia University, New York, U.S.A. (1975) | | Honorary Member American Society of Biological Chemists (1976) | | Intrascience Medalist, Santa Monica, California, U.S.A. (1976) | | Albert Lasker Basic Medical Research Award, New York, U.S.A. (1977) | | Honorary Degree of Doctor of Science, University of Chicago, Chicago, Illinois, U.S.A. (1978) | | Ciba Geigy Drew Award in Biomedical Research, Madison, New Jersey, U.S A. (1980) | | Member of the [Royal Swedish Academy of Sciences](http://www.kva.se/) (1981) | | Lewis S. Rosenstiel Award in Basic Medical Research, Brandeis University, Boston, Mass., U.S.A. (1981) | | Swedish Medical Association’s Jubilee Award, Stockholm, Sweden (1981) | | The Gairdner Foundation Award, Toronto, Canada (1981) | | Heinrich Wieland Prize, Munich, West Germany (1981) | | The Bror Holmberg Medal of the Swedish Chemical Society (1982) | | Honorary Member Association of American Physicians (1982) | | Member of the Mediterranean Academy, Catania, Italy (1982) | | Foreign Honorary Member of the American Academy of Arts and Sciences (1982) | | American Chemical Society Division of Medical Chemistry Award (1982) | | Waterford Bio-Medical Science Award, La Jolla, California, U.S.A. (1982) | | International Association of Allergology & Clinical Immunology Award, London, Great Britian (1982) | | Honorary Member, Swedish Medical Association, Stockholm, Sweden (1982) | | Honorary Degree of Doctor of Science, University of Illinois, U.S.A. (1983) | |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0597 |
| Biographical | I was born in Tardebigg, Worcestershire, on the 29th March 1927, one of three children, with an elder sister and brother. My father, Maurice Vane, was a son of immigrants from Russia and my mother, Frances Vane, came from a Worcestershire farming family.  We lived in a suburb of Birmingham where I attended the local state school from the age of five. I then went on to King Edward VI High School in Edgbaston, Birmingham. However, the war was beginning and the whole school was evacuated into the countryside, alongside Repton School in Derbyshire. The expected bombings did not take place, and early in 1940 the school moved back to Birmingham. The air raids then started, and for the next four years, my school and home life were coloured by the trappings of war. With my family, I spent nights in the air-raid shelter at the bottom of the garden and at school we firewatched and trained as (or pretended to be) young soldiers.  At the age of 12, my parents gave me a chemistry set for Christmas and experimentation soon became a consuming passion in my life. At first, I was able to use a Bunsen burner attached to my mother’s gas stove, but the use of the kitchen as a laboratory came to an abrupt end when a minor explosion involving hydrogen sulphide spattered the newly painted decor and changed the colour from blue to dirty green!  Shortly afterwards, my father, who ran a small company making portable buildings, erected a wooden shed for me in the garden, fitted with bench, gas and water. This became my first real laboratory, and my chemical experimentation rapidly expanded into new fields.  At High School I progressed through the pure sciences, and in 1944 it seemed natural to move to the University of Birmingham (which was just across the road from the school) to study Chemistry. However, the enthusiasm with which I had approached experimentation in Chemistry in the garden shed was soon dampened, for at university experimentation was nonexistent. The only unknown in the practical class was the percentage yield in the chemical synthesis involved. It was, I suppose, at this stage that I began to realise that my interest lay not in chemistry but more in experimentation. Thus, when Maurice Stacey, the Professor of Chemistry, asked me what I wanted to do when I graduated, I said “anything but chemistry”. Stacey then told me that he had received a letter that morning from Professor Harold Burn in Oxford asking whether he could recommend another young chemist (he had sent one the previous year) to go to Oxford to be trained in pharmacology. Without hesitation I grasped the opportunity and immediately went to the library to find out what pharmacology was all about! That brief exchange with Stacey reshaped my whole career.  I went to Burn’s department in 1946. I had no biological training of any sort and very little motivation. I found inspiration in working with him and caught his enthusiasm for pharmacology. If anyone can be said to have moulded the subject of pharmacology around the world, it is he. He did this through his particular style of research, through the lucidity of his writings, but most of all through the school which he founded. Young, impressionable scientists from various disciplines and older, less impressionable pharmacologists all came to work with him. His laboratory gradually became the most active and important centre for pharmacological research in the U.K. and the main school for training of young pharmacologists. It was his energy and inspiration that set my career into one of adventure in the fields of bioassay and pharmacology. It was Burn who reinforced for me the essence of experimentation and that is, never to ignore the unusual.  After qualifying for a B.Sc. in pharmacology, I spent a few months in Sheffield University as a research worker in the pharmacology department but then went back to Oxford to the Nuffield Institute for Medical Research in order to study for a D. Phil. with Dr. Geoffrey Dawes. In 1951 I was awarded the Stothert Research Fellowship of The Royal Society and this enabled me to complete my doctorate in 1953. Oxford was also an important milestone for it was there that my wife and I made our first home, and it was there that my daughters Nicola and Miranda were born.  In 1953, we all went to Newhaven, Connecticut where, at the invitation of Dr. Arnold Welch, who was then Chairman, I joined the Department of Pharmacology at Yale University as Assistant Professor in Pharmacology. That was a lively and bustling department, but after 2 years we returned to the U.K, where I started work with Professor W. D. M. Paton at the Institute of Basic Medical Sciences of the University of London in the Royal College of Surgeons of England. This was an unusual department, for the teaching was only for graduates, and was not time consuming, thus offering plenty of time for research. I stayed there for 18 years, progressing from Senior Lecturer to Reader to Professor of Experimental Pharmacology. From 1961 to 1973, Professor G. V. R. Born, a close friend from my Oxford days, was the Chairman of the Department and we enjoyed a strong symbiotic relationship, each maintaining an active group of graduate students and research workers. Interestingly, our fields of research endeavour (platelets and prostaglandins) only coalesced in a significant way after we had both moved on.  It was here that I developed, together with my group, the cascade superfusion bioassay technique for measurement of, dynamically and instantaneously, the release and fate of vasoactive hormones in the circulation or in the perfusion fluid of isolated organs. In the mid-1960’s, our attention was focused on prostaglandins, leading in 1971 to the forging of the link between aspirin and the prostaglandins.  In 1973, I was offered the position of Group Research and Development Director for The Wellcome Foundation. In making my decision, I was conscious that Henry Wellcome, seventy years before, had recruited [Henry Dale](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1936/index.html) to work in (and soon to direct) the Wellcome Physiological Research Laboratories, the forerunners of the present Research and Development Directorate. When Henry Dale, then at Cambridge, first received the offer from Wellcome, he hesitated over accepting it. “Friends to whom I mentioned this approach” he said, “were almost unanimous in advising me to have nothing to do with it. I should be selling my scientific soul for a mess of commercial potage”. Nevertheless, he accepted and had no regrets. I also found amongst a few of my friends a resistance to the idea of me entering into industrial science. It was as if to say that good science can only be promulgated in academia. Those friends were wrong; like Dale I accepted and had no regrets. I took with me from the Royal College of Surgeons a nucleus of colleagues, and this has expanded over the last few years into a Prostaglandin Research department under the leadership of Dr. Salvador Moncada. It was in this department that prostacyclin was discovered and its pharmacology developed.  Fellowships   |  |  | | --- | --- | | 1973 | Honorary Member of the Polish Pharmacological Society | | 1973 | Fellow of the Institute of Biology | | 1974 | Fellow of the Royal Society | | 1977 | Walter C. McKenzie Visiting Professorship, University of Alberta, Edmonton, Canada | | 1978 | Honorary Fellowship of the American College of Physicians | | 1978 | Member of the Royal Academy of Medicine of Belgium | | 1979 | Foreign Member of the Royal Netherlands Academy of Arts & Sciences | | 1979 | Visiting Professor, Harvard University, Cambridge, Mass., U.S.A. | | 1980 | Foreign Member of the Polish Academy of Sciences | | 1982 | Foreign Honorary Member of the American Academy of Arts and Sciences, U.S.A. | | 1982 | Honorary Fellowship of the Swedish Society of Medical Sciences | | 1983 | Foreign Associate of the National Academy of Sciences, U.S.A. |   Honorary degrees  1977  D. Med. (Hon. Causa) Copernicus Academy of Medicine, Cracow  1978Doctor Hon Causa René Descartes University, Paris  1980  Doctor of Science (Hon. Causa) Mount Sinai Medical School, City University of New York, U.S.A.  1983Doctor of Science, Aberdeen University  Medals, prizes and awards   |  |  | | --- | --- | | 1977 | Baly Medallist of the Royal College of Physicians | | 1977 | Albert Lasker Basic Medical Research Award | | 1979 | Joseph J. Bunim Medal of the American Rheumatism Association | | 1980 | Peter Debye Prize, University of Maastricht, Holland | | 1980 | Nuffield Lecture & Gold Medal, Royal Society of Medicine, England | | 1980 | Feldberg Foundation Prize | | 1980 | Ciba Geigy Drew Award, Drew University, U.S.A. | | 1981 | Dale Medallist, Society for Endocrinology | |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0598 |
| Biographical | Birthplace and Family: Born August 20, 1913, in Hartford, Connecticut to Francis Bushnell and Florence Kraemer Sperry of Elmwood, a small suburb. Father was in banking; mother trained in business school and after dad’s death, when I was 11 years old, she became assistant to the principal in the local high school. One brother, Russell Loomis, a year younger, went into chemistry. I was married to Norma Gay Deupree, December 28, 1949. We have one son, Glenn Michael (Tad), born October 13, 1953 and one daughter, Janeth Hope, born August 18, 1963.  Education: My early schooling was in Elmwood, Connecticut and William Hall High School in West Hartford, Connecticut. I attended Oberlin College on a 4 year Amos C. Miller Scholarship. After receiving the AB in English in 1935, I stayed on 2 years more in Oberlin for an MA in Psychology, 1937, under Professor R. H. Stetson. I then took an additional third year at-large at Oberlin to prepare for a switch to Zoology for Ph.D. work under Professor Paul A. Weiss at the University of Chicago. After receiving the Ph.D. at Chicago in 1941, I did a year of postdoctoral research as a National Research Council Fellow at Harvard University under Professor Karl S. Lashley.  Professional positions: Biology research fellow, Harvard University, at Yerkes Laboratories of Primate Biology (1942-46); Assistant professor, Department of Anatomy, University of Chicago (1946-52); Associate professor of psychology, University of Chicago (1952-53); Section Chief, Neurological Diseases and Blindness, National Institutes of Health (1952-53); Hixon professor of psychobiology, California Institute of Technology (1954-present).  Awards and Honors: Amos C. Miller Scholarship, Oberlin College (1931-35); National Research Council Fellowship (1941-42); Distinguished Alumni Citation; Oberlin College (1954); Elected National Academy of Sciences (1960); Elected American Academy of Arts and Sciences (1963); Howard Crosby Warren Medal, Society of Experimental Psychologists (1969); Distinguished Scientific Contribution Award, American Psychological Association (1971); California Scientist of the Year Award (1972); Co-recipient William Thomson Wakeman Research Award, National Paraplegia Foundation (1972); Honorary Doctor of Science degree, Cambridge University (1972); Passano Award in Medical Science (1973); Elected American Philosophical Society (1974); Elected Honorary Member American Neurological Association (1974); Co-recipient Claude Bernard Science Journalism Award (1975); Karl Lashley Award of American Philosophical Society (1976); Elected Foreign Member of Royal Society (1976); Honorary Doctor of Science Degree, University of Chicago (1976); Elected member of Pontifical Academy of Sciences (1978); Honorary Doctor of Science Degree, Kenyon College (1979); Wolf Prize in Medicine (1979); Ralph Gerard Award of the Society of Neurosciences (1979); International Visual Literacy Association Special Award (1979); Albert Lasker Medical Research Award (1979); Honorary Doctor of Science Degree, The Rockefeller University (1980); American Academy of Achievement Golden Plate Award (1980)  A vocational and anti-brain-strain: Collected and raised large American moths in grade school. Ran trap line and collected live wild pets during junior high school years. Three-letter man in varsity athletics in high school and college. Through middle life continued evening and weekend diversionary activities including sculpture, ceramics, figure drawing, sports, American folk dance, boating, fishing, snorkeling, water colors, and collecting unusual fossils – among which we have a contender for the world’s 3rd largest ammonite.  Selected Bibliography   1. The problem of central nervous reorganization after nerve regeneration and muscle transposition. R.W. Sperry. Quart. Rev. Biol. 20:311-369 (1945). 2. Regulative factors in the orderly growth of neural circuits. R.W. Sperry. Growth Symp. 10: 63-67 (1951). 3. Cerebral organization and behavior. R.W. Sperry. Science 133:1749-1757 (1961). 4. Chemoaffinity in the orderly growth of nerve fiber patterns and connections. R.W. Sperry. Proc. Nat. Acad. Sci. USA 50: 703-710 (1963). 5. Interhemispheric relationships: the neocortical commissures; syndromes of hemisphere disconnection. R.W. Sperry, M.S. Gazzaniga, and J.E. Bogen. In *Handbook Clin. Neurol.* P. J. Vinken and G.W. Bruyn (Eds.), Amsterdam: North-Holland Publishing Co. 4: 273-290 (1969). 6. Lateral specialization in the surgically separated hemispheres. R.W. Sperry. In *Neurosciences Third Study Program.* F. Schmitt and F. Worden (Eds.), Cambridge: MIT Press 3:5-19 (1974). 7. Mind-brain interaction: mentalism, yes; dualism, no. R.W. Sperry. Neuroscience 5: 195-206 (1980). Reprinted in *Commentaries in the Neurosciences.* A.D. Smith, R. Llanas and P.G. Kostyuk (Eds.), Oxford: Pergamon Press, pp. 651-662 (1980). 8. *Science and moral priority: merging mind, brain and human values.* R.W. Sperry. Vol. 4 of Convergence, (Ser. ed. Ruth Anshen) New York: Columbia University Press (1982). |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0599 |
| Biographical | I was born in 1926 in Windsor, Ontario. Three of my grandparents were also born in Canada: the fourth, my paternal grandfather, emigrated as a child to the U.S.A. from the Bavarian town of Nördlingen. He became a pharmacist and achieved some prosperity by inventing the first process for the mass producing of gelatin capsules. My parents were born and raised in Detroit, Michigan. My father, a chemical engineer, took a job across the Detroit River in Windsor, Ontario, became tired of commuting from Detroit, and finally moved to Canada. When I was born I acquired U.S. citizenship through my parents and Canadian citizenship by birth. (When it comes to prizes I don’t know whether each country gets half credit or both get full credit.) In 1929 my father moved to Montreal, where I grew up. From age six to eighteen I went to Strathcona Academy in Outremont, and owe much to the excellent teachers there, especially to Julia Bradshaw, a dedicated, vivacious history teacher with a memorable Irish temper, who awakened me to the possibility of learning how to write readable English. I owe much of my interest in science to my father, whom I plagued with endless questions. To my mother goes much of the credit for encouraging me to work for whatever objectives I set for myself. As a boy my main hobbies were chemistry (my friends, who consider me utterly ignorant of that subject, will be richly amused) and electronics. I soon tired of the electronics because nothing I built ever worked. But with chemistry I discovered potassium chlorate and sugar mixture and set off a small cannon that rocked Outremont, and I released a hydrogen balloon that flew all the way to Sherbrooke. At McGill College I did honors mathematics and physics, partly to find out why nothing worked in electronics, but mainly because it was more fun to do problems than to learn facts. I still much prefer to do science than to read about it. I graduated in 1947 and, almost on the toss of a coin, despite never having taken a course in biology (even in high school, where it was considered a subject only for those who could not do Latin or mathematics) I applied to Medical School at McGill. Rather to my horror I was accepted. At first I found it very difficult, given my total ignorance of biology and the need to memorize every muscular insertion in the body. I spent summers at the Montreal Neurological Institute doing electronics (I now had the theoretical basis but still no talent with a soldering iron) and there I became fascinated by the nervous system – small wonder considering that this was the period of culmination of the work of Penfield and Jasper. To my surprise I also found I enjoyed clinical medicine: it took three years of hospital training after graduation, (a year of internship and two of residency in neurology) before that interest finally wore off. The years of hospital training were interrupted by a year of clinical neurophysiology under Herbert Jasper, who was unequalled for his breadth and clarity of thinking in brain science. On setting foot into the United States in 1954 for a Neurology year at Johns Hopkins I was promptly drafted by the army as a doctor, but was lucky enough to be assigned to the Walter Reed Army Institute of Research, Neuropsychiatry Division, and there, at the age of 29, I finally began to do research. One then had little of the feeling of frenetic competition that is found in graduate students today; it was possible to take more long-shots without becoming panic stricken if things didn’t work out brilliantly in the first few months. We were not free from financial worries, as graduate students in biology by and large are now; until I entered the army my income was close to zero, and I owe a huge debt to my wife Ruth for supporting us through those lean and exploited years of residency and fellowship training.  Scientifically, I could hardly have chosen a better place than Walter Reed. In the neuropsychiatry division David Rioch had assembled a broad and lively group of young neuroscientists, notably M.G.F. Fuortes and Robert Galambos in neurophysiology, Walle Nauta in neuroanatomy, Joseph Brady and Murray Sidman in experimental psychology and John Mason in chemistry. As in Montreal, the focus was on the entire nervous system, not on a subdivision of biological subject matter based on methods. I worked under the supervision of Fuortes. We began by collaborating for six months on a spinal cord project, and it was then that I had my only apprenticeship in experimental neurophysiology. Fuortes had a genuine feel for biology that was rare among neurophysiologists in those days. I also learned and benefited much from a most able and helpful research assistant, Calvin Henson. My main project while at Walter Reed was a comparison of the spontaneous firing of single cortical cells in sleeping and waking cats. I began by recording from the visual cortex: it seemed most sensible to look at a primary sensory area, and the visual was easiest, there being less muscle between that part of the brain and the outside world. It was first necessary to devise a method for recording from freely moving cats and to develop a tungsten microelectrode tough enough to penetrate the dura. That took over a year, but in the end it was exciting to be able to record from a single cell in the cortex of a cat that was looking around and purring.  In 1958 I moved to the Wilmer Institute, Johns Hopkins Hospital, to the laboratory of Stephen Kuffler, and there I began collaboration with [Torsten Wiesel](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1981/index.html). A year later Kuffler’s entire laboratory (nine families) moved to Harvard Medical School in Boston, at first as part of the Department of Pharmacology under Otto Krayer, who was largely responsible for bringing Kuffler to Harvard. Five years later, in a move unprecedented for Harvard, we became the new Department of Neurobiology. My daily contacts with Stephen Kuffler (until his death a year ago) and with Edwin Furshpan, Edward Kravitz, David Potter and Simon LeVay have been both fun and enriching. During the past twenty two years, besides working with Torsten, I have collaborated briefly with Ursula Dräger, Helga Ginzler, and Ann Graybiel. At present I am working with Margaret Livingstone.  Since the age of five I have spent a disproportionate amount of time on music, for many years the piano, then recorders, and now the flute. I do woodworking and photography, own a small telescope for astronomy, and I ski and play tennis and squash. I enjoy learning languages, and have spent untold hours looking up words in French, Japanese and German dictionaries. In the laboratory I enjoy almost everything, including machining, photography, computers, surgery – even neurophysiology.  This is perhaps a suitable place to express my deep gratitude to the Eye Institute of the National Institutes of Health, to the U.S. Air Force, the Klingenstein Foundation, and to the Rowland Foundation for their generous support of our research. Also the Faculty of Harvard University deserves my thanks for tolerating such a truculent colleague. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | 0600 |
| Biographical | I was born in Uppsala Sweden in 1924, the youngest of five children. My father, Fritz S. Wiesel, was chief psychiatrist and head of Beckomberga Hospital, a mental institution located on the outskirts of Stockholm. We were brought up by my mother, Anna-Lisa (b. Bentzer), at the hospital and were sent by bus to Whitlockska Samskolan, a coeducational private school in the city. I was a rather lazy, mischievous student, interested mainly in sports. My election as president of the high school’s athletic association was my only memorable achievement during that period. Suddenly, at the age of 17, I became a serious student and I did reasonably well as a medical student. My curiosity about the workings of the nervous system was stimulated by the lectures of Carl Gustaf Bernhard and Rudolf Skoglund, my professors in neurophysiology. Because of my background I was also interested in psychiatry, and I spent one year while I was a medical student working with patients in different mental hospitals.  When my studies were completed I returned to Professor Bernhards’s laboratory at the [Karolinska Institute](http://www.ki.se/) in 1954 to do basic neurophysiological research. The following year I had the good fortune to be invited to the United States as a postdoctoral fellow in Dr. Stephen Kuffler’s laboratory at the Wilmer Institute, Johns Hopkins Medical School. Dr. Kuffler had just published his now classical study of the receptive field arrangements of cat retinal ganglion cells. This was an important extension of the pioneering work of Drs. [Hartline](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1967/index.html) and [Granit](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1967/index.html), for which they received the 1967 Nobel Prize. [David Hubel](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1981/index.html) joined the laboratory in 1968, and the two of us decided to explore the receptive field properties of cells in the central visual pathways. This marked the beginning of our twenty year collaboration.  In 1959 Dr. Kuffler was invited to become a professor of pharmacology at Harvard Medical School, and he brought a group of young and enthusiastic investigators with him from Johns Hopkins Medical School. The effectiveness of this group of neuroscientists in research and teaching, and the foresight of Dr. Ebert, then the Dean of the Medical School, led to the formation of the Department of Neurobiology with Stephen Kuffler as the chairman. In addition to David Hubel and myself, the original group of emigres from Johns Hopkins included Edwin Furshpan and David Potter; together with Edward Kravitz we became the original faculty of the new department. David and I now had the opportunity to continue our work in a stimulating environment. Our collaboration continued until the late seventies. In the past several years I worked with Charles Gilbert, a young investigator in the Department. In 1973 I was asked to be head of the Department of Neurobiology. Dr. Kuffler, who meant so much to all of us, continued his work as a University Professor until he died suddenly in 1980. My only regret is that he could not join David and me in the celebration of the Nobel Prize.  I was married to Teeri Stenhammar 1956-1970 and Ann Yee 1973-1981. My daughter Sara Elisabeth was born in 1975. Aside from my work my interests lie in the arts and in world affairs.   |  |  | | --- | --- | | Honors and Awards | | | 1967 | A.M. (Hon.), Harvard University2005 | | 1971 | The Dr. Jules C. Stein Award, presented by the Trustees for Research to Prevent Blindness | | 1972 | The Lewis S. Rosenstiel Prize, presented by Brandeis University | | 1972 | Ferrier Lecture (Royal Society of London) | | 1975 | The Freidenwald Award, presented by the Trustees of the Association for Research in Vision and Ophthalmology, Inc. | | 1976 | The Grass Lecture (Society for Neuroscience) | | 1977 | The Karl Spencer Lashley Prize, presented by the American Philosophical Society | | 1978 | The Louisa Gross Horwitz Prize, presented by Columbia University | | 1979 | The Dickson Prize, presented by the University of Pittsburgh | | 1980 | The Ledlie Prize, Harvard University | | 1980 | Society for Scholars (Johns Hopkins University) | | 1981 | The Nobel Prize in Physiology or Medicine | | 1983 | William D. Stubenbord Visiting Prof., Cornell Univ. Medical College, New York | | 1989 | W.H. Helmerich III Award, The Woodlands, Texas | | 1996 | Helen Keller Prize for Vision Research | | 1998 | Society for Neuroscience, Presidential Award | | 2005 | Institute of Medicine, David Rall Medal | | 2005 | The National Medal of Science (USA) | | 2006 | Spanish National Research Council (CSIC – Consejo Superior de Investigaciones Cientificas) Gold Medal | | 2007 | Marshall M. Parks MD Medal of Excellence [Shared with David Hubel], Children’s Eye Foundation |  **Addendum, October 2008** In 1983, I became the Vincent and Brook Astor Professor at The Rockefeller University, where I established a new Laboratory of Neurobiology and continued my close collaboration with Charles Gilbert on the circuitry of primary visual cortex. In close to 20 years of collaboration, Charles and I were able to describe the specificity and dynamic nature of the long-range horizontal connections that we discovered at Harvard.  After forty years in the lab, I was asked in 1991 to become president of The Rockefeller University. Unlike a working scientist, being president for seven years provided an opportunity to interact with scientists in many different fields and broadened my scope of the natural sciences. For example, it allowed me to take the initiative to create a Center for Studies in Physics and Biology. To my surprise, I enjoyed the challenges of administration, in particular assisting in the recruitment of new talent to the university. It was a privilege to be at the helm of such a great institution and to be a part of this unique community of scholars and university staff alike.  Since leaving the presidency in 1998, I have focused my efforts on many issues that have long concerned me and have devoted myself to programs for younger scientists. In the spring of 2000, I accepted the position of Secretary General of the Human Frontier Science Program (HFSP), an organization headquartered in Strasbourg that supports international and interdisciplinary collaboration between investigators in the life sciences and sponsors the training of post-doctoral students from different parts of the world.  While remaining at the Rockefeller University as director of the Shelby White and Leon Levy Center for Mind, Brain and Behavior, I continue to be an advisor to different countries and organizations, mainly helping to create opportunities for young scientists to carry out independent research, similar to what has become the established path for scientists working the United States. For over 15 years I have been involved with the Pew Charitable Trusts chairing both its Scholars Program and the Latin American Fellowship Program, which supports the training of students in the best laboratories in the U.S. Since 2002 I have co-chaired the board of governors of the Okinawa Institute of Technology (OIST), and since 2003 have chaired the advisory board of China’s National Institute of Biological Science (NIBS), in Beijing.  I continue to serve on the boards of the Pew Center on Global Climate Change, the Hospital for Special Surgery, and on the advisory board of the European Brain Research Institute (EBRI). For 10 years (1994-2004), I served as chair of the Committee of Human Rights of the National Academies of Science (U.S.A.) and the International Human Rights Network of Academies and Scholarly Societies, assisting colleagues who have been imprisoned or harassed for their peaceful opposition to the policies of their governments. I was also a founding member of the Israeli-Palestinian Science Organization (IPSO), a nongovernmental nonprofit established in 2004 to support collaborative research between scientists in Israel and Palestine to promote positive interactions between the two communities.  I also served as chair of the board of the Aaron Diamond AIDS Research Center (1995-2001), president of the International Brain Research Organization, IBRO, (1998-2004), chair of the Board of Governors of the New York Academy of Sciences (2001-2006), and on the board of directors of the Population Council (1999-2008).  In 2007, the Torsten Wiesel Research Institute was established by the World Eye Organization at West China Hospital in Chengdu, China, to engage in basic and clinical research, especially on eye diseases most prevalent in Asia. I was married to Jean Stein from 1995 to 2007. My grandson Owen Thomas Cullen was born on July 14, 2007. In 2008 I married Lizette Mususa Reyes. We presently divide our time between Strasbourg, Stockholm and New York. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q34 | Welcome to this Nobel interview, Professor Torsten Wiesel. You have devoted your long career in science to studies of the visual processing in the brain and now we can say, and we know, that this is not a simple thing, a simple process, rather a result of a long process that begins in the eyes but definitely does not stop here. |
|  | Correct. Of course it’s a very complex thing you’re asking the brain to do, because we can see details, colour, depth, moving objects, etc. Your camera cannot move without getting a slur in the image that is unclear, whereas your eye can move from one part of the room to another and still everything is clear. So this is a very complex machine that can carry out all these various functions, and we are, I think, still at a relatively primitive stage of a complete understanding of the neuro basis of perception. So it’s a long way still to go even if progress has been made. |
| Q23 | So this is not just a mechanical process? It is a question of interpretation? |
|  | Right. The brain has to decompose an image that falls on your retina and there are hundreds of millions of receptors in your eye, photo receptors that are sensitive to light and then there’s only one million fibres going from the eye into the brain. So already in the eye there’s some processing, complex processing of the image and then that’s sent into the brain and then it’s further composed together so that you can see all the things in detail. I used to say to students it’s not like a fax machine, that you send an image up to the brain and there are little people looking up in the brain at that picture, because you actually have to decompose the picture, send it like a message up and then rebuild it so you can perceive it and we know some of the code that is used by the brain to carry this out but we are still at an early stage of understanding that process. |
| Q23 | In spite of nearly 50 years of studies, I wonder what do you consider as the major step in our understanding of how the visual system works during these years. |
|  | During these last 50 years?  During your career, I would say.  Torsten Wiesel: During my career … You know, I came into a laboratory at Johns Hopkins University at the time. My mentor there was a man by the name of Stephen Kuffler and he had studied cells in the eye that leave the eye going to the brain and learnt about the way that these cells decode the visual image. Also the Swedish scientist by the name of [Ragnar Granit](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1967/granit-facts.html) was also very important in vision research and he received the Nobel Prize in 1967, I believe, for his work on the eye. My colleague David Hubel and I, we were fortunate when we started, in 1958 we started to work together, and try to understand how images sent in from the eye are handled by the brain and so that was some advances made during our collaboration. We worked together for 20 years in trying to understand how the first and second stage in the brain handle visual information and particularly in the visual cortexes, a primary visual cortex, it’s called. |
| Q34 | But even after the Nobel Prize you continued your research? |
|  | Yes. But you ask for the last 50 years with advances. So the reason why we got the Nobel Prize was because we made some advances obviously, and that was part of what I said, the decode, the fact that cells in visual cortex respond to contours of given orientations. So that then a phase, for example, is decomposed and then rebuilt perhaps cells responding to different orientation of your facial contours will feed and assemble cells responding in a particular way and the advances since that time scientists have recorded from higher visual areas, because first the signal from the eye goes to the primary cortex, then the second, the tertiary higher structures and we don’t have to go into the details, but at some stage, maybe three steps away, there are cells that actually respond to a face.  Not your face necessarily, but any face that is contoured like a face with eyes and nose and a mouth; those basic characteristics. So that is a major advance in the sense that cells can be so specific that they can respond to a particular object. There are probably other cells responding to a face or a form or shape. Of course these cells you’re not born with necessarily, because there’s a certain plasticity in the brain so that you can not only learn to recognise a new face but also objects which you never knew existed, like in modern art, for example, sometimes you see very abstract things which are invented by humans and you still can see them, recognise them and sort of store them as a visual memory like you store a face. |
| Q7 | But still I am not born with the cells that are focussed on modern art? |
|  | You’re born with the machinery to learn how to build an image. So these cells are sensitive to contours.  Very flexible machine.  … some part of our brains remain flexible all through life so you can learn new things …  Torsten Wiesel: You’re born with those cells. The newborn child can disseminate colour, it can see things, objects and so on. There’s a certain basic thing we are born with, but then of course you learn a lot of things. You recognise chairs and all kinds of things. So some part of our brains remain flexible all through life so you can learn new things, not only in vision but in language and movement etc. |
| Q34 | The field of brain studies has developed tremendously since you entered it in the ’50s. What do you find is the most interesting challenges in neurophysiology today? |
|  | Neuroscience is advanced to a large extent because new ways have developed to study subjects.  New instruments or new ways of thinking?  Torsten Wiesel: New instrumentation. Both new instrumentation and new conceptual questions perhaps asked. Sometimes you ask questions now that you didn’t ask earlier because there were no way of getting an answer.  What are these questions?  Torsten Wiesel: For example to ask the question that I said before that we want to understand the neuro basis of perception. That question wasn’t asked 50 years ago as a realistic scientific issue, but today it is realistic to try to actually have an experimental programme that tries to address that question so that’s the difference. And I think, you know, there are some people who feel that now it’s the right time also to understand not only neuro base of perception but also the higher issue of consciousness in general because in order to have perception you have to be conscious otherwise you don’t perceive. So those two are obviously linked very much.  So if you want to address a question of consciousness, then perhaps you have to do it in a context of a specific issue, like vision where you have a perception. You can when we know more perhaps about the sensory part of the brain in vision than in the other part of the brain because there has been a lot of interest, a lot of people have studied the various stages of the vision system both in psychophysics and in the laboratories, anatomy, physiology, chemistry etc. So there’s a lot of knowledge here, so I think the next decades in the future you are going to see more and a better understanding of the perception and consciousness related to that. |
| Q23 | Yes, there is this question, for example, when I see this flower and I see the red colour here, I recognise the colour here, I call it red. How can I be sure that the red colour that you see is the same that the one that I see? Do you think that neurophysiology can answer such questions? |
|  | Yes, of course it’s been known for a long time that colour vision varies between individuals because it depends very much on the visual pigment you have in your eye.  So maybe your red is my green, for example?  Torsten Wiesel: Most people have, not so much, but we have the cones; we have red, we have blue and we have green cones and they have their own spectre of sensitivity. Most people have very similar spectres and sensitivity of their cones but there are variations. So some in the red cone and maybe a slight difference in the peak sensitivity of the red cone, somebody else may have it in blue. So there may be slight variation, but then there are mutations. There are people who actually have no red cones or blue cones or green cones, so they have specific colour defects and it can be dangerous if you’re in the traffic and you know the red light and you don’t see red light and you have to know that the red is on top and the green is below.  So I think one has to assume that in most cases our perception of colour in this bouquet of flowers is probably similar, even if maybe somebody else would have a clear difference. I have a painter friend actually who had a deficit in his colour, his vision and his paintings reflected that. His colour scheme was kind of strange and some people found it very interesting but, you know, that was based on the fact that he saw the colours different from you and me perhaps. |
| Q45 | Yes, perhaps. But there still is this problem of consciousness of the subjective perception of the world. It’s sometimes called explanatory gap, how can our emotions and our perceptions translate into the hardware of the brain. Do you think that neurophysiology can jump over this gap or fill it in? |
|  | Knowledge advances in science at least, usually step by step, and depending on your background and the literature you read you may feel that there is a gap but some of us may feel there is no gap. It’s just a feel of ignorance. You have a knowledge here, up to this point and then you need to know more. You’re ignorant, you don’t understand something else and to have a complete basis for perception let’s say, because that’s what we’re talking about. So you can see that as a gap and it certainly is a gap in our knowledge but it’s not the conceptual gap. |
| Q3 | I have one last question about something else. You have left the research now and you have recently focussed your interest on other issues than doing research I would say. What engaged you most by now? |
|  | You know I was a professor at Rockefeller for a number of years.  Rockefeller University in New York, yes?  Torsten Wiesel: Rockefeller University in New York and I had been in Harvard. David Hubel and I worked together most of our time at Harvard, started out at Hopkins but then as a professor there was a need at a university so I was asked by the Board of Trustees to become president of that institution. It was in December ’91 and so I accepted to do that. So I did it for seven years. During that period it was very difficult for me to do experiments and I was 67 years old at the time. So after seven years I was close to 75 and the question was what … I was still full of interest and energy so instead of going to the laboratory I continued expanding, I should say, my interest in trying to help young scientists to have the same opportunities I had as a young scientist and to try to help to train students from developing countries. |
| Q43 | You mean to move from one country to another to come to good laboratories? |
|  | I’ve been running a programme for Latin American students, supported by the Pew Charitable Trust for ten years, bringing ten students a year from Latin America to come to the United States for training. Another interest I have … I’m now Secretary General for the Human Frontier Science Program which has headquarters in Strasbourg and we gave about 140 fellowships a year to students from all over the world, from 60 different countries.  As stipends for studies?  Professor Torsten Wiesel Stipend for studies. It’s now a three year programme and most of the students come to United States for studies and many of them stay in the United States because opportunities to do science there are usually better, particularly in the developing countries and I’m very interested to try to change that pattern so that we can help to provide opportunities for good training but also provide opportunity for young people coming back to their home country to carry out similar type of research as they did doing the training.So this is a major challenge I think that one should make serious effort.  … it’s difficult for young scientists to be independent, to get funds to do their own research …  It’s also provided opportunities, even in developed countries, it’s difficult for young scientists to be independent, to get funds to do their own research because Europe and also in Japan the professor is still taken very seriously whereas in United States a professor is not taken so seriously and the custom there is that as a young professor, assistant professor, you get your own lab, your own money and you’re doing your own research whereas in Europe and many part of the world it’s still not the case, you are still an assistant to the professor rather than independent scientists. This is an issue that I find very important for Europe and other parts of the world to develop really good science. It turns out the reason I think for the American success has been money but also the way science is organised. |
| Q43 | So you want to spread the idea of organising science because you yourself were born in Sweden but you have had your career in the States. |
|  | My scientific career in the States, yes, in part because of circumstances I had very good collaborator with David Hubel, we worked very well together. So that was one temptation. In science America became my homeland whereas when I come here I feel very much at home but it’s not as a scientists, it’s more as a person, a private person. |
| ID | 0601 |
| Biographical | I was born in Caracas, Venezuela, on October 29, 1920 of Spanish-Jewish ancestry. My father, a self-made business man, was a textile merchant and importer. He was born in Spanish Morocco, whereas my mother was born and raised in French Algeria and brought up in the French culture. When I was five years old, my family moved to Paris where we resided until 1939. My primary and secondary education was in French which had a lasting influence on my life. The second World War caused our return to Venezuela, where my father continued to have a thriving business. It was decided that I should pursue my education in the United States, and we moved to New York in 1940. I registered at Columbia University in the School of General Studies, and graduated with a Bachelor of Science Degree in 1942, having also completed the pre-medical requisites for admission to Medical School. By that time, I had elected to study biology and medicine, instead of going into the family business, as my father would have wanted. I did not realize, however, that admission to Medical School was a formidable undertaking for someone with my ethnic and foreign background in the United States of 1942. In spite of an excellent academic record at Columbia, I was refused admission by the numerous medical schools I applied to and would have found it impossible to study medicine except for the kindness and support of George W. Bakeman, father of a close friend, who was then Assistant to the President of the Medical College of Virginia in Richmond. Learning of my difficulties, Mr. Bakeman arranged for me to be interviewed and considered for one of the two remaining places in the Freshman class. I was accepted and began my medical studies in July 1942. While in medical school, I was drafted into the U.S. Army with the other medical students, as part of the wartime training program, and naturalized American citizen in 1943. I greatly enjoyed my medical studies, which at the Medical College of Virginia were very clinically oriented. I received what I considered to be an excellent medical education in the relatively short time of three war years. This busy time was rendered very happy by my marriage in 1943 to Annette Dreyfus, a French student, also a refugee from Paris, whom I had met at Columbia University. I trained as an intern at Queens General Hospital in New York City in 1945 and was commissioned First Lieutenant in the U.S. Army Medical Corps in 1946. After the usual six weeks of basic training at Fort Sam Houston, Texas, I was shipped to Germany with several thousand other physicians. I was happy to be assigned to France, first in Paris, then in Nancy, where my wife had joined me. I stayed there nearly two years, as the head of a medical unit where I enjoyed practising what today would be called community medicine. I was discharged in 1947 and, motivated by intellectual curiosity, decided upon a career in medical research at a time when such a choice was not fashionable. My interest was directed, from my medical student days, to Immunology, and particularly to the mechanism of hypersensitivity. I had suffered from bronchial asthma as a child and had developed a deep curiosity in allergic phenomena. I sought the advice of many scientists, among whom René Dubos at Rockefeller University, [John Enders](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html) at Harvard Medical School, and Jules Feund at the Public Health Research Institute in New York, to whom I had been recommended by members of the faculty in Richmond. I was strongly urged to work with a dynamic young immunochemist, Elvin Kabat, whose laboratories were at the Neurological Institute, Columbia University School of Physicians and Surgeons. Following an interview with Elvin Kabat, who offered me a Fellowship in his laboratory, I started my research career in February, 1948. Training with Elvin Kabat was one of the significant experiences in my development as a scientist. Elvin Kabat is a hard task-master with rigorous standards and an absolute respect for the quantitative approach to science. He felt that if a phenomenon could not be quantitated, it did not deserve to be studied. He taught me Immunochemistry and basic Immunology, but more importantly, I learned the significance of experimental proof, the need for intellectual honesty and scientific integrity. I was fortunate also that my first two years as a scientist were very productive and my initial goal of understanding experimental hypersensitivity mechanisms was in part fulfilled. My life for the next six years was very much influenced by family considerations. A daughter, Beryl, was born in 1949, and my parents had returned from Venezuela to their home in Paris. My father had suffered a severe stroke and was now a cripple. My wife’s family also lived in Paris. The attraction of moving to France and settling close to our respective families was very strong. Accordingly, we moved to Paris in mid-1949 and I accepted a position in Bernard Halpern’s laboratory at the Broussais Hospital. This position permitted me also to make frequent trips to Venezuela where my father’s business interests now required my personal involvement. During this period I was privileged to form a close relationship with a young Italian scientist who had also joined Halpern’s laboratory, Guido Biozzi. For six years we operated as a team and engaged in the study of reticuloendothelial function in relation to immunity. We developed the techniques to study the clearance of particulate matter from the blood by the RES, and formulated the equations that govern this process in mammalian organisms. After six years in Paris, I began to realize that as a foreigner to France, in spite of my French education, I would experience continuous difficulties in pursuing a scientific career and establishing an independent laboratory. This was made painfully clear to me by the chief of the laboratory, Dr. Halpern. The significance of this message was heightened by my unhappy discovery that I could not find another laboratory in Paris in 1956 that would give me a chance to work and establish myself. I decided therefore to return to the United States. I am deeply grateful to Lewis Thomas who offered me an appointment as Assistant Professor of Pathology at New York University School of Medicine and helped me develop my own laboratory and research support. I returned to my earlier studies on hypersensitivity mechanisms, but this time also developed an interest in cellular as well as humoral hypersensitivity. From 1956 to 1961, I worked on cellular hypersensitivity with Philip Gell, immune complex diseases with Robert McCluskey and Pierre Vassalli, anaphylactic hypersensitivity with Zoltan Ovary, tumor specific immunity with Lloyd Old, and the structure of antibodies, in relation with their specificity, with [Gerald Edelman](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1972/index.html). The years at New York University were very happy ones, and it was soon apparent that I had made the correct choice in returning to the United States. The scientific atmosphere at New York University during that period was particularly favorable to the development of Immunology. Numerous immunologists worked enthusiastically and interacted profitably: among these were Jonathan Uhr, Jeanette Thorbecke, Edward Franklin, Victor Nussenzweig, in addition to Robert McCluskey and Zoltan Ovary mentioned earlier. This is the time when I started to teach research fellows and students and realized that the training of young scientists was one of my most valuable and rewarding experiences. Later I chose “The Training of Scientists” as the topic of my presidential address to The American Association of Immunologists. Among the young immunologists with whom I had the pleasure and privilege to work at New York University are Lloyd Old, William Paul, Ira Green, Victor Nussenzweig, Michael Lamm, Pierre Vassalli, Stanley Cohen, Jeanette Thorbecke, Fred Kantor, Gregory Siskind, Stuart Schlossman, Kurt Bloch, Bernard Levine, Francois Kourilsky, Ted Brunner, and Takeshi Yoshida. During this period also I managed a New York bank, the Colonial Trust Company, which had been bought by my family and associates from Venezuela. However, the success of my laboratory made me realize that I had to choose between a scientific career and my business interests. I made the decision to devote myself solely to my laboratory and my students and to curtail my business career, as I felt the challenges were far greater in my chosen profession. This is precisely the time when I initiated the studies in Immunogenetics that resulted in my being awarded the Nobel Prize in Medicine. I made the observation that random bred animals immunized with antigens with restricted heterogeneity, such as hapten conjugates of poly L-lysine distribute themselves into two groups, responders and nonresponders. I sensed that this was an important phenomenon. I determined that responsiveness to these or other similar antigens is controlled by dominant autosomal genes termed immune response (Ir) genes. This was the beginning of a long and complex story that led to our understanding of the manner in which these genes, located in the major histocompatibility complex of mammals, exercise their function and determine immune responsiveness. By then I had become Professor of Pathology at New York University. The opportunity, however, arose at the request of John Seal to assume the Directorship of the Laboratory of Immunology of the National Institute of Allergy and Infectious Disease in Bethesda, where I moved in 1968 together with William Paul and Ira Green. Such a laboratory offered very attractive facilities and precious inbred guinea pig strains essential to my work in immunogenetics. Much of the insight on the mechanism of Ir gene function has indeed been obtained in that laboratory, from experiments of William Paul, Ira Green, Alan Rosenthal, Ethan Shevach, and Ronald Schwartz, with the systems I developed.  In 1970, Dean Robert Ebert offered me the Chair of Pathology at Harvard Medical School. I moved to Harvard because I missed the University environment and more particularly the stimulating interaction with the eager, enthusiastic, and unprejudiced young minds of the students and fellows. At Robert Ebert’s request, we initiated an interdepartmental immunology graduate program at Harvard Medical School which has developed very successfully under the stewardship of my colleague, Emile Unanue. At Harvard, I have continued my work on immune response genes and their role in the regulation of specific immunity with David Katz, Martin Dorf, Judith Kapp, Carl Pierce, Ronald Germain and Mark Greene. We also determined the role of immune response genes in the control of immune suppression phenomena with the help of Patrice Debré, Judith Kapp, and Carl Waltenbaugh; we analyzed the specificity of cytolytic T lymphocyte in relation to Ir gene function with Steven Burakoff and Robert Finberg and demonstrated how alloreactivity arises as a consequence of the commitment of T lymphocytes to recognize antigen in the context of autologous MHC gene products.  While reaching these scientific goals, I was elected President of the American Association of Immunologists in 1973, President of the American Society for Experimental Biology and medicine in 1974, President of the International Union of Immunological Societies in 1980. I was elected to the American Academy of Arts and Sciences in 1972, the National Academy of Science, U.S.A. in 1973, and I was appointed President of the Sidney Farber Cancer Institute in 1980.[1](https://www.nobelprize.org/prizes/medicine/1980/benacerraf/biographical/#not1)  I have received the following awards:  R.E. Dyer Lecture of National Institutes of Health 1969 Rabbi Shai Schacknai Lectureship and Prize in Immunology and Cancer Research, Hebrew University of Jerusalem 1974 T. Duckett Jones Memorial Award of The Helen Hay Whitney Foundation 1976 Honorary Degree of Doctor of Medicine, University of Geneva, Switzerland 1980 Waterford Biomedical Science Award 1980[2](https://www.nobelprize.org/prizes/medicine/1980/benacerraf/biographical/#not2)  My work has been generously and continuously supported since 1957 by the National Institute of Allergy and Infectious Diseases, and for the last decade also by the National Cancer Institute. I am very grateful for their enlightened support to me and my associates, which made our work possible. I am also particularly indebted to my many students and associates who have contributed so much to our common goal and whom I hold responsible in the largest measure for my achievements.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1980*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1981  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate. Addendum, May 2005 1. I was appointed President of the Dana-Farber Cancer Institute in 1980, a position in which I served until 1992. I was elected to the Institute of Medicine in 1985.  2. Honorary Degree of Doctor of Sciences, Virginia Commonwealth University 1981 Honorary Degree of Doctor of Sciences, New York University 1981 Honorary Degree of Doctor of Sciences, Yeshiva University 1982 Honorary Degree of Doctor of Sciences, Columbia University 1985 Rous-Whipple Award of the American Association of Pathologists 1985 Honorary Degree of Doctor of Sciences, Adelphi University 1988 Honorary Degree of Doctor of Philosophy, Weizmann Institute of Sciences 1989 National Medal of Science 1990 Honorary Degree of Doctor of Sciences, Gustav Adolphus University 1992 Honorary Degree of Doctor of Sciences, Harvard University 1992 Honorary Degree of Doctor of Sciences, Université de Bordeaux 1993 Honorary Degree of Doctor of Medicine, University of Vienna 1995 Gold Cane Award of the American Association for Investigative Pathology 1996 Charles A. Dana Award for pioneering achievements in Health and Education 1996  *Baruj Benacerraf died on 2 August, 2011.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0602 |
| Biographical | His mother originated from Lorraine, his father from the Pyrénées, two French provinces very distant from one another and with vast cultural differences. His parents met in Paris. During the First World War, his father, a doctor and captain in the army, sent Jean Dausset’s mother and the first three children to Toulouse. It was there that Jean Dausset was born, on 19th October 1916, and this region has held a strong attachment for him ever since.  After the war, his father worked as a physiotherapist and radiologist, dividing his time between Paris and the spa towns. Jean Dausset spent his early childhood in Biarritz, until the age of secondary school. Then, when he was 11 years old, his family came to settle permanently in Paris. He pursued his secondary studies at the Lycée Michelet and obtained his baccalaureate in mathematics.  His choice of career was almost dictated by that of his father, Henri Dausset, who pioneered Rheumatology in France. His medical studies progressed without incident until the advent of the Second World War, when they were interrupted. He was mobilized in 1939 and returned from the French Campaign in 1940 to a Paris occupied by the Germany Army. He began to devote his time ardently to the preparation of a competitive examination for the title of Intern of the Paris Hospitals. Upon receiving this title, he immediately left to join the fighting forces in North Africa. During the Tunisian Campaign, he performed blood transfusions in the army. This was his first introduction to immunohaematology.  While training in Algiers, he performed his first laboratory experiments and carried out his first scientific study on blood platelets.  On his return in 1944, to a liberated Paris, he was given the responsibility for collection of blood samples in the Paris area, working from the Regional Blood Transfusion Centre at Hôpital Saint-Antoine.  As soon as the war was over, he undertook his first real research study, in collaboration with Professor Marcel Bessis. Professor Bessis had just developed exchange-transfusion in new-born babies and adults. It is impossible to say how much time he spent treating, with this method, women who had become anuric following abortion manoeuvres resulting in septicaemia due to Clostridium perfringens – this was his first contact with kidney failure!  His clinical years oriented towards haematology and pediatrics, with a constant attraction to the laboratory. In 1948, he was sent, as a French trainee, to the Children’s Hospital in Boston (Professors L. K Diamond and Sydney Farber) where he worked in one of the Harvard Medical School laboratories.  On his return to France, he took up work again at the regional Blood Transfusion Centre, where he immediately became interested in the new immuno-haematology techniques for red blood cells. He decided to transpose these techniques to white blood cells and platelets.  The principal observation of leuco-agglutination and thrombo-agglutination was made in 1952. Since that time, he has retained a constant interest in the immunogenetics of blood cells.  In 1958, while Head of the Immuno-haematology Laboratory at the National Blood Transfusion Centre, he described the first leucocyte antigen, MAC, which has become known as HLA-A2.  Preoccupied with the state of medical research in France, he undertook with Professor Robert Debré, to institute radical reforms in the hospital and university structures. This work as Advisor to the Cabinet of the National Ministry of Education, spanned three consecutive years and culminated in the introduction of a law which established full-time employment in French hospitals, introducing to the hospitals professors of basic sciences, who were given hospital responsibilities. This reform permitted a soar in French biology and brought a new lease of life to French medical research.  Despite the administrative struggles which ensued during this period, he never abandoned his laboratory work. In 1958, he was named Assistant Professor of Haematology at the Faculty of Medicine in Paris, then Professor of Haematology in 1963 and was appointed Head of the Immunology Department at Hôpital Saint-Louis. Again, he devoted his time entirely to research and, in 1965, described the first tissue group system (Hu-1, later named HLA).  Thanks to the admirable volunteer blood donors, skin donors and skin recipients, grafted under the care of Professor F. T. Rapaport, correlations were established between graft survival and tissue incompatibility.  He participated in the creation of the Research Institute in Blood Diseases, directed by Professor Jean Bernard, and was Assistant Director there until 1968. One of the departments under his direction was the Research Unit on Immunogenetics of Human Transplantation, an INSERM (National Institute of Health and Medical Research) unit of which he has been director since 1968.  In 1977, the Collège de France called him to the Chair of Experimental Medicine, a position held by Claude Bernard from 1958 to 1978, but his research laboratory remained at Hôpital Saint-Louis.  In 1963, he married Rose Mayoral from Madrid who gave him two children, Henri and Irène.  In addition to his scientific interests, he has only two passions in life: his family and modern plastic art.   |  |  | | --- | --- | | Professor Honoris Causa |  | | University of Brussels | 1977 | | University of Geneva | 1977 | | University of Liège | 1980 | |  |  | | Membership of Academies |  | | Honorary foreign member of the Belgian Royal Academy of Medicine | 1969 | | Académie des Sciences de l’Institut de France | 1977 | | Académie de Médecine (Paris) | 1977 | | Hon. Member, American Academy of Arts and Sciences (Boston) | 1979 | | Hon. Member, Yugoslavian Academy of Arts and Sciences (Zagreb) | 1979 | |  |  | | Prizes |  | | Grand Prix des Sciences Chimiques et Naturelles (Académie des Sciences) | 1967 | | Médaille d’Argent du Centre National de la Recherche Scientifique | 1967 | | Grand Prix Scientifique de la Ville de Paris | 1968 | | Prix Cognac-Jay (Académie des Sciences de l’Institut de France) | 1969 | | Stratton Lecture Award (U.S.A.) | 1970 | | Landsteiner Award AABB, San Francisco (U.S.A.) | 1970 | | Gairdner Foundation Prize (Canada) | 1977 | | Koch Foundation Prize (Germany) | 1978 | | Wolf Foundation Prize (Israel) | 1978 |   From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1971-1980*, Editor Jan Lindsten, World Scientific Publishing Co., Singapore, 1992  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  Copyright © The Nobel Foundation 1980 Addendum, May 2005 Thanks to the Nobel Prize and the French Television, Jean Dausset received in 1984 for his laboratory a huge inheritance. With this unexpected gift, he created, with the collaboration of the Professors Howard Cann and Daniel Cohen, the Human Polymorphism Study Center (CEPH), which soon after became Foundation Jean Dausset-CEPH.  Numerous collaborators working on the same large families, as the ones collected by Prof. Jean Dausset for his studies on the HLA system, permitted to add numerous markers and thus to give the possibility to publish the first genetic map and, later on, the first physical map. The families of the Foundation Jean Dausset-CEPH are still today, in 2005, the families reference for the international scientific community.  On top of that, an exhaustive study of the worldwide populations has already given important publications : the search continues. Besides this, fratries of people over 95 years old and a bank of centenarians is an inestimable resource for the Foundation Jean Dausset-CEPH.  With his collaborator, Prof. Edgardo Carosella, Jean Dausset has always been interested in an atypical molecule of the HLA system, named the HLA-G, molecule of tolerance, unlikely to the other HLA molecules. Jean Dausset participated in the demonstration that HLA-G protected the incompatible foetus against the active cellules of the mother, resolving this way the millennium mystery of keeping the foetus into his mother.  Jean Dausset is still, in 2005, Chairman of the France Bone Marrow Grafts (France Greffe de Moelle). This institute searches for, among the 9 millions volunteers donators of bone marrow worldwide, the compatible donator, or, if possible, the identical one, with the patient.  At least, Jean Dausset took an active part of the huge problem of Humanity. He was, during nearly 20 years, Chairman of the Universal Movement of the Scientific Responsibility (MURS). He was also the Chairman of the Academy of Water.  To end with, Jean Dausset has written a book retracing his life. This book, entitled « Clein d’oeil a la Vie » published at Odile Jacob Editions, in Paris in 1998, was republished under the title « Sceau de l’Individualite ».  *Jean Dausset died on 6 June, 2009.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | **0603** |
| Biographical | My parents were both New Englanders, though my father was born in Minnesota where his father had moved from Massachusetts to join a frontier community. My father moved east as a young man, and for a number of years was YMCA secretary in Haverhill, Massachusetts. Subsequently he invented and worked in the application of a device for winding induction coils used in ignitors for the motorboat engines of that day. I was born in Bradford, Massachusetts, a suburb of Haverhill, in December 1903, the youngest of three children. My parents moved when I was four to the home built by my great grandfather in Brookline, Massachusetts, and it was in the excellent Brookline public schools that I received my pre-college education.  Science and mathematics were my favorite subjects. In spare time I read books on astronomy and physics as well as the usual boyhood classics. But I also enjoyed sports, and a group of five or six youngsters used to gather at our house to play touch football or scrub baseball in our yard or a neighboring vacant lot. Imaginative stories and games also were very much a part of my childhood.  In 1900, three years before I was born, my mother’s parents had purchased a run-down farmhouse and 70 acres of land in South Woodstock, Vermont. The house was gradually restored and furnished, and the summers I spent at “the farm” were among the delights of my childhood and youth. An interest in gardening, farming, and forestry have been a permanent legacy of the experience this home provided.  Music was a major interest of the whole family. My mother played the piano, and we did a great deal of family singing in which friends often joined. It has been a source of great pleasure that my wife is also a pianist.  I entered Darmouth College in 1922 and again found science and mathematics my favorite subjects. A course in genetics taught by Professor John Gerould proved particularly fascinating, and it was that course that led me to the choice of a career. When the decision was finally made to enter graduate school, it was on Professor Gerould’s advice that I enrolled as a graduate student with Harvard’s Professor Castle, the first American biologist to look for Mendelian inheritance in mammals.  My thesis work on linkage in mice largely determined my future work. Two years spent teaching and two years as a postdoctoral fellow under Herman Muller studying the genetic effect of x-rays on mice served to convince me that research was my real love. If it was to be research, mouse genetics was the clear choice and the Jackson Laboratory, founded in 1929 by Dr. Clarence Cook Little, one of Castle’s earlier students, almost the inevitable selection as a place to work. The Laboratory was a small institution when I joined the staff of seven in 1935, but under the talented leadership of Dr. Little and his successor, Earl Green, it has grown into the world center for studies in mammalian genetics. I owe a great deal to it for providing the ideal home for my subsequent research.  It was in Bar Harbor that I met and married Rhoda Carson, and where we raised our three sons, Thomas, Roy and Peter.  I have always enjoyed sports, with skiing, which I learned at Dartmouth, and tennis perhaps being my two favorites.  While for 25 years I concentrated almost exclusively on studies of histocompatibility genes and especially of the *H-2* complex, and for 35 years have pursued these subjects to some degree, I also have become involved in other areas. While working under Dr. Castle, I spent parts of two summers at Woods Hole with Dr. Phineas Whiting, an earlier student of Castle, studying the genetics of the parasitic wasp, *Habrobracon*. An outcome of this work was a paper on The Role of Male Parthenogenesis in the Evolution of the Social Hymenoptera. The problems of social evolution have remained a continuing interest, to which I am now returning in a more active way in retirement. The two years with Muller at the University of Texas resulted in the first demonstration of the induction by x-rays of chromosomal changes in mammals. My first several years at the Jackson Laboratory were spent in continuation of this work, and especially in the detailed genetic analysis of two of the induced reciprocal translocations. In the late 1930s, I became involved in problems of gene nomenclature in mice, and this, together with problems of strain nomenclature, remained a concern for many years. The efforts of the Committee on Standardized Nomenclature for mice have led to the universal acceptance of a well organized and convenient nomenclature system for this species. Some experiments, which I carried out at about the same time that I was becoming interested in histocompatibility genetics, led to the discovery of immunological enhancement, the curious inversion of the expected growth inhibition seen with certain tumors when transplanted to pre-injected mice. I soon found that I was not the first person to have seen this phenomenon, but the mouse system proved very amenable to further exploitation. I had to drop this topic in favor of the genetic studies, but it has been interesting to see it grow through the work of Dr. Nathan Kaliss and many others into a major area of research with possible implications for organ transplantation in man. A final interest, developed jointly with Dr. Marianna Cherry during my last few years at the Jackson Laboratory, concerned serologically demonstrable alloantigens of lymphocytes.  Much of the work sketched above was carried out on a collaborative basis. I cannot here give names, but I owe a great debt to the many wonderful people with whom it has been my privilege to work in these studies.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1980*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1981  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *George D. Snell died on June 6, 1996.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0604 |
| Biographical | My parents went from the north of Scotland to South Africa shortly before World War I. My mother had been a teacher and my father was an engineer with the Post Office. I was born in Johannesburg in 1924, the youngest of three children. My family moved around the country quite a lot, as did the families of many civil servants, but after my father’s death in 1936 we settled in Cape Town. There I attended the Rondebosch Boys High School and my interests outside my academic work were debating, tennis, and to a lesser extent, acting. I became intensely interested in astronomy and devoured the popular works of astronomers such as Sir Arthur Eddington and Sir James Jeans, from which I learnt that a knowledge of mathematics and physics was essential to the pursuit of astronomy. This increased my fondness for those subjects.  At that time the prospects for making a living as an astronomer were not good, so on going to the University of Cape Town, I followed in the footsteps of my father and brother and started to study electrical engineering. I was fortunate in that a new engineering curriculum had just been introduced by the then Head of the Electrical Engineering Department, Professor B. L. Goodlet. While serving with Mountbatten in the Far East he had seen the value for engineering of a better grounding in physics and mathematics than had previously been the case, and the new curriculum contained a lot of physics and mathematics. After a couple of years I abandoned engineering and turned to physics. At the University of Cape Town I spent most of my spare time mountaineering either on Table Mountain which was almost our back yard, or on the lovely mountain ranges of the Western Cape Province, and what spare time was not spent on climbing was spent listening to music.  After completing my Bachelor and Masters degrees at Cape Town I went to St. John’s College, Cambridge, as a Research Student. I worked at the Cavendish Laboratory under Prof. Otto Frisch on problems connected with He6. While I made some progress on these problems I did not complete them because of the following circumstances. I had met an American girl, Barbara Seavey, in Dirac’s lectures on quantum mechanics, and a year and a half later I wanted to marry her, but I was broke. An inquiry at the Physics Department at Cape Town elicited not only the information that there was a vacancy there, but also a telegram offering me a position as Lecturer. So in 1950 I returned to Cape Town with a bride but no cyclotron, and so no further work on He6.  Working on nuclear physics in Cape Town was lonely because there were very few nuclear physicists in the country, and the nearest one was six hundred miles away. However Professor R. W. James, head of the Physics Department and my mentor as a student, gave me my head and I learnt a lot and published a few papers. In 1956 I by chance became interested in a problem that is now known as CAT-scanning, but that story will be told elsewhere in this volume.  On my first Sabbatical leave it seemed only reasonable that since my wife had willingly come out to the wilds of Africa with me that I should go to the wilds of America with her. In addition the United States was a very good place to do research, and Harvard was a particularly good place to be in, so I spent my Sabbatical at the Harvard cyclotron doing experiments on nucleon-nucleon scattering with Professors Norman Ransey and Richard Wilson and then graduate student Joseph Palmieri. This was the beginning of a long and happy association with the people at the Harvard Cyclotron amongst whom I must mention particularly its present Director, Andreas Koehler.  While on this Sabbatical leave I was offered a position at Tufts University by the then Chairman of the Physics Department, Professor Julian K. Knipp. I accepted the offer and, except for a brief return to South Africa and a couple of Sabbatical leaves, I have been there ever since, progressing up the academic ladder and being Chairman of the Physics Department from 1968 to 1976. My main interest for most of this time was in nuclear and particle physics and I pursued the CT-scanning problem only intermittently, when time permitted. In 1963 and 1964 I published the results of this work, but as there was practically no response I continued my normal course of research and teaching. In the period 1970-72, I became aware of a number of developments in, or related to CT-scanning, and since then I have devoted much of my time to these problems.  Apart from a little swimming and sailing in the summer, I lead a rather sedentary life, spending a lot of time reading. Since my first discussions of ecological problems with Professor John Day around 1950 and since reading [Konrad Lorenz’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/index.html) “King Solomon’s Ring”, I have become increasingly interested in the study of animals for what they might teach us about man, and the study of man as an animal. I have become increasingly disenchanted with what the thinkers of the so-called Age of Enlightenment tell us about the nature of man, and with what the formal religions and doctrinaire political theorists tell us about the same subject. I recently read Edward Wilson’s book “On Human Nature”, and after this hectic two months of my life culminates in Nobel Week, I look forward to tackling his “Sociobiology”.  My wife and I have three children – Margaret, Jean and Robert. Since 1957 we have lived in the town of Winchester, Mass. which I appreciate for still being governed by that unique New England experiment in democracy: a (limited) Town Meeting and a Board of Selectmen. We enjoy the amenities of New England, particularly summers near, in, and on Lake Winnepesaukee, New Hampshire.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1979*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1980  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Allan M. Cormack died on May 7, 1998.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0605 |
| Biographical | I was born and brought up near a village in Nottinghamshire and in my childhood enjoyed the freedom of the rather isolated country life. After the first world war, my father had bought a small farm, which became a marvellous playground for his five children. My two brothers and two sisters were all older than I and, as they naturally pursued their own more adult interests, this gave me the advantage of not being expected to join in, so I could go off and follow my own inclinations.  The farm offered an infinite variety of ways to do this. At a very early age I became intrigued by all the mechanical and electrical gadgets which even then could be found on a farm; the threshing machines, the binders, the generators. But the period between my eleventh and eighteenth years remains the most vivid in my memory because this was the time of my first attempts at experimentation, which might never have been made had I lived in a city. In a village there are few distractions and no pressures to join in at a ball game or go to the cinema, and I was free to follow the trail of any interesting idea that came my way. I constructed electrical recording machines; I made hazardous investigations of the principles of flight, launching myself from the tops of haystacks with a home-made glider; I almost blew myself up during exciting experiments using water-filled tar barrels and acetylene to see how high they could be waterjet propelled. It may now be a trick of the memory but I am sure that on one occasion I managed to get one to an altitude of 1000 feet!  During this time I was learning the hard way many fundamentals in reasoning. This was all at the expense of my schooling at Magnus Grammar School in Newark, where they tried hard to educate me but where I responded only to physics and mathematics with any ease and moderate enthusiasm.  Aeroplanes interested me and at the outbreak of the second world war I joined the RAF as a volunteer reservist. I took the opportunity of studying the books which the RAF made available for Radio Mechanics and looked forward to an interesting course in Radio. After sitting a trade test I was immediately taken on as a Radar Mechanic Instructor and moved to the then RAF-occupied Royal College of Science in South Kensington and later to Cranwell Radar School. At Cranwell, in my spare time, I sat and passed the City and Guilds examination in Radio Communications. While there I also occupied myself in building large-screen oscilloscope and demonstration equipment as aids to instruction, for which I was awarded the Certificate of Merit.  It was very fortunate for me that, during this time, my work was appreciated by Air Vice-Marshal Cassidy. He was responsible for my obtaining a grant after the war which enabled me to attend Faraday House Electrical Engineering College in London, where I received a diploma.  I joined the staff of EMI in Middlesex in 1951, where I worked for a while on radar and guided weapons and later ran a small design laboratory. During this time I became particularly interested in computers, which were then in their infancy. It was interesting, pioneering work at that time: drums and tape decks had to be designed from scratch. The core store was a relatively new idea which was the subject of considerable experiment. The stores had to be designed and then plain-threaded by hand (causing a few frightful tangles on occasions). Starting in about 1958 I led a design team building the first all-transistor computer to be constructed in Britain, the EMIDEC 1100. In those days the transistor, the OC72, was a relatively slow device, much slower than valves which were then used in most computers. However, I was able to overcome this problem by driving the transistor with a magnetic core. This increased the speed of the machine so that it compared with that of valve computers and brought about the use of transistors in computing earlier than had been anticipated. Twenty-four large installations were sold before increases in the speed of transistors rendered this method obsolete.  When this work finished I transferred to EMI Central Research Laboratories, also at Hayes. My first project there was hardly covered in glory: I set out to design a one-million word immediate access thin-film computer store. The problem was that after a time it was evident that this would not be commercially viable. The project was therefore abandoned and, rather than being immediately assigned to another task I was given the opportunity to go away quietly and think of other areas of research which I thought might be fruitful. One of the suggestions I put forward was connected with automatic pattern recognition and it was while exploring various aspects of pattern recognition and their potential, in 1967, that the idea occurred to me which was eventually to become the EMI-Scanner and the technique of computed tomography.  The steps in my work between this initial idea and its realisation in the first clinical brain-scanner have already been well documented. As might be expected, the programme involved many frustrations, occasional awareness of achievement when particular technical hurdles were overcome, and some amusing incidents, not least the experiences of travelling across London by public transport carrying bullock’s brains for use in evaluation of an experimental scanner rig in the Laboratories.  After the initial experimental work, the designing and building of four original clinical prototypes and the development of five progressively more sophisticated prototypes of brain and whole body scanner (three of which went into production) kept me fully occupied until 1976. Since then I have been able to broaden my interest in a number of projects which are currently in hand in the Laboratories, including further possible advances in CT technology and in related fields of diagnostic imaging, such as nuclear magnetic resonance.  As a bachelor, I have been able to devote a great deal of time to my general interest in science which more recently has included physics and biology. A great deal of my adult life has centred on my work, and only recently did I bother to establish a permanent residence. Apart from my work, my greatest pleasures have been mainly out-of-doors, and although I no longer ski I greatly enjoy walking in the mountains and leading country rambles. I am fond of music, whether light or classical, and play the piano in a self-taught way. In company I enjoy lively way-out discussions.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1979*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1980  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Godfrey N. Hounsfield died on August 12, 2004.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0606 |
| Biographical | I was born on June 3rd, 1929 in Gränichen in the Canton of Aargau, Switzerland, where I went to the public schools until the age of 16. I then entered the gymnasium at the Kantonsschule Aarau where I got a B-type maturity in 1949. From 1949 to 1953 I studied towards the diploma in Natural Sciences at the Swiss Polytechnical School in Zurich. It is in the last year of this study that I made my first contacts with fundamental research, when working on the isolation and characterisation of a new isomer of Cl34, with a halflife of 1.5 seconds.  On the recommendation of my professor in experimental physics, Paul Scherrer, I took an assistantship for electron microscopy at the Biophysics Laboratory at the University of Geneva in November 1953. This laboratory was animated by Eduard Kellenberger and it had two prototype electron microscopes requiring much attention. In spite of spending many hours to keep the microscope “Arthur” in reasonable working condition, I had enough time not only to help developing preparation techniques for biological specimens in view of their observation in the electron microscope, but also to become familiar with fundamental questions of bacteriophage physiology and genetics, which at that time was still a relatively new and unknown field. My first contribution to our journal club concerned [Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) and [Crick’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) papers on the structure of DNA.  In the 1950’s the Biophysics Laboratory at the University of Geneva was lucky enough to receive each summer for several months the visit of Jean Weigle. He was the former professor of experimental physics at the University of Geneva. After having suffered a heart attack, he had left Geneva to become a researcher at the Department of Biology of the California Institute of Technology in Pasadena. There, he had been converted to a biologist under the influence of [Max Delbrück](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) and had chosen to study bacteriophage lambda. This is why the first electron micrographs of phage lambda were made in Geneva. Stimulated by Jean Weigle we soon turned our interests also to other properties of lambda, and the study of defective lambda prophage mutants became the topic of my doctoral thesis.  In the summer of 1956, we learned about experiments made by Larry Morse and Esther and [Joshua Lederberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html) on the lambda-mediated transduction (gene transfer from one bacterial strain to another by a bacteriophage serving as vector) of bacterial determinants for galactose fermentation. Since these investigators had encountered defective lysogenic strains among their transductants, we felt that such strains should be included in the collection of lambda prophage mutants under study in our laboratory. Very rapidly, thanks to the stimulating help by Jean Weigle and Grete Kellenberger, this turned out to be extremely fruitful. We could indeed show that lambda-mediated transduction is based on the formation of substitution mutants, which had replaced a part of the phage genes by genes from the bacterial chromosome. This made the so-called lambda-gal phage derivatives so defective that they were not able any longer to propagate as a virus. In fact, one of the at first sight rather frustrating observation was that lysates of lambda-gal, which indeed could still cause the infected host cell to lyse as does wild type phage lambda, did not contain any structural components of lambda (phage particles, heads or tails) discernible in the electron microscope. This was the end of my career as an electron microscopist and in chosing genetic and physiological approaches I became a molecular geneticist.  After my Ph. D. exam in the summer of 1958 I had the chance to receive an offer to work at the University of Southern California in Los Angeles with Joe Bertani, a former collaborator of Jean Weigle. Several years before, Bertani had isolated and characterised another bacteriophage of *E. coli,* P1. Phage P1 rapidly had become a very welcome tool of bacterial geneticists, since it gives general transduction, i.e. any particular region of the host chromosome gets at some low frequency wrapped into P1 phage particles if P1 multiplies in a cell, and this enables the geneticists to carry out linkage studies of bacterial genes. While working as a research associate with Bertani, I received P1 at first hand which enabled me to study phage Pl-mediated transduction of monomeric and dimeric lambda prophage genomes as well as of the fertility plasmid F.  In the meantime, my Ph. D. thesis on lambda-gal, although written in French, had been read, or, what is perhaps more essential, understood in its conclusions by many leading microbial geneticists.  This may be the reason why I received offers to spend additional postdoctoral time in several excellent laboratories. On the other hand, I had remained in close contact with Eduard Kellenberger, and he urged me to come back to Geneva in order to lead an investigation on radiation effects on microorganisms. As a compromise, I decided to return to Geneva at the beginning of 1960, but only after having spent several very fruitful weeks at each of the laboratories of Gunther Stent in Berkeley, Joshua Lederberg in Stanford and [Salvador Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) at the Massachusetts Institute of Technology, Cambridge.  At the end of the 1950’s, a special credit had been voted for by the Swiss Parliament for research in atomic energy, including radiation effects on living organisms. Eduard Kellenberger felt that important contributions to the latter questions could be expected from studies with microorganisms, and he had therefore submitted a research proposal which found approval by the granting agency, the Swiss National Science Foundation. The project could bring insight into the nature of radiation damage to genetic material and its repair mechanisms, as well as of the stimulation of genetic recombination by radiation. These topics had already engaged the attention of Jean Weigle and Grete Kellenberger for a number of years.  One of the first experiments after my return to Geneva was to render *E. coli* B and its radiation resistant strain B/r sensitive to phage lambda. The first step to accomplish this was easy thanks to a hint received from Esther Lederberg to look for cotransduction of the Ma1+ and lambdaS characters. However, the strains thus obtained still did not allow an efficient propagation of lambda. Very rapidly I realized that this was due to host-controlled modification, a phenomenon described for lambda and *E. coli* strains seven years earlier by Joe Bertani and Jean Weigle. However, I was not satisfied to know how to overcome this barrier. I was also anxious to know how the restriction of phage growth and the adaptation of lambda to the new host strain worked. When I started investigations on the mechanisms of host-controlled modification, I did not of course imagine that this sidetrack would keep my interest for many years. Otherwise I might not have felt justified to engage in this work because of its lack of direct relevance to radiation research. However, a lucky coincidence rapidly dissipated these concerns. At the same time, Grete Kellenberger had looked at the fate of DNA from irradiated phage lambda upon infection of host bacteria: part of it was rapidly degraded after injection into the host. And so was the DNA from unirradiated phage lambda used to measure adsorption and DNA injection into restrictive bacterial strains! This phenomenon became the topic of Daisy Dussoix’s doctoral thesis, who very carefully not only studied the DNA degradation of phage that was not properly modified, but who also tried to detect parallels between the fate of unmodified DNA in restrictive conditions and of irradiated DNA in normal host cells.  Within about one year of study, it had become clear that strain-specific restriction and modification directly affected the DNA, without however causing mutations. It soon also became obvious that restriction and modification were properties of the bacterial strains and acted not only on infecting bacteriophage DNA, but also on cellular DNA as manifested in conjugation experiments. These findings were reported by myself and Daisy Dussoix for the first time to the scientific community during the First International Biophysics Congress held in Stockholm in the summer of 1961. In a more extended version I presented them in 1962 to the Science Faculty of the University of Geneva as my work of habilitation as privatdocent. This work earned me in the same year the Plantamour-Prévost prize of the University of Geneva.  At a time before the Swiss Universities received direct financial help from the federal government, the Swiss National Science Foundation awarded “personal grants” to qualified researchers to allow them to guide projects of fundamental research at a Swiss University. I was lucky to benefit from such a support form 1965 to 1970. These years were devoted to hard work to consolidate the preliminary data and the concepts resulting from them, and to extend the acquired notions, in particular with regard to the mechanisms of modification by nucleotide methylation, with regard to the genetic control of restriction and modification and with regard to the enzymology and molecular mechanisms of these reactions.  This work would not have been possible without a very fruitful help by a large number of collaborators in my own laboratory and of colleagues working on related topics in their own laboratories. I was extremely lucky to receive in my laboratory in the basement of the Physics Institute of the University of Geneva a number of first class graduate students, postdoctoral fellows and senior scientists. It is virtually impossible to list them all in this context, but my warmest collective thanks go to all of them. In 1964 Bill Wood laid out a solid basis for the genetics of the restiction and modification systems *Eco*K and *Eco*B. Later, Stuart Linn, profiting from his fruitful contacts with Bob Yuan and Matt Meselson, who worked in the USA on the enzymology of *Eco*K restriction, set the basis for in vitro studies with *Eco*B restriction and modification activities. These studies culminated in the final proof that modification in *E. coli* B and K is brought about by nucleotide methylation. This concept had found its first experimental evidence during my two months’ visit in 1963 with Gunther Stent at the University of California in Berkeley. Several years later Urs Kühnlein, a Ph. D student, and John Smith, working for various lengths of time with us, succeeded in careful in vivo and in vitro measurements on methylation to validate and extend the earlier conclusions. Their experiments also brought important conclusions with regard to the concept of the sites of recognition on the DNA for the restriction and modification enzymes.  As an illustration that my work has not always been easy and accompanied by success, I would like to refer to my long, fruitless and thus largely unpublished attempts to find experimental evidence for the diversification of restriction and modification systems in the course of evolution. Systems *Eco*K and *Eco*B form a closely related family as judged from genetic and functional studies. Another family is formed by restriction and modification systems *Eco*P1 and *Eco*P15. One could expect that mutations affecting the part of the enzymes responsible for recognition of the specificity site on the DNA might result in new members of the family, recognizing new specificity sites on DNA. We have in vain spent much time in search for such evolutionary changes both after mutagenization and after recombination between two members of the same family of the above mentioned systems. That the basic idea for this search was good was recently shown by Len Bullas, Charles Colson and Aline van Pel (J. Gen. Microbiol. 95, 166- 172, 1976) who encountered such a new system in their work with *Salmonella* recombinants.  In 1965 I was promoted extraordinary professor for molecular genetics at the University of Geneva. Not only did I always enjoy a continued contact with the students, but I also considered teaching as a welcome obligation to keep my scientific interests wide. Although we had a few excellent students in our laboratories, the teaching of molecular genetics at the University of Geneva in the 1960’s suffered a bit from a lack of interest by the young generation. This might have been related to a more general lack of public interest for this field, which was perhaps due to the economic structure of the city of Geneva and its environments. These, at that time perhaps more subconscious concerns, might have helped me to accept in 1968 an offer for a professorship at the University of Basel, since I felt that more general interest would be given to molecular genetics in this city with a long tradition of biomedical research at its industries.  I started my new appointment at the University of Basel in October 1971 after having spent one year as a visiting Miller Research Professor at the Department of Molecular Biology of the University of California in Berkeley. In Basel, I was one of the first persons to work in the newly constructed Biozentrum, which houses several University Departments, in particular those of Biophysics, Biochemistry, Microbiology, Structural Biology, Cell Biology and Pharmacology. This diversity within the same house largely contributes to fruitful collaborative projects and it helps to keep horizons broad both in research and teaching. Additional contributions to this goal come from contacts with other nearby University Institutes as well as with the private research Institutions in the city.  Since my coming to Basel, I devoted relatively little of my time to further studies on restriction and modification mechanisms. Not that I have lost my interest in them. On the contrary, I was fortunate to be able to set up a junior group which under the leadership of Bob Yuan and more recently of Tom Bickle, became rapidly quite independent, and it continues to be very successful in its investigations on the more detailed aspects of the molecular mechanisms of restriction and modification. This allowed me to turn my main interests back to other mechanisms affecting either positively or negatively the exchange of genetic material. For a number of years Nick Gschwind, a Ph. D. student, and Dorothea Scandella, a postdoctoral fellow, explored two other mechanisms found in some *E. coli* strains or mutants and affecting more specifically than restriction and modification systems particular steps in the propagation of bacteriophage lambda.  For the last several years I have turned my principal interests to the intriguing activities of insertion elements and transposons, which by their actions on genetic rearrangements, seem to be the main driving forces of evolution in microorganisms. Because of their independence on extended nucleotide homologies these forces bring about exchange of largely unrelated genetic materials. Our postdoctoral workers Katsutoshi Mise, Shigeru Iida and Jürg Meyer brought important contributions to the understanding of these phenomena, mainly by the use of the bacteriophage P1 genome as a natural vector of transposable elements. But general knowledge on this to my mind extremely important field is still very scarce and deserves continued attention.  Solid notions on naturally occurring genetic exchange between organisms that are not directly related will also form a good basis for a scientific evaluation of conjectural risks of in vitro recombinant DNA research. Since this research largely makes use of restriction enzymes, although it in no way fully depends on them, I consider it a personal obligation to contribute to the best of my abilities to the solution of questions which arose in the scientific and public debate on this research in the last few years. I see two ways to reach this goal. The first is scientific and tends as just stated to better understand what nature does in its nonhomologous genetic exchange. The second is rather political and it consists in actions to stimulate continued awareness of responsibility to work with a maximum of care in all scientific investigations, which should, however, be allowed to be done under optimal academic freedom.  A curriculum vitae would be incomplete without reference to my private life. I am fortunate to have found a continued support and steady encouragement by my family, in particular by my parents, and, since we became married in 1966, by my wife Antonia. In response to their interest and understanding for my scientific activities, I have tried to give them my personal affection needed for a harmonious life. Our two daughters Silvia and Caroline were born in 1968 and in 1974, respectively. When Silvia learned that I had been honored by the Nobelprize she not only wanted to know what this is, but also why I was chosen as a Laureate. After explaining her in simple terms the basic concepts of the mechanisms of restriction enzymes, she, after some reflection, reexpressed this message in her own terms by a tale, which in the meantime has found wide diffusion around the world. It might thus be justified to finish this curriculum vitae by its reproduction:  *“The tale of the king and his servants*  When I come to the laboratory of my father, I usually see some plates lying on the tables. These plates contain colonies of bacteria. These colonies remind me of a city with many inhabitants. In each bacterium there is a king. He is very long, but skinny. The king has many servants. These are thick and short, almost like balls. My father calls the king DNA, and the servants enzymes. The king is like a book, in which everything is noted on the work to be done by the servants. For us human beings these instructions of the king are a mystery.  My father has discovered a servant who serves as a pair of scissors. If a foreign king invades a bacterium, this servant can cut him in small fragments, but he does not do any harm to his own king.  Clever people use the servant with the scissors to find out the secrets of the kings. To do so, they collect many servants with scissors and put them onto a king, so that the king is cut into pieces. With the resulting little pieces it is much easier to investigate the secrets. For this reason my father received the Nobel Prize for the discovery of the servant with the scissors”. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q6 | Though some years have passed since you were receiving the big honour. At the time, what did you think would come out of being given the prize? Did it change your scientific work in any way, or your general life? |
|  | When I got the prize, 25 years ago now, of course I pretended it shouldn’t change my life, I did try to behave as before. I got, however, quite frequently obvious contacts from persons, from organisations, from groups, to ask me for giving some of my opinions, help in committees and so on and I did realise rather rapidly that that was a good opportunity for me. I had the liberty to choose, to say “no” or to say “yes” and I think I made usually a good choice sometimes. When I discovered that I shouldn’t have said “yes” I tried to get out of the business and … |
|  | Give us an example, what was a good outcome after the prize so to speak … |
|  | I have for example been asked in the 1980s, I was at the University of Basel and I had been asked whether I would be willing to become rector of that university for two years’ time. In fact, I would be a member of directorate during six years because there was a rector designated a period of two years then a rector in full office and a past rector for another two years so that was the group of directorates. After some reflection I accepted and it was really well seen, you know, that having been honoured by the Nobel Prize, I wasn’t thinking that I should do only science and that brought me into science politics and then sometime after I had been asked to become a member of the Swiss Science Council in which I have also been more than ten years and that brought me into really problems of science politics which I think was good for my own country and also for the world altogether. |
| Q38 | … there are, people said there are many risks, can you see those risks today, why people … |
|  | OK. When I made the specific discoveries in 1960 of course it wasn’t obvious at that moment what that would lead to. It needed to have the enzymes purified, that took another almost ten years and other people in our own lab contributed essentially to that and it is then in the early 1970s that the enzymes which are able to cut the DNA into fragments, which allows to act, to analyse the genetic information more properly than if you have the very long chromosomal filaments. At that moment it became clear that certain fragments could be recombined differently together and also amplified in so called gene vectors which could be viruses or other small DNA molecules, that actually gave rise to genetic engineering, the recombinant DNA techniques and at that moment the question was raised whether there were contractual risks into doing so. Now I felt, because I had contributed to the knowledge that there are these enzymes and then the enzymes were used, I felt also more of an obligation to think about more deeply on these risks and from today’s point of view I think I did contribute a lot for the evaluation of such more long-term risk which would relate to the biological evolution. I have studied for the last about 30 years intensively the molecular processes of molecular revolution, how do genetic variations which is the basis for evolution occur in nature and are these similar or very different from what the genetic engineer can do in the laboratory.  I work with bacteria and this I found out that there is a big opportunity to understand molecular processes by which the genetic information spontaneously undergoes changes. This can be compared with what in genetic engineering is done reflectively, by human beings and perhaps I could just tell you that there are a relatively big number of natural processes on work too which contribute each in its proper way to the formation of genetic variations at very low frequencies of course because for any living being the genetic information must have quite good stability. However, it’s not absolute. If the stability would be absolute there wouldn’t be any evolution and the evolution is a source of biodiversity. I think it’s a wonderful thing. |
| Q38 | But if you then go in and if you can control it, the humans can go on. |
|  | If you look at which kind of changes nature does spontaneously there are in fact three strategies, one strategy is within the genetic script, changing one or very few letters, these are local changes. The second strategy is within the genetic information of the organism rearrange longer segments of that DNA and sometimes duplicate one thing and delete it or invert it or put it in another sector within the DNA and the third large strategy is to acquire from another organism by horizontal gene transfer a segment which that receiving organism hadn’t had before. These are the three much natural strategies of genetic variation and their qualities of course with regard to contribution to evolution is different. Now, if one looks at what in genetic engineering has done where also artificially reflected the DNA sequences are changed in order to make mutants on which one want to study what is the effect of such changes on the life, on the phenol type, that can be locally, it can be by deleting a segment, by inserting another segment from another origin and so on and so forth. So, the strategies are just the same and my conclusion for the time being is that we shouldn’t worry too much about the risk of genetic engineering because the risks are very similar to absolutely normal, natural evolution which is actually a natural phenomenon without which we wouldn’t live today and our surrounding world wouldn’t be as it is. |
| Q59 | Somebody said to me that the scientists who are dealing with basic science, are different to those who maybe do medical research or develop certain kinds of products and so on with the technique so that the moral high ground is high within the researchers and the scientists so to speak, the basic scientists, but there might be other people who are not as morally, they might have other interests, financial interests. |
|  | OK, you’re right, if a technique has proven to be applicable to something of course the inventor of that technique has no guarantee that someone else will misuse it for another purpose, that’s clear, but this is true in any human doing so that’s a general problem and it can be properly contained I think by bringing this particular issue into the political legislation so that some things are actually favoured and other things should be not allowed, that’s the usual case but of course I do realise that this takes quite a number of years going through all this political debate and so on to have it finally implemented. |
| Q59 | So it would be good from your point of view to have some kind of similar legislation all over the world on these issues? |
|  | Harmonisation of the legislation in these fields would be very appropriate and thanks to not at least through the activities of the scientists themselves I have already recalled the Asilomar conference more than 25 years ago, have helped enormously to make all the countries attentive to these developments and in many countries the laws have been adapted to really conduct the appropriate research properly. |
| Q23 | To be able to understand this valuable research that scientists are doing and which often takes many, many years, you then have to be able to explain it as well and I read a beautiful story that your daughter came up with. Could you just briefly relate them to us, as a way of describing what you found out. |
|  | Sylvia was ten years old when I got the announcement of the prize in October of 1978 and the next weekend we went to some walks and we talked about what has happened during that week which was really also impressing our two children and then Sylvia said, “If the children in school tomorrow ask me what was that all about, what should I tell them?” And then I tried to explain to Sylvia in relatively simple terms what my contributions were and after some reflection she came up with some comparisons saying “Well, DNA, is that correct, DNA is like the king? And these enzymes which you found, the restriction enzymes, are like some of the servants of that king?” And I said “Well, that’s perfect, good comparison. What is the role of the servants?” And she said “If a foreign king, another DNA molecule tries to penetrate into these cells, the servants kill that invading king by cutting it into fragments” and then I said “It’s perfect, Sylvia” and then I asked Sylvia “Why don’t you write this story up?” and she wrote it and I then included it into my CV for the book which the Nobel Foundation gives out and therefore later on it has spread worldwide, it’s a nice story. |
| Q73 | Is it important to be able to, in simple terms, describe science today, natural science to make it more popular and more understood? |
|  | I think it is important, but it also has some throwback. One has to be careful enough so that it’s not being misinterpreted. Simplifications help to understand better, but they also could lead to some misunderstanding, in this particular case of the king and his servants I think it’s no big problem but if one uses simplifications too often, that can at long term be a source of misunderstandings of some principles of nature. |
| Q59 | Some people have the feeling that there is now a mistrust between the general public and natural scientists. Have you got that feeling and why is that in that case or is it rather mistrust of what one can do with science so to speak? |
|  | It is, there is a certain mistrust, I think it has to do with human conservative opinions, humans, many humans are conservative for whatever and if they don’t see a much benefit for their own life, they are often very hesitant to accept technological progress, I think that’s a normal human behaviour and some of these mistrusts can under certain circumstances be misused by political movements, you know, taking this on their flack. I think good examples have been the use of, peaceful use of atomic energy and genetic engineering is another example which has sometimes been misused in that sense. |
| Q72 | For example, do you mean the debate around, could we say genetically modified food or genetically modified species like for example Dolly … |
|  | It goes in this direction, yes, without precisely what is behind, but I might add to this question, going further you know, after understanding how the molecular process of genetic variation works. Me as well as quite a number of other colleagues have realised that these are in fact in most of the cases done in nature by the help of particular enzymes. Enzymes are products of genes and these enzymes often do nothing else than helping genetic variation to occur and also, that’s quite important, to not occur too frequently. So I’d say there are gene products which are generated of genetic variation and some do it themselves and some other gene products are modulators of the frequency of genetic variation, to keep it low enough so that the species guarantees a certain genetic stability. |
| Q23 | The positive uses though of your achievements are many, the way research, medical research, have gone further. There have been a number of examples, for example in the cancer research. Would you just give us an example that you are really feeling particularly proud of, where you know that your work has really benefited medicine? |
|  | If you go into the field of medicine, I think any, very active protein like, let’s say interferons have been isolated, thanks to these techniques and then the question was, how should one apply them? In which kind of medical problems? Some, there were some deceptions but there were also discoveries that in certain other fields these products were very useful. Another example which has been widely successful is the product of human insulin which made medicine largely independent of insulins harvested from living animals and I think if one looks at these things these are really very good examples. They are also in human populations in the society relatively well accepted while in other fields on which either people themselves or people in their families or in the neighbourhood were not profiting from a treatment, people hesitate much more to accept genetic engineering and their products. |
| Q38 | Were there times when you really despaired, said No, I think I’m going to give this up, it’s too much work, or too much people might not believe in what I’m doing? |
|  | I had periods in which for long periods of time my expectations were not fulfilled. I can remember that I had searched for recombinants, giving a new type of research in enzymes by either mutation or recombination. I worked on that for more than one year quite intensively, without success, and I was very pleased only two or three years later that some other scientists working with a related system, but not with the one of ours, just found that spontaneously. We had been working on the rock system, the principle can be found, I also know why in my system with which I worked, it would be much, much more difficult to find this kind of thing which I looked for, but that stimulates you, that indeed you’re convinced that sometimes even if your ideas might be wrong, you don’t find the result but that’s how scientific life is. One shouldn’t be disappointed.  So you need to be flexible, you need …  Werner Arber: Yes, I think it is important, yes. |
| Q20 | And you need to share information with other scientists as well. |
|  | Yes. The bad thing is, let’s say if that happens to a very young scientist in his first experimental investigation, that’s relatively bad for her or him. What I told you occurred to me what was it, about 15 years of experience and I was immune against reacting to that, I think, at that moment.  So sometimes it can just be luck as well, hard work and luck?  Werner Arber: Yes, and you have to your eyes open, you know I was finding, identifying the molecular basis of these research in enzymes by working on a completely different project, that was is in 1960, a time when the governments gave extra money to study the peaceful use of atomic energy, power plants, but some of the money had to be given for by safety. We did some experiments in such a project which was trying to find out the effect of different types of radiation on bacteria and in doing that they ran into the phenomenon of restriction and they within just a few months of additional experiments I could show that the phenomenon has to do really properly with DNA, the modification is a mutilation. Once I’d seen that I felt Oh, this is an important discovery. I have, you have to have your eyes open and take your liberty to do a few experiments to clarify what it is and later on I also had of course to tell those people who guided the project that I had done something different than what I was supposed to do but they understood that actually after all it wasn’t so bad and it was alright. |
| Q12 | How do you relate that to young students of today, your story and the way you worked and what qualities do they have to have to go on? |
|  | It needs of course interest, some degree of curiosity for how nature works. You have to overcome short periods of mis-success and as I said before you have to have your eyes open to the unexpected, sometimes, you know, each experiments that you do, you do it in order to show something which is in your mind but the experiments may be not giving that answer which you expected but another answer and if you just say the experiment failed and you discard it, you make never a new discovery so, but it’s not an old favour that a new discovery of course is inborn so … |
| Q34 | What are the big issues yet to be found out? |
|  | Oh, there are many. There are so many. Of course we go more and more into trying to understand complexity, complex systems and there’s a lot of questions which even haven’t been formulated yet I think, there are more. How proteins, which are gene products, mutually influence each other in their activities and so on and also what I found in my own research, the co-existence within the genome of genes which are actually not working for your own personal life, your individual life, but for the biological evolution of the population. These, I call these evolution genes, variation generators and modulators of the frequency of variation which I mentioned already and of course the majority of the genes are other genes which are making your life possible. I mean bacteria, plants, animals and humans and this is a very high philosophical content here, identifying that within the genome there are not only genes whose product work for me but contribute for further evolution, not only for human beings but this is a general phenomenon, bacteria, all the living world and gives the guarantee that nature itself takes care of the biological evolution, rather than that as you still read in many textbooks that evolution only benefits from errors and mistakes occurring to the DNA. Many, practically all of these changes in variations are actively introduced at very low frequencies into the genetic information and of course natural selection, that’s Darwinism, will eventually decide whether such normal mutation is maintained or discarded. |
| Q23 | But that is amazing, so those evolutionary genes, the way I could relate to, is that somehow, we are connected, all of us. |
|  | That’s correct, yes, particularly since there is this third strategy of horizontal gene transfer, whatever somewhere in nature normal genetic gadget has been developed, has some chance at some later time by chance at low frequency to be horizontally transferred to other organisms so you can benefit from that perhaps in some future time so we are interconnected of course by common origins in the past but we are also interconnected into the future by possibilities that profit from other developments made by others. |
| Q23 | That just makes this absolutely amazing. |
|  | Yes, it is, yes, so that is a kind, for me, you know, if you come to that kind of insight, if it touches you. The first time you think, well it must be wrong, then you reflect it, then what is the consequence of it? There are a lot of philosophical, even theological consequences of that, creation and evolution were often in conflict, but what is going on in nature is in fact the permanent slow process of creation and that gives us a guarantee that also in future times, even if some living conditions are going to change, there is an internal natural potential that by diversity will be amplified again. Of course I have to add to that without your question you may ask this not necessary is developing from humans to superhumans but somewhere else in that evolutionary tree there will be the branches growing. |
| Q72 | You mention theology, as you said there has often been a conflict but theology has, a lot of people who are believers of any different disciplines of religion, always have this sort of saying the connection between all human and actually all living beings in some of the … |
|  | Yes, that’s right, yes, actually I think my understanding of molecular evolution is something which can give from the side of molecular biology, a confirmation of these opinions of continuous creation, also I have talked to theologians and it’s an interesting aspect, the question is if you are believers on some religion like Christianism, the question comes up sooner or later why does God, who actually likes creation, his work, and likes the organisms of creation including the human beings, why does he allow that sometimes a genetic variation is against the positive life, genetic inheritance, inheritable diseases and this has been my latest quest. But the duality of the genome having genes working for your own on the one hand and working for evolution on the other hand and we do know that not all genetic variations are beneficial. The majority in fact is detrimental so genetic diseases are among those detrimental ones so God, I believe, according to Genesis, found evolution as good and that implies that mechanism, that once in a while there’s a sacrifice of an individual getting by chance a bad mutation so that’s how I think one could think about, I’m not sure whether that interpretation is correct, but it leads me into really considerations of this kind. |
| ID | **0607** |
| Biographical | My parents came to the United States in the early years of this century as part of a wave of Russian Jewish immigrants seeking freedom and opportunity in the New World. My mother, Sarah Levitan, came to America when she was 18. My father, Samuel, rebelling against an orthodox family, left home in his midteens and made his way to the United States a few years later. They were married in Philadelphia in 1910. As the last of their nine children I was born in 1928 in Wilmington, Delaware, on the eve of the great depression. Soon after, my father lost his small business and was for some time unemployed. Our house was cold and leaky, and (I learned later) my parents sometimes went hungry. Yet they generally managed to retain their good humor and certainly their hopes for their children. I have only fond memories of this period, no doubt due to the special attentions of an affectionate family.  My education began in the public schools of Wilmington. During most of these years, from about age 10, I also worked at some job or other after school, on weekends, and in the summer months. Following in the footsteps of my brothers and sisters, I went on to the University of Delaware, where I studied chemistry, philosophy, and literature. Although I enjoyed science and mathematics, what I remember most vividly is a small, stimulating circle of professors and students (including a number of veterans just back from the war), interested in philosophy and politics. To my father my interest in natural science meant “medicine”, and becoming a physician also seemed more attractive to me than any other alternative I knew about. So I applied to medical school and received a scholarship at Washington University in St. Louis. Washington University turned out to be a lucky choice. The faculty was scholarly and dedicated and accessible to students. A wonderful summer of research with Oliver Lowry, Professor of Pharmacology, convinced me that a career in medical research and teaching suited me better than medical practice. After getting an M. D. degree in 1954, I went to the Columbia-Presbyterian Medical Center in New York for an internship in medicine with Robert Loeb, a masterful clinician and medical scientist. That was one of the most valuable years of my life. The glimpses of human strength and frailty that a physician sees are with me still. I spent two more years at Columbia as a medical resident, interrupted by service as a Clinical Associate at the National Institutes of Health in Bethesda. During my years in Bethesda, I married Joanne Gomberg, and our son Eli was born.  While at the National Institutes of Health I developed an interest in the biosynthesis of proteins as a result of a study with Michael Potter and John Fahey of myeloma protein formation in plasmacytoma cells. This led me to [Fritz Lipmann’s](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1953/index.html) laboratory at the Rockefeller Institute in 1959. Here I identified the bacterial “elongation factors” involved in the addition of amino acids to growing peptide chains, worked on the mechanism of action of puromycin as an inhibitor of this step (with Amos Neidle), and in a collaborative study with Norton Zinder, demonstrated that RNA from a bacterial virus directed the synthesis by cell extracts of viral coat protein. During those years in the invigorating atmosphere of Lipmann’s laboratory and the Rockefeller Institute, I learned a geat deal, and Lipmann’s artistry made a lasting impression on me. I also found out that I liked biochemical research and that I could do it. The intention of returning to a department of medicine was abandoned, and I accepted a position at Johns Hopkins University School of Medicine in the Department of Microbiology, headed by Barry Wood, an inspiring former teacher at Washington University. During the years in New York our son Jeremy was born, and soon after our move to Baltimore in 1962, my wife gave birth to our youngest son, Ben.  In Baltimore I became head of a one-man “Division of Genetics” which gradually developed substance with the recruitment of [Hamilton Smith](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1978/index.html), Bernard Weiss, Kenneth Berns, Thomas Kelly, and recently, John Morrow. My initial research at Hopkins was a continuation of studies on the in vitro translation of bacteriophage RNA, particularly its regulation by phage coat protein and the location of genes by translation of fragments of the RNA. My co-workers during these years were Yoshiro Shimura, Max Oeschger, Gerardo Suarez, Robb Moses, Kathleen Eggen, Roy Schmickel, Herbert Kaizer, Marilyn Kozak, and Susan Polmar.  In the mid 60’s I became interested in viral tumorigenesis and spent the first half of 1969 learning about animal cells and viruses at the Weizmann Institute of Science in Rehovot, Israel, with Leo Sachs and Ernest Winocour. That spring a letter from Hamilton Smith telling me about the restriction endonuclease he had discovered in *Hemophilus influenzae* aroused my interest in the possibility of using restriction enzymes to dissect the genomes of DNA tumor viruses. Back in Baltimore in the summer and fall of 1969, Stuart Adler and I surveyed the known restriction enzymes for their ability to cleave the DNA of Simian Virus 40, one of the simplest animal viruses that transform cultured cells to tumorigenicity. Using fragments of Simian Virus 40 DNA produced by Smith’s enzyme and by similar enzymes discovered subsequently, Kathleen Danna and George Sack constructed a cleavage map of the viral DNA. With this map in hand, other co-workers proceeded to localize viral genes and template functions along the molecule, to construct deletion mutants and later point mutants at pre-selected restriction sites, and to analyse the genomes of naturally arising variants of the virus. Associates in these later studies were Elena Nightingale, Ching-Juh Lai, Theresa Lee, William Brockman, Mary Gutai, Walter Scott, Nicholas Muzyczka, and David Shortle; and collaborators from other laboratories were George Khoury, Malcolm Martin, Kathleen Rundell, and Peter Tegtmeyer.  As I look back on the last few decades of my life, I am struck by the good fortune that came my way. Throughout my schooling there was an abundance of opportunity and encouragement. Several of my teachers were remarkable individuals who had a lasting influence on me. At every stage of my career I have had interesting and cordial colleagues, some of whom are close friends. My field of research is as exciting to me as ever, and it remains essentially a “cottage industry” effort. I have had talented students who are a source of much enjoyment, and I anticipate more to come as their careers develop. And most important, my wife and sons have created in our home an atmosphere of joy and harmony, so essential to everything else.   |  | | --- | | Vita | | Born 30 October, 1928, to Samuel and Sarah (Levitan) Nathans in Wilmington, Delaware, U. S.A. | | Married 4 March, 1956, to Joanne Gomberg. Three children: Eli, Jeremy, Ben. | | B. S. in Chemistry (1950), University of Delaware, Newark, Delaware. | | M. D. (1954), Washington University, St. Louis, Missouri. | | Intern (1954-1955) and Resident (1957-1959) in Medicine, Columbia-Presbyterian Medical Center, New York. | | Clinical Associate (1955-1957), National Institutes of Health, Bethesda, Maryland. | | Guest Investigator (1959-1962), Rockefeller Institute for Medical Research, New York. | | Faculty member (1962-present), The Johns Hopkins University School of Medicine, Baltimore, Maryland. Since 1972, Boury Professor and Director of the Department of Microbiology. | | American Cancer Society Scholar (1969), Weizmann Institute of Science, Rehovot, Israel. | | National Academy of Sciences’ U. S. Steel Foundation Award in Molecular Biology (1976). | | Fellow, American Academy of Arts and Sciences (1977). |   From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1978*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1979  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Daniel Nathans died on November 16, 1999.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | 0608 |
| Biographical | My mother and father each came from simple country backgrounds, but both showed an early inclination for scholarly pursuits. They eventually met as school teachers in a local Panama City, Florida high school and were married in 1929. The following year, my father was appointed Assistant Professor of Education at the University of Florida at Gainesville, and in that year my brother was born. In 1931, my father went on leave to Columbia University in New York City to complete his doctoral work in education. I was born there on August 23, 1931 while he was a graduate student. Though the family commuted annually between New York City and Gainesville over the next five years, I retain the strongest memories of our life in the city. In particular are recollections of life in a small, intimate apartment, walks in the city parks, and quiet evenings spent with my mother and father who entertained us with arithmetic problems and a small Gilbert chemistry set.  In 1937, our family moved to Champaign-Urbana, Illinois. My father had joined the faculty of the Department of Education at the University of Illinois and was to spend the major part of his academic career there until retirement. My entire boyhood was spent in this small midwestern academic community. Despite the fact that our life in Urbana spanned the late depression years and World War II, the community continued to function pretty much as if untouched by world events. At home, an atmosphere of intense intellectualism was maintained. My father was perpetually working and writing. At the same time, my mother struggled to establish herself as a writer, but she was to remain frustrated in her ambitions. However, she, in particular, imbued us with a respect and desire for the creative life.  My brother and I received private French lessons during our pre-teen years. I began piano lessons at age eight and my brother took up violin. We studied with a talented musical family, the Fosters and Sonderskovs. I was in no way gifted and found practice to be a chore until one memorable day when I was about age thirteen. On that day, a friend introduced me to the local music shop and by chance I picked up a recording of Artur Rubinstein playing Beethoven’s Pathetique Sonata. I had been struggling with the piece for sometime, but had never appreciated its dramatic beauty. Listening to Rubinstein’s magnificent performance for the first time was a truly awakening experience. From then on I became a devoted pupil and music lover.  My boyhood friends were mostly sons of university faculty. Our interests included football, basketball, music, chemistry, electricity, and electronics. My brother and I spent many hours in our basement laboratory stocked with supplies purchased from our paper route earnings. We attended University High School, a superb small college preparatory school with an array of exceptionally talented students drawn largely from university faculty families. To my knowledge, two Nobel Laureates are counted among “Uni-High’s”graduates, as well as numerous successful professionals, and no less than three current professors at Johns Hopkins. I completed high school in three years largely due to a wonderful science teacher, Wilbur E. Harnish, who allowed me to complete chemistry and physics during the two summers preceding ninth grade. Two other teachers at “Uni-High” influenced my development profoundly: Vynce Hines, who taught me the beauties and rigor of plane geometry and Miles C. Hartley, who gave me a sound foundation in algebra.  After completing high school, I matriculated at the University of Illinois, majoring in mathematics for which I had a flair but no deep talent. I had not yet decided on a particular field of science. My brother, who was considerably more gifted in the abstract areas than I, was studying theoretical physics, but this did not appeal strongly to me, nor was I interested in pure chemistry. At that time biology, as taught, was largely descriptive. It was not especially appealing for one brought up on “real” science. However, during my sophomore year, my brother introduced me to a book on mathematical modeling of central nervous system circuits by a biophysicist named Rashevsky. It caught my interest and I began reading about the nervous system. I continued this interest after transferring to the University of California at Berkeley in 1950. There, for the first time, I found courses in cell physiology, biochemistry, and biology that interested me. I recall in particular at that time, a guest lecture by [George Wald](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1967/index.html) describing his studies of retinal biochemistry. I was converted overnight into an avid student of visual physiology. It had become clear that mathematics, while providing an excellent basic training, was not my real interest. With a broadening appreciation of biology and a budding interest in human visual- and neurophysiology, I decided to apply to medical school.  In 1952, I began my studies at the Johns Hopkins University Medical School in Baltimore, Maryland. I was immediately caught up in the excitement of a new kind of life, and without firm commitments to any particular area of research, I was to continue a fairly conventional medical career for several years. I received my M. D. degree from Hopkins in 1956 and proceeded to Barnes Hospital in St. Louis for a medical internship. There I experienced for the first time a true feeling of freedom and independence. In my second month of internship I met Elizabeth Anne Bolton, a young nursing student. She was from a family of doctors and engineers, had been born in Spain, reared in Mexico City, and had come to the States for college and nurses’ training. We immediately liked each other, and a few months later, were married.  In July, 1957, I was called up in the Doctor’s Draft, and rather than seek any of several avenues of deferment, decided it was an opportune time to be done with my service obligation. I chose the Navy and we received a two year assignment in San Diego, California. It was a relaxed and easy time for us after so many years of schooling. For the first time in my life I was faced with greatly reduced demands on my time and the problem of idleness. I began to search for ways to occupy myself. A report of the then new research in human chromosomal aberrations caught my interest. Soon I was reading textbooks on genetics. Because of my mathematical background, I delved deeply into the population genetics of Sewell Wright and Ronald Fisher.  In 1959, with the Navy service completed, my wife and I moved to Detroit, Michigan with our one-year old son to begin my medical residency training at the Henry Ford Hospital. There I found a well-stocked library that included “Bacteriophage” by Mark Adams, the first issues of the Journal of Molecular Biology containing the classical [Jacob](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html) and [Monod](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html) paper describing the operon model for gene regulation, and two collections of papers by Adelberg and Stent. I suddenly became aware of the beautiful work of the “phage school” and of [Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) and [Crick](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) and DNA. After many years of haphazard searching for the “right” area of research, I knew I had found it.  In 1962, armed with a N.I.H. postdoctoral fellowship, I began my research career with Myron Levine in the Department of Human Genetics at the University of Michigan in Ann Arbor. Mike was a geneticist studying *Salmonella* Phage P22 lysogeny. The choice to work with him, while governed more by expediency than by considered planning, turned out to be most fortuitous. Mike was an easy-going young investigator with a solid phage background and well established among the phage crowd. He allowed me just the right blend of independence and encouragement. Together we carried out a series of studies demonstrating the sequential action of the P22 *C*-genes which controlled lysogenization. In 1965, we discovered the gene controlling prophage attachment, now known as the *int* gene. By 1967, I had published this work and had carried out a study of defective transducing particles formed after induction of *int* mutant prophage. During 1966-67, Mike took a sabbatical year with [Werner Arber](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1978/index.html) in Geneva and through correspondence, I learned for the first time about Arber’s remarkable work on restriction and modification phenomenon in bacteria.  In 1967, I came to Johns Hopkins as an Assistant Professor of Microbiology and have remained there since. My research work includes studies of restriction and modification enzymes, enzymology of genetic recombination, mechanism of bacterial transformation, and genetic regulation in prokaryotes and eukaryotes. In 1975-76, as a Guggenheim Fellow, I collaborated with Max Birnstiel at the University of Zurich in Switzerland on histone gene arrangement and sequence. It was a superbly enriching year for both myself and for my family.  My wife, Elizabeth, is artistically inclined, enjoys a variety of “Handarbeit”, sings in a church choir, enjoys classical music, and is a moderately proficient linguist (English, Spanish, German, and French). My major non-scientific diversions are classical music and piano. We have four sons and a daughter, none of whom currently indicate a strong interest in science.   |  | | --- | | Principal works | | Smith, H.O. and Wilcox, K.W. A restriction enzyme from *Hemophilus influenzae*. 1. Purification and general properties. J. Mol. Biol. *51*, 379 (1970). | | Kelly, T.J., Jr. and Smith, H.O. A restriction enzyme from *Hemophilus influenzae*. 11. Base sequence of the recognition site. J. Mol. Biol. *51*, 393 (1970). | | Roy, P.H. and Smith, H.O. The DNA methylases of *Hemophilus influenzae* Rd. 1. Purification and properties. J. Mol. Biol. *81*, 427 (1973). | | Roy, P.H. and Smith, H.O. The DNA methylases of *Hemophilus influenzae* Rd. 11. Partial recognition site base sequences. J. Mol. 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| Autobiographical |  |
| Podcast |  |
| Telephone  interview | 0608 |
| Interview |  |
| Q76 | Three days ago, there was a major announcement, a major event in science, you could say, a joint announcement by groups in the United States and the United Kingdom about, I would say, a high-quality DNA sequence of the entire human genome and the significance of this event was underlined by the fact that two heads of state, Bill Clinton and Tony Blair, had joined the press conference. We are happy to have here among us two Nobel Laureates in Physiology or Medicine, Professor or Doctor Richard Roberts and Hamilton Smith who have been involved in various capacity in the human genome project. In fact, one of you was actually present at the White House during this press conference. Would you like to take it on from here? |
|  | I’m actually an employee of Celera Genomics, which is a company in Rockville Maryland that has been single-handedly determining the human genome sequence in what many have called a race with the rest of the world, with the public efforts which carried on in the United States, England, Germany and Japan and I think some other countries. The White House ceremony was an attempt to get a cooperation between the public effort and the private effort, not a collaboration but a cooperation where we would agree to not say bad things about each other’s approaches or data or personalities and that we would try to do joint publications in a scientific journal, sometime near the end of the year 2000. Not papers that have joint authorship between the groups but separate publications where we present our accomplishments. I think it’s been a very good thing actually to do this, it takes the focus of the press coverage away from the warring parties and gets it back to what’s really important, namely getting the sequence and getting it out to the public.  The ceremony itself, President Clinton gave a short talk of about 4-5 minutes and then, by a TV hook-up in England, Tony Blair came on and said a few words in his best oratorical style and then President Clinton introduced briefly Francis Collins, who’s head of the public effort in the US and of course there were words said about the DoE part of the effort and there were nice things said all over the place. It was really a pretty good show and then Craig Venter was the last speaker. I was wondering when he went up to the microphones, whether there was anything left to be said but Craig, I think, handled this situation extremely well and got across how Celera fits into this accomplishment. So, we had a press conference afterwards. I think it was not only a truce between the public and private efforts but also an announcement that each of the groups had achieved their goals. The public human genome project announced that they had completed a working draft of the genome which represents about a 90% coverage of the genome but without a complete assembling of the genome and Celera announced that they had a 99% random coverage of the genome with an assembly of those sequences, so that genes are laid down linearly along the chromosomes. |
| Q23 | Now that we have two independent groups who have come to an agreement about the general structure of the human genome, maybe you are able to answer the question, how many genes are there in the human genome. It’s a question you get when you lecture in this field and I’ve heard widely varying figures so, now if you get the question, what would your answer be? |
|  | Hamilton Smith: I think at this moment we still are in considerable doubt, but at Celera we’re also sequencing the mouse genome which will be complete sometime before the end of the year, to the extent that we can compare the mouse sequence to the human sequence. The protein coding regions of the mouse and human are sufficiently similar that they can be aligned, whereas the so called junk DNA, the 97% of the genome which doesn’t code for …  Richard Roberts: You’re talking about this stuff I discovered, are you?  Hamilton Smith: Yes, something like that.  Richard Roberts: The junk.  Hamilton Smith: Yes, the junk.  Hamilton Smith: … is more dissimilar, so it should be possible to simply read the two genomes in six frames and with high probability overlap the protein coding regions and get a fairly precise count of how many genes are present and that’s really the strategy that we’re pursuing. We have the mouse sequence, or we will have the mouse sequence and we’re the only ones in the world that will have it, so I think Celera will have the most accurate annotation. |
| Q24 | Because people are betting on the number and there is a need for an authoritative answer to this question from the gambling point of view and from the human centred views that we entertain. To drive these large projects, the human genome project, obviously there have been precursors, people have got news from physics now that they are enormous projects, big physics and you now have big biology coming around, so once the human genome project has been completed, how will we proceed? I think we would agree that the most important thing now is to find out how the genome functions and we now enter then a type of research where we want to study the ultimate products, the proteins. Since there are many ways in which you can process the information from the DNA and the genome, at the RNA level, there are many more proteins to be found. This field of studying the proteins made in biological systems is called proteomics, so do you see any such big proteomics coming along and what can be done in terms of technology to speed up the analysis of the much larger number of proteins than the number of genes? |
|  | Hamilton Smith: I mean, I can say pretty much what we are planning at Celera. Celera I think is unique in its ability to do very large scale surveys. We don’t like really doing anything unless we can do 100,000 a day of whatever it is, so this is a way Craig Venter thinks and it allows us to do things that can’t be done easily in the university setting or in most other companies. What we’re planning of course is to move into proteomics using new instrumentation from PE Bio systems, mass spectrometers that can analyse tens of thousands of samples per day of protein. The plan would be to, the big interest initially I think is to see the spectrum of proteins that are being made in specific tissues, normal or diseased tissues, cancer, whatever. The plan would be to separate these proteins from say a cancer tissue on two-dimensional gels and then each single protein spot on the gel would be analysed in the mass spectrometer. Essentially hit by a laser blown into fragments of the protein which would then be matched with the genomic sequence and by computer, one should be able to predict the protein peptide spectrum that you would get for each of the genes in the human genome. Let’s say there are 50,000, so that we would get a virtually instantaneous identification of the particular gene product for each of the spots and we could say then that a given tissue is expressing certain genes and we form a database of this kind of information and again we sell that to our subscribers. This is sort of a first step of something that we can easily see ahead that we could produce this. I don’t know where we’re going beyond that but maybe Rich could.  Richard Roberts: The real problem with proteomics is that much of the technology that you need to relate function back to the gene is not in place at the moment, so one issue is well what is being expressed, how much is being expressed if we look at particular tissues, if we look at the brain, if we look at skin, if we look at liver, what kinds of proteins are taking place? At the moment we are able to look at what messenger RNAs are taking place, but we know also from other experiments that the amount of protein very often does not match the level of RNA, so we need both to be able to look at RNA and to look at the protein. One way to look at the protein is to use the kind of technology that Ham just talked about. |
| Q3 | You made a point in one of the sessions at this meeting that once you study microbial genomes and there is a project called the minimal genome project which tries to define what’s the minimum number of genes. Wouldn’t such a system be the most suitable in finding out the function of various genes, because the human with this much larger genome and many genes is incredibly more complex? |
|  | Richard Roberts: Right. I think there are two separate issues, one issue relates to what is it that really makes life, what do you need, what is the minimum set of instructions that you need to make a living cell? And one way to do that is to take the very smallest cell that we know that is free living, as Clyde Hutchison is doing, and try to remove the genes that look as though they’re not necessary, get down to the minimum set, understand that in completion. Then one will at least know what is the minimum thing you need for life but that’s likely to be less than 500 genes and those 500 genes are a small set of what is present in a human cell. So, I think what will come from say the minimal genome project will be a working definition of kind of what is the minimum of life but there’s so much more to life than that. We need to know what is the precise biochemical function of each of the gene products, what reactions does it catalyse? That is something that for most proteins is not easy to do and we’re working ourselves at the moment on a bunch of proteins that are present in every organism for which the genome has been sequenced so far.  We think that this particular protein transfers methyl groups from S-Adenosyl methionine onto something, but we don’t know what and it’s not easy to find out, it’s not easy to prove that. But it is an interesting protein, it’s present in every genome but we don’t know what it does, no-one has stumbled upon it by genetics or by biochemistry yet, to know what it does and there are many such proteins. In the human genome, there are going to be thousands of these proteins for which we need to define function so what we need is to find high throughput ways, fast ways in which we can get clues to function. One high throughput way is to use computation to try to do that, so you look through the protein sequences, you try to find the little protein sequence motifs that in other proteins we know interact with ATP or they interact with DNA or they’re RNA binding proteins or whatever, so this can give you a clue, but you need to do the biochemistry afterwards to show that the clues that were given were correct or not and we don’t have good methods for doing that at the moment.  Hamilton Smith: Another approach to the minimal genome is the synthetic approach which I think is intriguing, creating “life” in the laboratory. The idea there would be again working with the mycoplasma genitalium is sort of the basic tools or parts for it. Having some idea from the other studies as to what genes are essential, one could actually make a synthetic chromosome that contains the set of proteins that have been identified as essential and then put that synthetic chromosome into a cell from which the natural chromosome has been removed and then see if you get something that will grow in the laboratory. Of course it probably won’t work the first time, maybe not the 100th time either, it could be somewhere to cloning Dolly and in the beginning you had to do hundreds of them before you got a successful attempt. But it would be a spectacular event if one could create a new genome.  Richard Roberts: I guess, when you start to think about the real importance of microbiological research, within the context of the human genome, the methodology that will need to be developed to understand how something as simple as mycoplasma genitalium work is going to methodology that can be applied to the human genome. So if we can learn to do this thing properly and if we can learn to do it in a fast manner for the small bacterial genomes, where in principle everything is a lot easier, we should be able to apply that methodology to these much more complicated systems too and in the meantime of course, we will find out much about what is really important in order to make life. What is it about these proteins and these genes that really makes something living as opposed to just a collection of chemicals in a test tube. |
| Q34 | If we look at the biomedical benefits of the DNA sequence of the human genome, I’m sure when [Jim Watson](https://www.nobelprize.org/prizes/medicine/1962/watson/facts/) went to congress, he had many ideas on what the benefits would be and tried to convince the congress and I noticed also that Bill Clinton mentioned cancer, the cure of cancer would be something that would be following after the sequencing. How do you see the immediate consequences in the biomedical field of our knowledge of the human genome sequence? |
|  | Hamilton Smith: I don’t think I can foresee all of the benefits or consequences, we’re going to have to work into it gradually, but I it seems clear that it would facilitate much of the work that’s going on. A lot of work over the past few years has gone into hunting for genes in the genome and sub-cloning them and so on and so forth. This should short circuit all of that, I mean you should be able to in many cases find a gene or several duplications of the gene in the genome and proceed from that sort of jumpstart. I think an example would be, there are several groups of proteins that have demonstrated therapeutic benefits, for example the interferons and already we have an example by the genome sequencing of a new interferon which was previously not detected. With the whole genome you can look and often find members of a protein group that you didn’t know about, so these are new potential products. We could discover new epogen type proteins as well or growth factors that can stimulate certain tissues simply by analogy to ones that are already known. |
| Q77 | Will it be possible to sequence a genome of individuals in the short time, in such a short time that it would be important in medical practice, in designing the therapy one is planning for a certain disease? |
|  | Hamilton Smith: Not with current technology, it’s too expensive. Eventually I think that we will need some sort of a physical method for single molecule sequencing. Once that arrives, we might be able to tackle the whole individual, but one of the big areas of effort now is large scale genotyping using various arrays of genes. My dream would be to be able to take a single drop of blood from an individual and within a few hours, determine 100,000 single nucleotide polymorphism mutations in that individual, I shouldn’t say mutations but indifferences in that person’s genome. In other words develop an immediate genotypical profile for an individual that could be used in judging what treatments would be best for that individual or what possible genetic diseases that person might encounter in life. I think that’s coming, probably in the near future.  Richard Roberts: I guess the real point that you’re getting at here is that one would like to take individuals and get some idea of their genetic makeup. One way to do that is to get the complete DNA sequence, but in fact you can get a lot of information without looking at the complete DNA sequence because as a result of these things called single nucleotide polymorphisms, we know that approximately every 300 bases or so, along with human genome, there is a region that varies, quite often from one individual to another. By just looking at those regions, in essence just sampling a one three hundredth of the genome instead of looking at the whole thing, one can actually tell a lot about the genetic propensity of various people.  For instance, we know that there are genes that if they go wrong, if they have some particular polymorphism, they have one sequence as opposed to another, that that leads to problems and the first classic example of this was sickle cell haemoglobin where we knew that a single base change in the DNA sequence for haemoglobin rendered the haemoglobin not quite so effective. This was a mutation that had been well kept within the human population in Africa because when you had heterozygous for this condition, when you had one sickle cell gene and one normal gene, you had resistance to malaria which, if you live in Africa, this is quite an important thing to have. That has been maintained in the population, even though the selection no longer applies among blacks who have moved from Africa into the US or into England or into Western Europe and they maintain this mutation because evolution is slow, it takes a long time for it to get out of, and there are many diseases for which this kind of thing is true. |
| Q78 | You mentioned the probability of finding an SNP /- – -/ that the human genomes that have been sequenced a body, say a single group and then the sphere group have been different and can you already now see evidence of SNPs if you compare your sequences with each other? |
|  | Richard Roberts: Yes.  They shouldn’t be entirely equivalent, I would imagine.  Richard Roberts: No, basically what’s happened so far is that the main sequence that’s come from Celera is from one individual. There are other individuals who are being sequenced at Celera at a level sufficient to identify single nucleotide polymorphisms. The public human genome project, they have sequenced many individuals, a much larger number than Celera have been dealing with and so there are single nucleotide polymorphisms that are apparent within their data already and there is in fact something called the SNIP consortium which are a group of labs who are specifically looking for single nucleotide polymorphisms. These have been funded by both government agencies and by commercial companies and this data is all being placed in the public domain, so the answer is we know of a lot of snips already but we don’t know enough to do a complete genotype on someone.  Hamilton Smith: Nor do we know which of those snips really are clinically relevant, I mean the large proportion of them are probably pretty neutral changes. We don’t know how many would be medically significant or genetically significant.  Richard Roberts: But this is what will come out of the next stage of the human genome project where one tries to assign function and identify the genes, because many of these we know that these are important for this disease or for that, we will probably find homologs of some of these genes and we don’t know whether they’re important yet, so that will need to be tested. In many ways, we’re really at the beginning of the human genome project, not at the end, so even though we have announced we’ve gotten through this first stage, it very much is a beginning. Biology has undergone this revolution in the last few years where it’s gone from being really an observational science, in which people have been looking at phenomenon and trying to understand them and trying to figure out what was going on, to become a hard science like chemistry or physics where we can really now look at a complete genome and put some bounds on the problem. If we want to explain how a small bacterium works, we can say we’ve found there are 4,000 genes or 5,000 genes, we need to explain this organism in term of these 5,000 genes, if we’re going to do a genetic experiment in which we change one of these genes and we know what to look for, we know we have to look and see what happens to all of the other genes, in order to begin to understand. I think we’re very much at the start of biology, which is a wonderfully exciting time for us, you know I mean this is the time I would love to be a graduate student again, this is the time to be a graduate because there are many discoveries to make, many more Nobel Prizes coming out of this field.  Hamilton Smith: In science, one tends to go from simple to complex and then hopefully back to simple again. We’re in the complex phase right now.  Richard Roberts: We would hope not. |
| Q12 | So your supervisor buys a licence maybe, to have the detailed sequence for a certain genome, so does that leave the individual graduate student then with trying to define the role of specific proteins or signalling systems? |
|  | Richard Roberts: That’s certainly one possibility. Basically what you have is this enormous textbook, except that instead of being a textbook with diagrams and clear headings telling you what everything is, you’ve got a textbook, it’s full of words but we don’t know what the headings are and we don’t know how to put in the diagrams to explain how this little bit relates to this little bit. This is for the graduate student to start to work out.  Hamilton Smith: Each gene with an unknown function is a PhD degree, if you can figure it out. |
| ID | **0609** |
| Biographical | I was born in France on January 11, 1924 in the small town of Dijon, the capital of Burgundy. I was educated there in the public schools and the lycée. I entered medical school in Dijon in 1943 and received the M.D. degree from the Faculté de Médecine of Lyon in 1949, – the two schools were then administratively connected, with the larger school of Lyon granting the degrees. All my medical studies and training were totally clinically oriented, with three years of what we could call rotating internship. There was no laboratory facility of any sort in Dijon, except for gross anatomy. Dark years of no fun youth these were; France had fallen to the Germans in 1940; Dijon was from then on occupied by the German army until liberation days in 1944.  During these five years of medical studies, I had always been interested in endocrinology, probably because two of my best teachers of clinical medicine, P. Etienne-Martin and J. Charpy were themselves interested in what were in those days the early concepts of endocrinology and the beginning logical therapy it appeared to offer. I always hoped that somehow I could one day work in a laboratory. In France you had terminated your medical studies after 5 years of curriculum; you could then practice medicine – which I did for some time. To obtain the degree of Doctor in Medicine you had to write and defend a dissertation, a thesis; that was usually *pro forma*. I decided, however, to write a dissertation for the M.D. degree that I would enjoy, hopefully on some work I could perform in a laboratory.  One day, I learned that Hans Selye would lecture in Paris on his alarm reaction and the endocrinology of the general adaptation syndrome. I went to hear him. The magnetism of the man was extraordinary. I went to talk to him after one of his lectures. A few months later I was in Selye’s newly created Institute of Experimental Medicine and Surgery at the University of Montreal, with a modest fellowship from Selye’s funds. In one year I completed some experimental work on desoxycorticosterone-induced hypertension in bilaterally nephrectomized rats kept alive for several weeks by peritoneal dialysis; that constituted the material for the thesis necessary in the French system to obtain the M.D. degree, which I obtained in Lyon upon the defense of that dissertation, in 1949. Not much interested in the academism and formalism of a research career within the French system that was then open to me, I returned to Selye’s Institute, and three years later eventually obtained a Ph.D. degree in physiology in 1953. In these four years I had learned experimental endocrinology in a remarkable program jointly conducted between McGill University and the University of Montreal. In 1953, I joined the staff of the Department of Physiology at the Baylor University College of Medicine in Houston, Texas, as a young assistant professor. I taught physiology at Baylor College of Medicine for 18 years, until 1970. While in Selye’s department, I had become interested in the problem of the physiological control of the secretion of the pituitary gland as it was involved in the acute response to stress. This was due particularly to friendly contacts with Claude Fortier and to a long visit by Geoffrey W. Harris from London.  I have recounted in some details in a chapter of Volume 2, of *Pioneers in Neuroendocrinology*, J. Meites (ed.), Plenum Press Publ., 1978, how I became more and more involved in the search for the chemical mediators of hypothalamic origin, suspected to control the functions of the pituitary gland; how [Schally](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1977/index.html) came to me at Baylor from the laboratory of Murray Saffran at McGill immediately after he had obtained there his Ph.D. degree in biochemistry – as we both thought that we would solve in no time the problem of the nature of CRF (the corticotropin releasing factor); how I went back to France in 1960, – on academic promises that did not materialize, thus returned to Houston in 1963, and later, in 1970, went to the Salk Institute to establish our present Laboratories for Neuroendocrinology. That chapter written in a light anecdotal manner, along with two reviews, one concerning the isolation and characterization of the first of the hypothalamic releasing factor, TRF (in *Vitamins and Hormones, 29,* 1-39, 1971), the other concerning the isolation of the luteinizing hormone releasing factor (in *Am. J. Obs. and Gynecol., 129,* 214-218, 1977) will give the interested reader a good historical description of these early years of, indeed, true pioneering in neuroendocrinology.  I served for 11 years on several advisory groups (Study Sections) of the National Institutes of Health (NIH) – an experience that was as rewarding as it was exhausting – as a member of the Council of the American Endocrine Society from 1969-1973.  I was elected a member of the National Academy of Sciences of the USA, in 1974, a member of the American Academy of Arts and Sciences in 1976. I have been honored by several national and international scientific recognitions: among which The Gairdner International Award, Toronto, Canada, 1974; The Dickson Prize in Medicine, The University of Pittsburgh, Pennsylvania, 1976; the Passano Award in the Medical Sciences, Baltimore, Maryland, 1976; the Lasker Award in Basic Sciences, New York, 1975; and recently the National Medal of Science presented by the President of the USA.  I have received honorary degrees, from the University of Rochester (D.Sc.), 1976; the University of Chicago (D.Sc.), 1977; and the Légion d’Honneur from the French government in 1973.  I consider as major honors to have been asked to deliver numerous memorial lectures, in particular the Harvey Lecture, The Rockefeller University, New York, 1974; the Jane Russell Wilhelmi Memorial Lecture, Emory University, Atlanta, Georgia, 1976; the Geoffrey W. Harris Memorial Lecture, International Congress of Endocrinology, Hamburg, Germany, 1976; The Gregory Pincus Memorial Lecture, The Laurentian Hormone Conference, 1976; The Herbert M. Evans, Memorial Lecture, University of California in San Francisco, 1977.  In Houston, in Paris, in La Jolla, where I set up shop – sometime simultaneously as in the days of commuting between Paris and Houston – I have had the extraordinary privilege to work with wonderful collaborators some so much more knowledgeable in their own field than I was (or still am), all full of enthusiasm and sharing common ethics of science. The work recognized in this Nobel Prize was a group effort and achievement. I started writing the list of these colleagues, collaborators, students who worked with me, starting in 1953; I stopped when I realized more than one hundred names were involved. Of unique roles and significance in the saga of the hypothalamic hormones in which I was involved, I must call to the lime light Edvart Sakiz, now in Paris, Roger Burgus, now in La Jolla, Wylie Vale who came to me as a graduate student, now in La Jolla, Nicholas Ling and Jean Rivier, both now in La Jolla. They, and their own students, are and will be the future of this expanding field or research.  My wife is a musician of talent and, so far, five of our six children are already in artistic careers or show a definite preference for artistic endeavors; one only, may be a biologist some day. And all that is fine with me. Since 1970 when we came to the Salk Institute, we have lived in La Jolla, a suburb of San Diego, in a Mediterranean house which we have filled, if not overfilled, with many contemporary paintings French and American, sculptures and potteries mostly from pre-Columbian Mexico and also from New Guinea. Several keyboards and string instruments are also part of the enjoyable living environment of that happy house. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0609** |
| Interview |  |
|  |  |
| ID | **0610** |
| Biographical | I was born in Wilno, Poland on November 30, 1926, being of Polish, Austro-Hungarian, French and Swedish ancestry. My father, a professional soldier trained in the military academies of Vienna, Austria and St. Cyr, France, had to leave his family when the Second World War broke out to fight with the Allied Forces. My life and outlook were influenced by the harsh childhood which I spent in the Nazi-occupied Eastern Europe, but I was fortunate to survive the holocaust while living among the Jewish-Polish Community in Roumania. I used to speak Polish, Roumanian, Yiddish, Italian and some German and Russian, but I have almost completely forgotten them, and my French in which I used to excel is also now far from fluent. In 1945, I moved via Italy and France to England and Scotland. In spite of post-war economic and nutritional austerity, the United Kingdom seemed like a paradise to me because of the respect for human rights. Since that time, I have always had a profound friendship for the British. I received my high school diploma in Scotland in 1946 and afterwards studied chemistry in London. I adored English and Scottish association football and I even tried out as an inside forward for some English and Scottish football clubs, but since I could not devote enough time to training I never made regular First Division teams. However, since 1946 I have always stayed in excellent physical shape by swimming daily and practicing other sports. “Mens sana in corpore sano” has always truly been my motto. In England I also developed a great liking for classical music, especially Beethoven, Brahms and Liszt.  My interest in medical research started at the age of 23, when I joined the National Institute of Medical Research (NIMR, MRC) Mill Hill, London, England. I was fortunate to work with and be exposed to the stimulating influences of such scientists as Dr. D. F. Elliott, Sir Charles Harington, Dr. [R.R. Porter](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1972/index.html), Dr. [A.J.P. Martin](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1952/index.html), Dr. R. Pitt-Rivers, Dr. J. Gross, Dr. T. S. Work, Dr. H. Fraenkel-Conrat, and Dr. [W. Cornforth](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1975/index.html), several of whom later won Nobel Prizes for chemistry or physiology and medicine. Although my position was very junior at Mill Hill, my work was appreciated and this was a source of tremendous satisfaction for me, inasmuch as this recognition came from scientists of such caliber. I learned much in those 2 1/2 years, not only technical expertise but also the philosophy of research and a systematic approach to scientific investigations. These years of instruction (1950-1952) were decisive in providing inspiration, training, and laboratory discipline and profoundly influenced the course of my career. In fact, it was at NIMR, Mill Hill where I endured my “baptism of fire” in medical research and became addicted to it. In May, 1952, I moved to Montreal, Canada where I was given the opportunity to work and study at McGill University. There I learned endocrinology from the brilliant lectures by Professor D. L. Thomson and from my work with Dr. M. Saffran in the laboratory of experimental therapeutics of the Allan Memorial Institute of Psychiatry headed by Dr. R. A. Cleghorn. The work at this laboratory was devoted to ACTH and adrenal cortical steroids. That period marked the beginning of my interest in the relationship between brain function and endocrine activity, and it was there in 1954 that my involvement in the hypothalamic field began.  In 1955, using *in vitro* systems, Dr. M. Saffran and I demonstrated the presence of corticotropin releasing factor (CRF) in hypothalamic and neurohypophysial tissue. This was the first experimental proof of the existence of hypothalamic hormones regulating pituitary function postulated with prophetic insight by Dr. G. W. Harris. I obtained my doctorate at McGill University in May, 1957, and in September of the same year I was able to secure a position which enabled me to continue my work on CRF at Baylor University College of Medicine in Houston, Texas, where I was associated with Dr. [R. Guillemin](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1977/index.html). My years in Houston (1957-1962) where I was Assistant Professor of Physiology and a Senior Research Fellow of the U.S. Public Health Service were discouraging and frustrating because of problems with the isolation of CRF. Our failure to obtain enough CRF to determine its structure tended to cast doubt on the initial findings. We encountered much skepticism, but I remained unshaken in my confidence in the correctness of the observations on CRF and in the postulation of other hypothalamic hormones regulating anterior pituitary function.  In 1961 I spent about one month at the Institute of Biochemistry in Uppsala with Dr. J. Porath where I gained useful experience in the use of Sephadex and column electrophoresis. I also visited Dr. V. Mutt and the late Professor E. Jorpes in Stockholm, in connection with our collaboration on gastrointestinal hormones, and I was encouraged that they and other astute scientists had confidence in our work and the foresight to appreciate the possible scientific and medical importance of hypothalamic hormones.  I was grateful for the opportunities I was given in the United States, for which I felt a complete allegiance, and in 1962 became a naturalized citizen. When Dr. Joe Meyer, then head of the Veterans Administration (VA) basic research, offered in June, 1962, to set up a VA laboratory devoted to research on the hypothalamus and make me its chief, I accepted since this gave me a clear opportunity to be in complete command of such an effort. The support of a number of individuals, including Dr. E. H. Bresler, then Associate Chief of Staff for Research of the New Orleans VA Hospital, Dr. C. Y. Bowers and Dr. G. Burch of the Department of Medicine of Tulane University School of Medicine, and Dr. W. Locke of the Ochsner Foundation Hospital, was instrumental in helping me establish the laboratory in New Orleans. In December of 1962, I was appointed Chief of the Endocrine and Polypeptide Laboratories at the VA Hospital in New Orleans and Associate Professor of Medicine at Tulane University, and, in 1966, Professor. The earliest members of our 1962 VA-Tulane team were T. W. Redding, W. H. Carter, and M. Tanaka. They have stayed with me all these years, and without their devoted help we could not have resolved the many problems associated with our work on TRH in 1969, LH-RH in 1971, and porcine somatostatin in 1975. Working in a clinical environment, I became more aware of the need for better diagnosis and treatment of patients than I had been before. It occurred to me early that problems with infertility on the one hand and the necessity for population control on the other would make a breakthrough in the control of reproduction particularly desirable from the standpoint of society, and therefore I became especially interested in reproductive endocrinology. To broaden our knowledge of reproductive processes at the brain level, we studied the central effects of contraceptive steroids and clomiphene. In some of the early studies on LH-RH, before its isolation, we collaborated with one of the pioneers of the hypothalamus and the man I always admired deeply, Professor C. H. (Tom) Sawyer and also with Drs. J. Hilliard, D. Holtkamp, A. Parlow and W. F. White.  It was my good fortune that in 1964 Dr. A. J. Kastin and in 1965 Dr. A. Arimura came to join our laboratory. Dr. Abba Kastin was mainly interested in continuing his work on control of release of MSH and in helping us in clinical work on hypothalamic hormones. He quickly became my best friend and a most efficient collaborator. Dr. Akira Arimura was an experienced physiologist and endocrinologist. Because of his great knowledge, enthusiasm and very hard work, he made great contributions in all phases of our program, and also broadened it with many independent ideas, especially in immunology. Other excellent collaborators at that time included Drs. I. Ishida, A. Kuroshima, T. Saito, and S. Sawano from Japan, and Dr. E. E. Muller from Italy.  All during the period since 1962, I had been hard at work on TRH with Cy Bowers and Tom Redding. In 1966, we reported for the first time the isolation of porcine TRH and determined that it contained three amino acids (glutamic acid, histidine, and proline) in equimolar ratio, but did not take full advantage of this original early finding, as we were preoccupied with parallel studies on reproduction and growth hormone-releasing hormone (GH-RH). However, when R. Burgus and R. Guillemin announced at the 1969 Tucson, Arizona, conference that they also found the same three amino acids in ovine TRH, I realized that we had the right substance. The same year I established the correct amino acid sequence of porcine TRH with Dr. R. M. G. Nair in New Orleans. Subsequently, with help from Drs. F. Enzmann and J. Bøler working in K. Folkers laboratory in Austin, Texas, we were able to determine the structure of porcine TRH and synthesize it. We have shared the credit with R. Burgus, W. Vale and R. Guillemin, who elucidated the structure of ovine TRH at about the same time.  The identification of TRH removed the skepticism surrounding the work on the hypothalamus and I realized that many workers would now be attracted to the field. We therefore redoubled our efforts on LH-RH.  In 1965, in Mexico City, I met Dr. C. Gual of the National Institute of Nutrition who invited me to collaborate with him in the clinical testing of hypothalamic hormones in Mexico. We took advantage of this invitation and in 1968 demonstrated, with Cy Bowers, that preparations of natural TRH are active in humans. Subsequently, again in collaboration with Carlos Gual, Abba Kastin and I established that highly purified porcine LH-RH unequivocally released LH and FSH in men and women under a variety of conditions. It was clear that LH-RH might be useful clinically and this encouraged us to continue the agonizing effort involved in the isolation of this hormone. Although I consider myself an endocrinologist or neuroendocrinologist, with considerable interest in clinical endocrine research and not a biochemist, I personally carried out the isolation work on TRH, LH-RH, somatostatin, and other hormones. Only a person such as myself with strong faith in the presence of these materials would have the patience to go through the many fastidious steps of the isolation procedure, since the effort required in isolating exceedingly small quantities of gradually purer and purer materials from a crude hypothalamic exctract is so enormous. I was able to isolate a small amount (800 µg) of LH-RH from 160,000 hypothalami and proved it to be a polypeptide. This tiny amount of material was passed to our chemists, Dr. H. Matsuo and Dr. Y. Baba, with suggestions for a structural approach. Since I did not think that amounts of LH-RH on hand would be enough to complete our structural work, I decided to isolate additional amounts of LH-RH. Drs. Matsuo and Baba worked hard and efficiently, and we were able to determine the complete structure of LH-RH with the 800 µg material. After confirming the structure by synthesis, we were in a position to present our findings at the Endocrine Society meeting in San Francisco, California, in June 1971. It was one of the high points in my life to be able to report for the first time the solution to the problem which had preoccupied me and others for so long.  Physiological and subsequently immunological studies with natural and synthetic LH-RH in our laboratory by Drs. A. Arimura, L. Debeljuk, J. Reeves and M. Saito, and with others demonstrated that LH-RH was indeed the physiological hormone. With the synthetic LH-RH readily available, Dr. Kastin and I continued to carry out a variety of clinical studies in Mexico in association with Dr. Gual and later with Drs. A. Zarate and D. Gonzalez-Barcena. I also did parallel clinical tests with Dr. J. Zanartu in Chile and in Argentina with Drs. L. Schwarzstein, N. Aparicio, and the late R. Mancini.  The importance of analogs, particularly with respect to the possibility of developing a new birth control method was uppermost in my mind. I was very fortunate in being able to induce Dr. D. H. Coy, a superb peptide chemist and his wife Esther, also a researcher, to join our laboratory in 1972. More than 300 analogs of LH-RH were synthesized by the Coys with the help of Drs. Y. Hirotsu, K. Nikolics and J. Seprödi in our laboratory between 1972 and 1977. We were particularly interested in stimulatory long-acting superactive analogs for clinical use and in inhibitory analogs which would block LH and FSH release. We were joined in this important work by researchers from many countries. The work of Drs. J. Vilchez from Venezuela, A. de la Cruz from Peru, E. Pedroza from Colombia, and N. Nishi from Japan established in 1976 that the antagonists of LH-RH can indeed completely block ovulation in animals. Very recently with Dr. D. Gonzalez-Barcena in Mexico we showed that these analogs are also active in humans. This of course raises the possibility that such analogs could eventually form the basis of a new birth control method. However, much work is still needed to make my dream of being able to control reproduction at the central level come true.  In 1971, immediately after solving the LH-RH problem, I decided to reinforce our attacks on PIF and GH-RF next, but six years of hard work with Dr. A. Arimura and Drs. J. Sandow from Germany, A. Dupont from Canada and J. Takahara from Japan resulted only in a demonstration that hypothalamic catecholamines and gamma-amino butyric acid (GABA) may be involved in the control of release of prolactin, but did not yet lead to the development of any clinical agents. In our preoccupation with PIF and GH-RH, we did not work on factors inhibiting growth hormone release but after P. Brazeau and collaborators in 1973 announced the isolation and structure of ovine somatostatin, we purified this hormone from porcine hypothalami, determined its structure and synthesized it. We also carried out much physiological and immunological work (some in collaboration with Dr. F. Labrie in Quebec, Canada), as well as clinical work which convinced us of its importance. Particularly important was the establishment of a radioimmunoassay for somatostatin by Dr. Arimura. The clinical work on somatostatin was carried out mainly in England. Brilliant clinicians Professor R. Hall from the Royal Victoria Infirmary in Newcastle-upon-Tyne and Professor G. M. Besser of St. Bartholomew’s Hospital in London were our leaders of two clinical teams which also included excellent collaborators such as Drs. A. Gomez-Pan, D. Evered, C. Mortimer, S. R. Bloom, and others. These clinical studies in England (based in part on some of our suggestions) showed that somatostatin inhibits the release of GH, TSH, glucagon, insulin, and gastrin. Basic studies carried out in England in collaboration Dr. A. Gomez-Pan and in Poland with Professor S. Konturek showed that somatostatin also inhibits gastric acid and pepsin secretion, and the release of duodenal hormones, secretin and cholecystokinin. Since the immunological work of Dr. Arimura showed the presence of somatostatin in the pancreas, stomach and intestine, we then suggested that this substance may be involved in the control of secretion not only of the pituitary, but also of the pancreas, stomach and duodenum. Since somatostatin has multiple short-lived effects, Drs. D. H. Coy and C. Meyers are achieving considerable success in the synthesis of long-acting and selective analogs of somatostatin, some of which could be more practical clinical agents.  Also among our present projects is the isolation of all the compounds with PIF activity, of PRH, GH-RH, CRF, and other hypothalamic substances. In addition to authoring or co-authoring many publications, I take satisfaction from the fact that I helped Dr. W. Locke write a book for clinical endocrinologists.  Since much work with hypothalamic hormones and their analogs is being carried out in Latin America and Spain, my ability to communicate in Spanish and Portuguese has aided me greatly, and resulted in the formation of many beautiful friendships. However, the greatest reward for learning Spanish and Portuguese came when, in 1974, in the course of my work in Brazil I met a very charming endocrinologist, Ana Maria de Medeiros-Comaru (M.D.). Our friendship soon deepened into love and led to our marriage.  I have had the satisfaction that my work in the hypothalamus was honored by top U.S., Canadian and Spanish awards: Van Meter Prize of the American Thyroid Association; Ayerst-Squibb Award of the U.S. Endocrine Society; William S. Middleton Award, the highest award of the VA; Charles Mickle Award of the University of Toronto; Gairdner Foundation International Award, Canada; Edward T. Tyler Award; Borden Award of the Association of American Medical Colleges; Albert Lasker Basic Medical Research Award, and the Laude Award, Spain. In 1973 I was made a Senior Medical Investigator by the Veterans Administration, an honor reserved for only a few. When I learned about my Nobel Prize, I was too grateful and too moved to be overcome with joy, but that came a few hours later when my friends from all over the world began to phone or wire. However, I do not feel that these prizes will have an adverse effect on my future productivity. I am still as keen as ever to make new discoveries and useful contributions to endocrinology.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)*. The Nobel Prizes 1977*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1978  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1977 Addendum, April 2005 In the years 1972-1978, I developed agonistic analogs of LH-RH (also called GnRH) and in 1981 was the first to show that they inhibit growth of prostate cancer in rats. On this basis, I organized with Dr. George Tolis the first clinical trial with LH-RH agonists in patients with advanced prostate cancer in 1982. This trial demonstrated the clinical efficacy of LH-RH agonists in palliative treatment of androgen-dependent prostate cancer. I then helped develop sustained delivery systems (microcapsules) for agonists of LH-RH and participated in evaluations of their efficacy. Sustained delivery systems of various LH-RH agonists (microcapsules or implants) now provide the preferred method for the treatment of advanced prostate carcinoma. Previous primary endocrine treatment modalities for advanced adenocarcinoma of the prostate based on the work of [Charles Huggins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1966/index.html) (Nobel Prize in Medicine for 1966), used since the 1930s, included orchiectomy or administration of estrogens (DBS). However, surgical castration (bilateral orchiectomy) is associated with psychological impact and estrogens such as DES have serious cardiovascular, hepatic and mammotropic side effects. Treatment with LH-RH agonists is as effective as orchiectomy and offers the advantage of avoiding castration. The therapy with agonists of LH-RH is presently the preferred method of treatment for men with advanced prostate cancer and in about 70% of cases, LH-RH agonists are selected for primary treatment.  I helped Prof. R. Hall and Prof. M. Besser in the first clinical evaluations of somatostatin in normal subjects and patients with neuroendocrine tumors in England and I was profoundly influenced by its effects. Based on this experience, I became one of the pioneers in the development of analogs of somatostatin for oncological uses and demonstrated their antitumor activity in animal models of various tumors. I have been credited with influencing the thinking in the field of oncological applications of somatostatin. Analogs of somatostatin are used now for treatment of acromegaly and endocrine tumors, including carcinoid tumors. The fact that few relevant clinical benefits have been obtained in patients with pancreatic, colorectal, prostatic, breast and other cancers treated with somatostatin analogs is due to a low expression of SST receptor subtypes 2 and 5 in these malignancies that preferentially bind octapeptide somatostatin analogs. However, the expression of these subtypes should be high enough to permit therapy with targeted cytotoxic somatostatin analogs synthesized by my group or somatostatin analogs labeled with various radionuclides developed in the meantime in Europe. Radiolabelled somatostatin analogs pioneered in Holland are now extensively used for tumor localization. Among my other major accomplishments is the development of antagonistic analogs of LH-RH, the demonstration of their antitumor activity in experimental cancer models and with my associates of clinical efficacy of these antagonists in patients with prostate cancer, endometriosis and leiomyomas. My late wife Ana Maria Comaru-Schally also showed that antagonists of LH-RH could be used as a therapy for benign prostatic hyperplasia (BPH).  My group demonstrated that the receptors for LH-RH, somatostatin and bombesin are present in various tumors, including human prostatic, mammary, endometrial and ovarian cancers. Based on this demonstration of receptors for peptides in various tumors, I started in 1995 the development of modern cytotoxic analogs of LH-RH, bombesin and somatostatin, which can be targeted to peptide receptors on various primary cancers and their metastases. We demonstrated in experimental models of human cancers that these hybrids produce tumor regression or eradication. Because the receptors for these peptides are present on many cancers, targeted chemotherapy based on cytotoxic analogs of these peptides should be more efficacious and less toxic than the currently used systemic chemotherapeutic regimens and might permit dose escalation. My group also developed bombesin antagonists aimed at decreasing EGF receptor levels in tumors and growth hormone-releasing hormone (GH-RH) antagonists, which suppress IGF-I and -II levels and block tumoral receptors for GH-RH and showed that they inhibit a variety of experimental cancers, including androgen-independent prostate cancers, estrogen independent breast cancers, ductal pancreatic cancers, colorectal cancers, lung cancers and brain tumors. My associates and I also demonstrated that GH-RH, which we found in mammary, ovarian, endometrial lung cancers and other tumors, is probably an autocrine growth factor. Our work suggests that cytotoxic somatostatin analog AN-238, cytotoxic LH-RH analogs AN-152 or AN-207 and GH-RH antagonists could be used in the management of patients with advanced prostatic carcinoma who relapsed androgen ablation. Cytotoxic LH-RH analogs or GH-RH antagonists might also be considered for improvement of primary hormonal therapy for prostate cancer.  In September 2004, my wife Ana Maria Comaru-Schally, M.D., F.A.C.P. died suddenly from thyroid cancer. I was profoundly hurt by the unexpected passing of my wife after 28 years of wonderful marriage, which was preceded by 2 years of an exciting and emotional romance. She was an ideal wife, companion, collaborator and my best friend. She will be sorely missed by me and many friends in various countries. Her death was the hardest blow and the biggest tragedy in my life. I am seeking consolation and comfort by continuing my work in cancer research. I believe that this is what she would want me to do.  In conclusion, since receiving the Nobel Prize, I developed the preferred method for treatment of advanced prostate cancer based on LH-RH agonists. My group synthesized several new classes of antitumor peptides such as LH-RH antagonists, somatostatin analogs, bombesin/GRP antagonists, GH-RH antagonists and targeted cytotoxic analogs of LH-RH, bombesin and somatostatin. I then proposed, and with my associates experimentally demonstrated, the efficacy of new approaches to therapy of prostatic, mammary, ovarian, endometrial, renal, pancreatic, colorectal, gastric and lung cancer (SCLC and non-SCLC), osteosarcomas, melanomas, non-Hodgkin’s lymphomas and brain tumors based on these antitumor peptides.  I have been credited with extending the concepts of hormone-dependent tumors beyond the pioneering work of the great Charles Huggins. Hormonal therapies that I proposed are based on the peptide analogs of hypothalamic and other hormones and are relatively free of side effects, in contrast to radiation and chemotherapy. I am gratified that my discoveries have led to many practical clinical applications that are widely used and highly effective. It is my hope that the significance of these discoveries and their applications to oncology will increase in the future.  I now have over 2200 publications, more than 1200 of which were published after I received the Nobel Prize. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
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| ID | **0611** |
| Biographical | I was born on July 19, 1921 in New York City and have always resided and worked there except for 3 1/2 years when I was a graduate student at the University of Illinois.  Perhaps the earliest memories I have are of being a stubborn, determined child. Through the years my mother has told me that it was fortunate that I chose to do acceptable things, for if I had chosen otherwise no one could have deflected me from my path.  My mother, née Clara Zipper, came to America from Germany at the age of four. My father, Simon Sussman, was born on the Lower East Side of New York, the Melting Pot for Eastern European immigrants. Neither had the advantage of a high school education but there was never a doubt that their two children would make it through college. I was an early reader, reading even before kindergarten, and since we did not have books in my home, my older brother, Alexander, was responsible for our trip every week to the Public Library to exchange books already read for new ones to be read.  By seventh grade I was committed to mathematics. A great chemistry teacher at Walton High School, Mr. Mondzak, excited my interest in chemistry, but when I went to Hunter, the college for women in New York City’s college system (now the City University of New York), my interest was diverted to physics especially by Professors Herbert N. Otis and Duane Roller. In the late ’30’s when I was in college, physics, and in particular nuclear physics, was the most exciting field in the world. It seemed as if every major experiment brought a Nobel Prize. Eve Curie had just published the biography of her mother, Madame [Marie Curie](https://www.nobelprize.org/nobel_prizes/physics/laureates/1903/index.html), which should be a must on the reading list of every young aspiring female scientist. As a Junior at college, I was hanging from the rafters in Room 301 of Pupin Laboratories (a physics lecture room at Columbia University) when [Enrico Fermi](https://www.nobelprize.org/nobel_prizes/physics/laureates/1953/index.html) gave a colloquium in January 1939 on the newly discovered nuclear fission – which has resulted not only in the terror and threat of nuclear warfare but also in the ready availability of radioisotopes for medical investigation and in hosts of other peaceful applications.  I was excited about achieving a career in physics. My family, being more practical, thought the most desirable position for me would be as an elementary school teacher. Furthermore, it seemed most unlikely that good graduate schools would accept and offer financial support for a woman in physics. However my physics professors encouraged me and I persisted. As I entered the last half of my senior year at Hunter in September 1940 I was offered what seemed like a good opportunity. Since I could type, another of my physics professors, Dr. Jerrold Zacharias, now at Massachusetts Institute of Technology, obtained a part time position for me as a secretary to Dr. Rudolf Schoenheimer, a leading biochemist at Columbia University’s College of Physicians and Surgeons (P&S). This position was supposed to provide an entrée for me into graduate courses, via the backdoor, but I had to agree to take stenography. On my graduation from Hunter in January 1941, I went to business school. Fortunately I did not stay there too long. In mid-February I received an offer of a teaching assistantship in physics at the University of Illinois, the most prestigious of the schools to which I had applied. It was an achievement beyond belief. I tore up my stenography books, stayed on as secretary until June and during the summer took two tuition-free physics courses under government auspices at New York University.  In September I went to Champaign-Urbana, the home of the University of Illinois. At the first meeting of the Faculty of the College of Engineering I discovered I was the only woman among its 400 members. The Dean of the Faculty congratulated me on my achievement and told me I was the first woman there since 1917. It is evident that the draft of young men into the armed forces, even prior to American entry into the World War, had made possible my entrance into graduate school.  On the first day of graduate school I met Aaron Yalow, who was also beginning graduate study in physics at Illinois and who in 1943 was to become my husband. The first year was not easy. From junior high school through Hunter College, I had never had boys in my classes, except for a thermodynamics course which I took at City College at night and the two summer courses at NYU. Hunter had offered a physics major for the first time in September 1940 when I was an upper senior. As a result my course work in physics had been minimal for a major – less than that of the other first year graduate students. Therefore at Illinois I sat in on two undergraduate courses without credit, took three graduate courses and was a half-time assistant teaching the freshman course in physics. Like nearly all first-year teaching assistants, I had never taught before – but unlike the others I also undertook to observe in the classroom of a young instructor with an excellent reputation so that I could learn how it should be done.  It was a busy time. I was delighted to receive a straight A in two of the courses, an A in the lecture half of the course in Optics and an A- in its laboratory. The Chairman of the Physics Department, looking at this record, could only say “That A- confirms that women do not do well at laboratory work”. But I was no longer a stubborn, determined child, but rather a stubborn, determined graduate student. The hard work and subtle discrimination were of no moment.  Pearl Harbor on December 7, 1941 brought our country into the war. The Physics Department was becoming decimated by loss of junior and senior faculty to secret scientific work elsewhere. The campus was filled with young Army and Navy students sent to the campus by their respective Services for training. There was a heavy teaching load, graduate courses, an experimental thesis requiring long hours in the laboratory, marriage in 1943, war-time housekeeping with its shortages and rationing, and in January 1945 a Ph.D. in Nuclear Physics. My thesis director was Dr. Maurice Goldhaber, later to become Director of Brookhaven National Laboratories. Support and encouragement came from the Goldhabers. Dr. Gertrude Goldhaber, his wife, was a distinguished physicist in her own right, but with no University position because of nepotism rules. Since my research was in nuclear physics I became skilled in making and using apparatus for the measurement of radioactive substances. The war was continuing. I returned to New York without my husband in January 1945 since completion of his thesis was delayed and I accepted a position as assistant engineer at Federal Telecommunications Laboratory, a research laboratory for ITT – the only woman engineer. When the research group in which I was working left New York in 1946, I returned to Hunter College to teach physics, not to women but to returning veterans in a preengineering program.  My husband had come to New York in September 1945. We established our home in an apartment in Manhattan, then in a small house in the Bronx. It and a full-time teaching position at Hunter were hardly enough to occupy my time fully. By this time my husband was in Medical Physics at Montefiore Hospital in the Bronx. Through him I met Dr. Edith Quimby, a leading medical physicist at P&S. I volunteered to work in her laboratory to gain research experience in the medical applications of radioisotopes. She took me to see “The Chief”, Dr. G. Failla, Dean of American medical physicists. After talking to me for a while, he picked up the phone, dialed, and I heard him say “Bernie, if you want to set up a radioisotope service, I have someone here you must hire.” Dr. Bernard Roswit, Chief of the Radiotherapy Service at the Bronx Veterans Administration Hospital and I appeared to have no choice; Dr. Failla had spoken.  I joined the Bronx VA as a part time consultant in December 1947, keeping my position at Hunter until the Spring Semester of 1950. During those years while I was teaching full-time, I equipped and developed the Radioisotope Service and started research projects together with Dr. Roswit and other physicians in the hospital in a number of clinical fields. Though we started with nothing more than a janitor’s closet and a small grant to Dr. Roswit from a veterans’ group, eight publications in different areas of clinical investigation resulted from this early work. The VA wisely made a commitment to set up Radioisotope Services in several of its hospitals around the country because of its appreciation that this was a new field in which research had to proceed pari passu with clinical application. Our hospital Radioisotope Service was one of the first supported under this plan.  In January 1950 I chose to leave teaching and join the VA full time. That Spring when he was completing his residency in internal medicine at the Bronx VA, Dr. Solomon A. Berson and I met and in July he joined our Service. Thus was to begin a 22 year partnership that lasted until the day of his death, April 11, 1972. Unfortunately, he did not survive to share the Nobel Prize with me as he would have had he lived.  During that period Aaron and I had two children, Benjamin and Elanna. We bought a house in Riverdale, less than a mile from the VA. With sleep-in help until our son was 9, and part-time help of decreasing time thereafter, we managed to keep the house going and took pride in our growing children: Benjamin, now 25, is a systems programmer at the CUNY Computer Center; Elanna, now 23, is a third year doctoral candidate in Educational Psychology at Stanford University. She has just married Daniel Webb and is with us on part of her honeymoon.  But to return to the scientific aspects of my life, after Sol joined our Service, I soon gave up collaborative work with others and concentrated on our joint researches. Our first investigations together were in the application of radioisotopes in blood volume determination, clinical diagnosis of thyroid diseases and the kinetics of iodine metabolism. We extended these techniques to studies of the distribution of globin, which had been suggested for use as a plasma expander, and of serum proteins. It seemed obvious to apply these methods to smaller peptides, i.e., the hormones. Insulin was the hormone most readily available in a highly purified form. We soon deduced from the retarded rate of disappearance of insulin from the circulation of insulin-treated subjects that all these patients develop antibodies to the animal insulins. In studying the reaction of insulin with antibodies, we appreciated that we had developed a tool with the potential for measuring circulating insulin. It took several more years of work to transform the concept into the reality of its practical application to the measurement of plasma insulin in man. Thus the era of radioimmunoassay (RIA) can be said to have begun in 1959. RIA is now used to measure hundreds of substances of biologic interest in thousands of laboratories in our country and abroad, even in scientifically less advanced lands.  It is of interest from this brief history that neither Sol nor I had the advantage of specialized post-doctoral training in investigation. We learned from and disciplined each other and were probably each other’s severest critic. I had the good fortune to learn medicine not in a formal medical school but directly from a master of physiology, anatomy and clinical medicine. This training was essential if I were to use my scientific background in areas in which I had no formal education.  Sol’s leaving the laboratory in 1968 to assume the Chairmanship of the Department of Medicine at the Mount Sinai School of Medicine and his premature death 4 years later were a great loss to investigative medicine. At my request the laboratory which we shared has been designated the Solomon A. Berson Research Laboratory so that his name will continue to be on my papers as long as I publish and so that his contributions to our Service will be memoralized. At present my major collaborator is a young, talented physician, Dr. Eugene Straus, who joined me in 1972, first as a Fellow, then as Research Associate and now as Clinical Investigator.  Through the years Sol and I together, and now I alone, have enjoyed the time spent with the “professional children”, the young investigators who trained in our laboratory and who are now scattered throughout the world, many of whom are now leaders in clinical and investigative medicine. In the training in my laboratory the emphasis has been not only in learning our research techniques but also our philosophy. I have never aspired to have, nor do I now want, a laboratory or a cadre of investigators-in-training which is more extensive than I can personally interact with and supervise.  The laboratory since its inception has been supported solely by the Veterans Administration Medical Research Program and I acknowledge with gratitude its confidence in me and its encouragement through the years. My hospital is now affiliated with The Mount Sinai School of Medicine where I hold the title of Distinguished Service Professor. I am a member of the National Academy of Sciences. Honors which I have received include, among others: Albert Lasker Basic Medical Research Award; A. Cressy Morrison Award in Natural Sciences of the N.Y. Academy of Sciences; Scientific Achievement Award of the American Medical Association; Koch Award of the Endocrine Society; Gairdner Foundation International Award; American College of Physicians Award for distinguished contributions in science as related to medicine; Eli Lilly Award of the American Diabetes Association; First William S. Middleton Medical Research Award of the VA and five honorary doctorates. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0611** |
| Interview |  |
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| Biographical | I was born in 1925, in New York City, the second of three children of Meyer and Ida Blumberg. My grandparents came to the United States from Europe at the end of the 19th century. They were members of an immigrant group who had enormous confidence in the possibilities of their adopted country. I received my elementary education at the Yeshiva of Flatbush, a Hebrew parochial school, and, at an early age, in addition to a rigorous secular education, learned the Hebrew Testament in the original language. We spent many hours on the rabbinic commentaries on the Bible and were immersed in the existential reasoning of the Talmud at an age when we could hardly have realized its impact.  After attending Far Rockaway High School I joined the U.S. Navy in 1943 and finished college under military auspices. I was commissioned as a Deck Officer, served on landing ships, and was the commanding officer of one of these when I left active duty in 1946. My interest in the sea remained. In later years I made several trips as a merchant seaman, held a ticket as a Ships Surgeon, and, while in medical school, occasionally served as a semiprofessional hand on sailing ships. Sea experience placed a great emphasis on detailed problem solving, on extensive planning before action, and on the arrangement of alternate methods to effect an end. These techniques have application in certain kinds of research, particularly in the execution of field studies.  My undergraduate degree in Physics was taken at Union College in upstate New York, and in 1946 I began graduate work in mathematics at Columbia University. My father, who was a lawyer, suggested that I should go to medical school, and I entered The College of Physicians and Surgeons of Columbia University in 1947. I enjoyed my four years at the College immensely. Robert Loeb was the chairman of the Department of Medicine and exerted a marked influence on the entire college. There was a strong emphasis on basic science and research in the first two years (we hardly saw a patient till our third year), and we learned practical applications only in our last years.  Between my third and fourth years, Harold Brown, our professor of parasitology, arranged for me to spend several months at Moengo, an isolated mining town, accessible only by river, in the swamp and high bush country of northern Surinam. While there we delivered babies, performed clinical services, and undertook several public health surveys, including the first malaria survey done in that region. Different people had been imported into the country to serve as laborers in the sugar plantations, and they, along with the indigenous American Indians, provided a richly heterogeneous population. Hindus from India, Javanese, Africans (including the Djukas, descendants of rebelled slaves who resided in autonomous kingdoms in the interior), Chinese, and a smattering of Jews descended from 17th century migrants to the country from Brazil, lived side by side. Their responses to the many infectious agents in the environment were very different. We were particularly impressed with the enormous variation in the response to infection with *Wuchereria bancroftia* (the filariad which causes elephantiasis), and my first published research paper was on this topic. This experience was recalled in later years when I became interested in the study of inherited variation in susceptibility to disease. Nature operates in a bold and dramatic manner in the tropics. Biological effects are profound and tragic. The manifestations of important variables may often be readily seen and measured, and the rewards to health in terms of prevention or treatment of disease can be great. As a consequence, much of our field work has been done in tropical countries.  I was an intern and assistant resident on the First (Columbia) Division at Bellevue Hospital in lower New York from 1951 to 1953. It is difficult to explain the fascination of Bellevue. In the days before widespread health insurance, many of the city’s poor were hospitalized at Bellevue, including many formerly middle class people impoverished by the expenses of chronic illness. The wards were crowded, often with beds in the halls. Scenes on the wards were sometimes reminiscent of Hogarth’s woodcuts of the public institutions of 18th century London. Despite this, morale was high. We took great pride that the hospital was never closed; any sick person whose illness warranted hospitalization was admitted, even though all the regular bed spaces were filled. A high scientific and academic standard was maintained. Our director, [Dickinson W. Richards](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html), and his colleague, [André F. Cournand](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html), received the Nobel Prize for their work on cardio-pulmonary physiology. Anyone who has been immersed in the world of a busy city hospital, a world of wretched lives, of hope destroyed by devastating illness, cannot easily forget that an objective of big-medical research is, in the end, the prevention and cure of disease.  I spent the following two years as a Clinical Fellow in Medicine at Columbia Presbyterian Medical Center working in the Arthritis Division under Dr. Charles A. Ragan. I also did experimental work on the physical biochemistry of hyaluronic acid with Dr. Karl Meyer. From 1955 to 1957, I was a graduate student at the Department of Biochemistry at Oxford University, England, and a member of Balliol College. I did my Ph.D. thesis with Alexander G. Ogston on the physical and biochemical characteristics of hyaluronic acid. Professor Ogston’s remarkable combination of theory and experiment guided the scientific activity in his laboratory. He has served as a model to me on how to train students; I hope I have measured up to his standard. [Sir Hans Krebs](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1953/index.html) was the chairman of the Department of Biochemistry. I have profited by conversations with him, particularly when (in 1972) I was a visiting fellow at Trinity College and we had opportunities to discuss our mutual interests in the history of science.  Oxford science at that time was influenced by the 19th and 20th century British and European naturalists, scientists and explorers who went to the world of nature – often to distant parts of it – to make the observations which generated their hypotheses. Anthony C. Allison was then working in the Department of Biochemistry and introduced me to the concept of polymorphism, a term introduced by the lepidopterist E. B. Ford of the Department of Zoology. In 1957 I took my first West African trip (to Nigeria) and was introduced to the special excitement of that part of the world. I found the Nigerians warmhearted and friendly with a spontaneous approach to life. We collected blood specimens from several populations (including the nomadic pastoral Fulani and their domestic animals) and studied inherited polymorphisms of the serum proteins of milk and of hemoglobin. This approach was continued in many subsequent field trips, and it eventually led to the discovery of several new polymorphisms and, in due course, the hepatitis B virus.  I worked at the National Institutes of Health from 1957 until 1964. This was during a period of rapid growth for the NIH, and I continued to develop my research on polymorphisms and their relation to disease. This led to the formation of the Section on Geographic Medicine and Genetics, which was eventually assigned to an epidemiology branch directed by Thomas Dublin, from whom I learned the methods of epidemiology. The NIH was a very exciting place, with stimulating colleagues including J. Edward Rall, Jacob Robbins, J. Carl Robinson, Kenneth Warren, Seymour Geisser, and many others. The most important connection I made, however, was with W. Thomas London (who later came to The Institute for Cancer Research), who has become a colleague, collaborator, and good friend with whom I have worked closely for fifteen years. Tom was an essential contributor to the work on Australia antigen and hepatitis B, and without him it could not have been done.  I came to The Institute for Cancer Research in 1964 to start a program in clinical research. The Institute was, and is, a remarkable research organization. Our director, Timothy R. Talbot, Jr., has a deep respect for basic research and a commitment to the independence of the investigators. Above all, people are considered an end in themselves, and the misuse of staff to serve some abstract goal is not tolerated. Jack Schultz was a leading intellectual force in the Institute, and his foresighted, humane view of science, his honesty and his good sense influenced the activities of all of us. Another important characteristic is the dedication and intelligence of our administrative and maintenance staffs, which contributes to the strong sense of community which pervades our Institute.  Over the course of the next few years we built up a group of investigators from various disciplines and from many countries (Finland, France, Italy, Poland, Venezuela, England, India, Korea, China, Thailand, Singapore) who, taken together, did the work on Australia antigen. Alton I. Sutnick (now Dean of the Medical College of Pennsylvania) was responsible for much of the clinical work at Jeanes Hospital. Some of the early workers included Irving Millman, Betty Jane Gerstley, Liisa Prehn, Alberto Vierucci, Scott Mazzur, Barbara Werner, Cyril Levene, Veronica Coyne, Anna O’Connell, Edward Lustbader, and others. There were many field trips during this period to the Philippines, India, Japan, Canada, Scandinavia, Australia, and Africa. It has been an exciting and pleasant experience surrounded by stimulating and friendly colleagues.  At present, we are conducting field work in Senegal and Mali, West Africa, in collaboration with Professor Payet of Paris, formerly the Dean of the Medical School of Dakar, with Professor Sankalé, his successor in Dakar, and a group of other French and Sengalese colleagues, including Drs. Larouzé and Saimot.  I am Professor of Medicine at the University of Pennsylvania and attend ward rounds with house staff and medical students. I am also a Professor of Anthropology and have taught Medical Anthropology for eight years. I have learned a great deal from my students.  My non-scientific interests are primarily in the out-of-doors. I have been a middle distance runner (very non-competitive) for many years and also play squash. We canoe on the many nearby lakes and rivers of Pennsylvania and New Jersey. I enjoy mountain walking and have hiked in many parts of the world on field trips. With several friends we own a farm in western Maryland which supplies beef for the local market. Shoveling manure for a day is an excellent counterbalance to intellectual work.  My wife, Jean, is an artist who has recently become interested in print making. We have four children of whom I am very proud: Anne, George, Jane, and Noah. They are all individualists, which makes for a turbulent and noisy household, still we miss the two oldest who are now away at college. We live in the center of old Philadelphia, a few blocks from Independence Hall. The city has appreciated its recognition by the Nobel Award in our Bicentennial Year.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1976*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1977  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1976 Addendum, August 2006 The editors of the Nobelprize.org website of the Nobel Foundation have asked me to provide a supplement to the autobiography that I wrote in 1976 and to recount the events that happened after the award. Much of what I will have to say relates to the scientific developments since the last essay. These are described in greater detail in a scientific memoir first published in 2002 (Blumberg, B. S., Hepatitis B. *The Hunt for a Killer Virus*, Princeton University Press, 2002, 2004).  The Nobel award led to profound changes in my professional and personal life. There was some excitement in Philadelphia – a Nobel Prize had not been awarded to one of our citizens since 1972 and only two since then – but that soon quieted down. The most important effects had to do with our research. By 1976 there was general agreement on the identification of the hepatitis B virus (HBV) and the work on the molecular biology had started, much of it at the Fox Chase Cancer Center. The immunodiffusion test for detecting the virus was widely used to prevent the use of blood donations from carriers of HBV. This program became more effective with the introduction of the specific HBV radioimmunoassay we had invented, and improved further when more sensitive and convenient tests developed by other laboratories became available. Within a few years, post transfusion hepatitis due to HBV had been essentially eliminated in the United States and many other countries. This however did not completely solve the problem of post transfusion hepatitis and it became apparent that there was an additional blood borne virus that also caused post-transfusion hepatitis. This was referred to temporarily as the non-A, non-B virus until the hepatitis C virus was discovered in the mid-1980s and there was a second dramatic drop in post transfusion hepatitis. The tests for HBV and HCV are now used widely and post transfusion hepatitis is well controlled in most countries with good medical and public health facilities.  A major focus of our research at the time the prize was awarded was the etiological relation between HBV and primary cancer of the liver (hepatocellular carcinoma, HCC). As early as 1969 Bruce Smith and I had postulated that HBV was a cause of primary cancer of the liver. By the mid-1970s we were fully engaged in testing this model in Senegal in collaboration with Senegalese and French colleagues and other investigations were in progress in several laboratories in Asia and elsewhere (see below). A very important contribution was a prospective epidemiological study in Taiwan by Beasley and his colleagues. They determined that carriers of HBV had more than a 200 times higher risk of developing HCC than controls who were not carriers.  In the following sections I will describe what I believe to be the high points of the 30 years since the Nobel award.  China These findings precipitated what was probably the most important field trip of my life, a life that has included many field trips. In the mid-1970s I read an abstract of a paper presented at an international cancer congress held in Florence, Italy describing the epidemiology of cancer of the liver in China. The prevalences cited were extremely high; HCC was one of the most common cancers in the most populous country on the globe. Our earliest studies showed a high frequency of Australia antigen, the surface antigen of HBV, in Asians and Pacific Islanders. This combined with our invention of the vaccine, whose development by drug companies was just starting, made it clear that it was important to visit China to tell scientists and public health officials about HBV research and its practical applications, and to learn more about the situation in China. This would be of help, not only to the Chinese populations, but to those at risk of developing chronic liver disease and HCC worldwide.  Recall that this was at a time when the United States and the Peoples Republic of China did not have diplomatic relations. Contacts between the two countries had been few and sporadic. The US Ping Pong team had, unexpectedly, been invited to visit their colleagues in China from April 11th to 17th 1971. President and Mrs. Nixon had visited China February 21-27, 1974 but the US and China did not exchange Ambassadors and have regular diplomatic relations until January 1, 1979. In the interim, there was a Liaison Office; George H.W. Bush, later the President of the US, was the United States liaison in the mid-1970s. During this period there were occasional visits by scientific and other groups from the United States and elsewhere.  Beginning in the early 1970s we had contacted the Committee for Friendly Cooperation with China, a US Government related organization formed to facilitate scientific and cultural interactions between China and the United States. Through them I had been in contact with the Chinese Medical Association; letters were exchanged, but there was no further progress. Soon after the award of the Nobel Prize in 1976, I received an invitation from the Association to visit China as their guest for several weeks. I believe that the invitation was a consequence of the Prize and, in the view of my Chinese hosts, the status that it conferred. This was an early example of the advantages that accompanied the prize.  I flew first to Japan and met with my colleague Professor K. Nishioka. He told me that, in 1974, a deputation from China had come to Tokyo to learn the methods for detection of HBV. Later, while in China, I learned that Premier Chou En-lai had favored the introduction of these techniques against a prevailing political opposition that regarded any foreign technology as suspect. On 10.07.77 I flew to Peking (now Beijing ) from Tokyo and was greeted by representatives of the Chinese Medical Association and officials of the Communist party. The CMA was a non-governmental organization but there were always Party officials among those who formally greeted me at the several cities I visited. Thereupon followed a hectic visit traveling by car, train, crowded airplanes, and foot. I spoke to several thousand scientists at well attended lectures many lasting for three or more hours. I told them of the recent advances in HBV research, described the procedures in place for testing donor blood, and gave them a copy of our HBV vaccine patent and other information on the production and use of the vaccine. (At that time the Chinese did not respect patent protection.) I put them in contact with Merck & Company, Inc. whom we had licensed to produce the HBV vaccine, and they eventually arranged an exchange of technical information that allowed the Chinese to produce vaccine in-country. For years afterwards on my return visits to China and in speaking with the many Chinese scientists who came to study and work in the United States and Britain (where I lived between 1989 and 1994) they told me that they had heard me speak during the 1977 visit and that it had influenced their work. I believe, though of course it is difficult to be certain, that my visit accelerated the research on HBV and its application to testing and, in particular, in moving forward the vaccination program. If so, then the visit could have been responsible for saving many lives.  My strongest memories of the trip were not the intense scientific discussions I had with the many scientists and others I met, but rather the time that I spent walking or running by myself through the early morning streets of Peking (Beijing), Shanghai, Quilan, Canton (as it was then), and in rural locations. During the day and in the evening I was accompanied by a political guide and an eminent Chinese scientist, Dr. Sun Tsung-tang – himself a pioneer in hepatitis research – but no one seemed to mind when I arose early in the morning and ran for miles through the places we were visiting. A running, middle aged, bald American was not a common site in Tiananmen Square, or the other venues for my runs, but it allowed me to see the everyday life of the China of that time. The country was emerging from the great Cultural Revolution, and the “Gang of Four”, including Mao’s wife had only recently been deposed. There were few automobiles, the streets of Beijing were dominated by masses of bicycles, and government control was still very obvious. It was far different from contemporary China that I saw on visits more than 25 years later, a country that had vigorously entered the world’s industrial and information revolution.  The following year, 1978, I visited Taiwan. Research on HBV was already well advanced and testing of donor blood for HBV carriers was nearly universal. They were preparing for vaccination programs even though the vaccine was not yet tested or approved. I visited the blood bank and was impressed with the organization of their testing facilities and the quality of the data management for the donor blood testing. I asked what they did with the blood donor units that were positive for HBV; they told me that they were stored for a period and then disposed of. I suggested that they acquire deep freeze units, store the separated plasma and that, in time, when the production of vaccine began, they could be used as a source of the surface antigen that was used to make the vaccine. (The vaccine we had invented was made from the surface antigen particles of HBV found in great quantities in the blood of HBV carriers.) When I returned to Taiwan in June of 1986 I was invited to visit the Taipei Blood Donor center. My host told me that they had a new building since my last visit and that there were other new blood bank building elsewhere on the island. They had followed my suggestion, stored the sera of the carriers and sold it for the manufacture of vaccine! I was surprised to find my picture on the wall commemorating my earlier visit. As the years go by, I seem to be asked for advice on a wide variety of subjects but this was one of the rare times that it was actually followed.  Hepatocellular Carcinoma and West Africa As already noted, a major focus of our research in the mid-1970s had been on the relation of HBV to primary cancer of the liver. My laboratory was at the Fox Chase Cancer Center, an institution dedicated to the treatment, cure and prevention of cancer. When I started the research on blood polymorphisms, the Australia antigen, and later the hepatitis B virus, there was little evidence that it had any relation to cancer. Our Center emphasized basic research on the nature of the normal cell and on genetics with the expectation that this research, in turn, could lead to a better understanding of the cancer process. We were given wide latitude in our choice of research topics and they did not have to pass the test of relevance to cancer. However, in time, the sponsoring agencies for the research, primarily the National Cancer Institute of the National Institutes of Health, did want some reassurance that, eventually, the research would impact on the group of diseases that it was empowered to fund.  Primary cancer of the liver (HCC) is not common in the United States. Where should we do our research? We needed to study the problem in the field and in a location where there was both a high prevalence of HBV and of HCC, along with a felt concern in the population about the diseases that would stimulate interest and collaboration.  In 1972, while I was the Visiting Fellow in Oxford, Dr. Bernard Larouze, at that time at Hôpital Claude Bernardpital Claude Bernard*,* in Paris in the Department of Professor Maurice Payet came to visit me in my office at the Laboratory of Genetics (then headed by Professor Sir Walter Bodmer) in the Department of Biochemistry. He asked if I could collaborate with him, his Professor, and Senegalese scientists at the University of Dakar to work on hepatitis and HCC. We agreed and for the next twenty years our research group had an ongoing program in Senegal. I visited Senegal and Mali on several occasions and once again enjoyed the ambience of West African life. Our work contributed to the understanding of the etiological association of HBV with HCC and we helped to establish some of the criterion for a vaccination program. In particular, in a multiple year study in Thies, a provincial center to the east of Dakar, we showed that children were often infected by their HBV carrier mothers, probably at the time of birth or soon afterwards, but that the carrier state was not manifest until several months after birth. This provided an interval when vaccination could be effective. Interestingly, in Asia, the carrier state was detected much sooner after delivery than in Senegal, but even there the vaccine proved to be effective if administered at birth or soon thereafter. This suggested that the vaccine might protect even after infection but before the carrier state was established.  It was nothing short of providential that the vaccine was effective in newborns because, in time, when the vaccine became available in commercial quantities (more about this later) extensive vaccination programs could be launched that protected even the children of carrier mothers from the development later in life of chronic liver disease and primary cancer of the liver. This was one of the most gratifying consequences of all our research. At a meeting in Barcelona (05.07.90), Dr. P. Pasquini of the Instituto Superiore di Sanita in Rome thanked me for saving some 9000 lives per year in Italy and, if I recall correctly, specifically extended the thanks of tens of thousands of Italian women who could now have children without fear of transmitting HBV to them.  My colleague, Tom London, had the major role in the Senegal program and continued it for many years when I stepped down as the Principal Investigator of our group at FCCC in 1989. He and his colleagues undertook a large epidemiological study in Senegal and, at the same time, in coastal China. They made fundamental contributions to the understanding of the dynamics of viral carcinogenesis that will inform the prevention program, treatment, and the search for other viral-caused cancers.  Hepatitis B vaccine We invented (and the Fox Chase Cancer Center had patented) the vaccine for HBV in 1969, but it would take some time before we could interest a pharmaceutical company to help develop and produce it. Vaccines are not an attractive product for pharmaceutical companies in that they are often used once or only a few times and they ordinarily do not generate as much income as a medication for a chronic disease that must be used for many years. Also, the medical research community was, in the early 1970s, far from convinced that we had identified the virus and much less that we had produced a vaccine using a non-conventional method. However by the mid-1970s we reckoned that there was sufficient evidence for a concerted campaign to find a company that we could license. The National Institutes of Health, who had financed much of the research, retained the domestic rights to the patent but granted FCCC the foreign rights. Irving Millman, the co-inventor, and I sought an appropriate manufacturer. On 08.07.76, FCCC signed an agreement with Merck & Company, Inc., whose vaccine facilities were located near Philadelphia, to produce the vaccine using the novel method we had designed. The vaccine was made from small HBV surface antigen particles, made in the liver cells of the human host guided by the surface antigen gene introduced by the virus. This was a unique method for producing a vaccine that had never been attempted before.  The vitally important next step was the field testing of the vaccine. For a variety of reasons we had decided that we would not be directly involved in the testing of the vaccine. That task was undertaken by Dr. Wolf Szmuness and his colleagues at the New York Blood Bank. Ordinarily, vaccine field trials involve thousands or even hundreds of thousands of individuals; for example, 1.8 million people were involved in the testing of the Salk polio vaccine. Dr. Szmuness’s study required less than a thousand volunteers, but the results were convincing. He showed that the vaccine was highly effective – over 90% protection rate – and it appeared to have no deleterious side effects. He published his report in 1980; within a few years the vaccine was approved by the US Food and Drug Administration primarily based on his HBV vaccine trial. After some hesitation in its use because of the initial high cost, universal national vaccination programs became widespread.  Use of the vaccine was greatly increased after it was produced by the recombinant method by several companies in the US and elsewhere. This was the first widely used vaccine produced by the recombinant method and for many years it was the only one. By the turn of the millennium over a billion doses had been administered and, by May 2003, 151 (79%) of the 192 members countries of WHO had national vaccination programs. It is now one of the most widely used vaccines in the world. The prevalence of HBV carriers and cases has dropped dramatically in the impacted populations. To cite one example of many, in a study in China the prevalence of HBV carriers dropped from the pre-vaccination prevalence of 16.3% to 1.4% after the program had been in place for several years.  The vaccination program has also decreased the incidence of primary cancer of the liver. In a study in Taiwan, the incidence of HCC dropped by two thirds after the program had been in place for only a decade. HBV vaccine is the first “cancer vaccine”, that is, a vaccine that prevents cancer. HBV vaccination is second only to the smoking prevention campaigns as a cancer prevention program. The apparent success of the program has raised expectations that other virally caused cancers caused by cancers may be prevented. The second “cancer vaccine” – against Papilloma virus that causes many cases of cancer of the cervix – has been successfully tested and will probably be widely deployed within a few years. It is likely that many more vaccines to prevent cancer will become available in the future and, I hope, Fox Chase Cancer Center will take a major role in this program.  Plant studies In the late 1980s another project began to dominate the research in our laboratory. Would it be possible to devise a therapy for the millions of patients with HBV including many of the approximately 375 million HBV carriers in the world? The concept of rationale design for drug discovery was (and is) in vogue at this time; it is an approach that is based on a molecular understanding of the disease process and the identification of biochemical or biophysical processes of disease at which a medication could be designed to interfere to abort or eliminate the disease. However, most drugs in use have been derived from already existing “natural” chemicals found in plants or other biological material. I decided to look for a medication in the plants that had been used in indigenous medical systems – folk medicine – to see if any of these contained constituents that were anti-viral. My colleagues and I consulted the many texts on folk uses and made a list of all the plants that had been used to treat yellow jaundice, the most obvious symptom of hepatitis. Jaundice can be the result of many diseases, for example, hemoglobinopathies, but probably the most common cause worldwide would be viral, including HBV infection. This resulted in a list of over a thousand plant species. I then sorted the list by the country where the folk medicine was used and identified plant genera that were used on three or more continents or geographic regions. This decreased the number of candidate plants and we finally chose a small weedy plant, *Phyllanthus amarus* for further study*. Phyllanthus* species were widely used in India, China, elsewhere in Asia, South and North America, Africa, and in the Pacific for the folk treatment of jaundice. It was also selected because P.S. Venkateswaran, the natural products chemist in our laboratory had known of this plant in his youth. There were also other plants on the short list with which a more limited series of studies were done.  During the next five years or so we collected many of these plants in their native habitat. This resulted in some interesting field trips. I had already engaged in many trips during our research on the distribution of polymorphic traits and in the HBV studies. But this was different. Medical field research is usually done indoors, observing patients in hospitals and populations in villages, towns, and cities. Collecting plants meant that one was outdoors, in the field, forest and jungle; and I enjoyed that very much. There were collecting trips to India (including a fascinating few days in the jungles of the Western Ghats in Karnataka), Nepal (including a long trek in the Himalayas ), England, France, Ireland, Korea, Singapore, Taiwan, and Trinidad and Tobago. There were also extensive collections in the United States ; in California, Colorado, Florida, Hawaii, Louisiana, Maine, Maryland, Massachusetts, New Jersey, New York, Oregon, Pennsylvania, South Carolina, Texas, Vermont, Virginia, and Washington. I usually did these trips when I was traveling for other reasons, to attend meetings or consultations, in order to minimize travel costs.  This research required the establishment of a whole new range of activities in the laboratory. We added a natural products chemist, and a botanist, and developed a series of tests to determine if the medication had any effect on the replication mechanism of HBV. There were no established laboratory animals that could be infected with HBV nor was there then an adequate tissue culture system. However, woodchucks or groundhogs, (*Marmota monax*) are infected with woodchuck hepatitis virus (WHV) that is very similar to HBV. Hence, we developed skills for trapping and testing woodchucks and raising them in a laboratory setting, a very complicated and difficult operation.  Professor S.P. Thyagarajan at the University of Madras, India had done a controlled clinical trail on the effectiveness of *Phyllanthus amarus* on the HBV levels in carriers. We helped in the testing of the serum samples from the study and the analysis of the data. This first trial showed an impressive clinical effect. However, subsequent trials in other Asian locations did not confirm the results. We continued in our efforts to isolate the active principles and several other laboratories and commercial companies worldwide have continued research on the preclinical science. Although the plant continues to be used widely in India and elsewhere it has not (at least so far) resulted in a tested and widely used proprietary medication. Research continues and there may be one day another medication to add to the treatment of HBV and other viruses.  India In January of 1986 my wife Jean and I flew to Bangalore, India where, for the next three months, I served as the Raman Professor of the Indian Academy of Sciences at the Indian Institute of Sciences (IISc). We lived in the guest house on the campus of the IISc but I traveled extensively around India giving lectures, consulting with colleagues and collecting information with which to write a report on hepatitis control. India, as many visitors will tell you, is one of the most fascinating places the world. The contrasts were enormous; rural and urban illiteracy and poverty were widespread, but there were large numbers of well educated people and brilliant intellectual communities. I have rarely met such a large number of intelligent academics in one place as at the IISc and several of the other institutions where I was a guest. Bangalore was just beginning to become the center of the information revolution that has spread so rapidly over the world in the past decade.  On 01.20.86 I met with the Prime Minster, Rajiv Ghandi (who was tragically assassinated in 1991) and described my findings for the report that I prepared on the hepatitis problem. I was very impressed with his understanding of the problem and his interest in moving forward with it. In the report I made broad suggestions beyond the issue of vaccine production. I recommended the establishment of graduate level Schools of Public Health. India had several hundred conventional and traditional medical schools at the time but, I believe, only one school of Public health. The use of disposable needles is one of the most important measures to prevent the spread of HBV, HIV, HCV and other blood borne agents. At the time, there were no manufacturing facilities in India for this product and I recommended that they be established. I also commented on an upgrading of water supply in the large cities. Many water systems had been in place for decades without replacement and breaks in the water supply and waste disposal plumbing were common. Since they were sometimes laid near each other, cross contamination, with subsequent disease was common. I also recommended national testing for the prevalence of HBV that could be coupled with surveys for HIV that was then just beginning to spread in India. I also included recommendations on the manufacture of vaccine.  I submitted the report after my return to Philadelphia, and received an acknowledgement of its receipt. Did the report have any effect? It is difficult to know. However, some years later, several schools of public health were established. In 2002 the Hepatitis B Project was initiated in India with the support of the Global Fund for Vaccines and Immunization and, I understand, the vaccination program is accelerating. There are also voluntary programs to encourage vaccination. I became aware of these several years ago when Professor S.P. Singh, Head of the Department of Gastroenterology at SCB Medical College in Cuttack, India wrote to say that July 28, my birthday, would be the date for their annual Hepatitis B Eradication Day in their city. In 2006 it was extended to other parts of India.  Balliol College, Oxford 1989 brought with it a major change in the direction of my scientific career and our family life. I had been a graduate student in Biochemistry at Oxford University in 1955. At Oxford, students become members of one of the colleges; I was attached to Balliol College where my supervisor Alexander Ogston was a Fellow. The years we spent in England still at that time recovering from the economic, social, and psychological damages of World War II, were among the happiest of our married life. The College, possibly the oldest in Oxford, dates to 1263 when John de Balliol, along with his wife Dervorguilla of Galloway, founded the College. Dervorguilla continued his benefactions after his untimely death and gave our College its first code of Statutes, still retained in our archives, that differs remarkably little from the current code. Their son, also named John, was subsequently crowned King of Scotland and there has been a thread of attachment between the College and Scotland from early days.,  I retained a strong affection for Oxford and returned to the University on sabbatical leave in 1972 when I was a Visiting Fellow at Trinity College (of which my biochemistry mentor at Sandy Ogston had become the President), and again in 1983 as the Eastman Professor at Balliol. We had a wonderful time during these years. The Eastman Professorship provided a comfortable home well positioned adjacent to the Balliol cricket pitch and carried very few responsibilities. I gave a series of lectures on scientific process, attended nearly exclusively by members of my family, my squash partners, and fellow rowers. The Balliol graduate accommodation was near our house and we frequently entertained the eclectic bunch of students that made up the international, multi-disciplined, intelligent and very interesting group of young people. I organized the Balliol College Running Group and we hade several happy long distance competitions in the inevitable rain and gloom of an Oxford winter.  But that was not the end of our Oxford experience. In 1988, to my surprise, I was asked if my name could be put forward as a candidate to be the Master of Balliol. I readily agreed and, again to my surprise, was elected. Jean and I came to Balliol in September 17, 1989 to begin my term of office. I was somewhat disappointed that the Porter at the massive gates of the College did not know who I was nor where we were to stay. Despite, or perhaps because of, these initially humbling experiences our five years at Balliol were grand. We entered a world totally different from urban Philadelphia. It included, educational and administrative issues I had not before encountered, interacting with a lively student body and dedicated teaching and research Fellows, formal entertainments at our College and others, and meeting leaders in British and international politics, science, and society. Administering a College in which the Master had no power, but a great deal of influence, were all part of this exciting time.  Did I make much of an impact on the College and its future? It is hard to say. I introduced a “development” program that is an office to solicit funds from alumni, foundations, companies, and others. This form of educational support had not been common in Oxford and Balliol was among the first of the colleges to have a program. I sought to bring the Old Members (alumni) back into the orbit of the College by organizing Master’s Seminars on topics of broad interest to which we invited the Old Members, students, and the Fellows of the College. Balliol has many alumni in the former colonies and current members of the Commonwealth. I traveled extensively (usually in conjunction with scientific meetings and field trips) to meet and speak with them and to take part in seminars away from the College. There were meetings in Toronto, Hong Kong, Singapore, New York, Washington, Tokyo, Paris, and elsewhere.  The college was mainly celebrated for its program in Politics, Philosophy and Economics (“PPE”) that attracted many who subsequently went into government and politics. It had strengths in classics, history, and the humanities. But, we also had a fair share of scientists, particularly at the graduate level. I was, to my knowledge, the first scientist who was Master of Balliol, with the possible exception of an alchemist who served in the 14 th century. I tried to increase the number of students reading science by visiting schools and encouraging science students to apply. But, this was a period in Britain as it was, and is, in the United States, when science was not a popular career choice for young people. We had some success in recruitment and, I like to think, it may have had a long term effect. The social life was demanding. Events, dinners, meetings and parties kept me busy four or five evenings a week and occasionally more. This was a major change from our quite science oriented life in Philadelphia. Our lives were also enriched by our children who, I suppose fortuitously, were in England for long periods during our five years stay. Our oldest daughter Anne was married in the garden of our home, the King’s Mound. My youngest daughter Jane had married Mark Thompson, an Englishman (later, the Director General of the BBC) and they and their growing family would often visit us on weekends. Our second grandchild was delivered in Oxford and Jane stayed with us at the Master’s residence during that time. Another child was born to them during our tenure. If nothing else, that happy event will connect us indelibly with Balliol and Oxford. In the last few years of our stay my oldest son, George, came to Oxford with his family to complete the research for a D. Phil. (Ph.D.) degree. He had been away at school, living in Europe and out of our home for several years. It was a joy to encounter him, each of us on our bicycles, on the narrow streets of central Oxford, and stop for a beer at one of the many pubs that grace the University town. One of his children was also born in Oxford. It was a busy time for reproduction.  I bicycled daily. The automobile traffic in the city was (and is) horrific, but distances are short in central Oxford and I could get anywhere in minutes of earnest peddling. Strangely, among my happiest memories of our stay were the long cycling trips I took into the wonderful Oxfordshire countryside, wrapped in layers of warm clothing, and enclosed in a water resistant outer layer to protect against the frequent rains of the winter (and autumn, spring and summer).  I learned important lessons about management as the Head of an Oxford College. Balliol was originally a collection of clerics who, for a fee, tutored the sons of the wealthy in classics, theology, and a smattering of mathematics, and provided food, lodging, and protection from a sometimes hostile world. To increase their effectiveness, they formed into groups, rented, bought or built, houses in Oxford, and appointed one of their number as the head of the House with different titles (Master, Provost, President, etc.). He (and much later, she) was granted certain stated powers of governance but, over the years, the Fellows (the other clerics), who voted on all issues, took back any absolute powers the Master may have gained. Hence, the Master was accorded honors and privileges, had a great deal of responsibility (if anything went wrong it was the fault of the Master), but no power. Nor did he or she have any staff to speak of. I once asked my predecessor, Sir Anthony Kenny if he could tell me who my staff were. He responded, “What do you mean by Staff?” I replied, “If I tell them to do something, they do it.” He responded, succinctly, but gently, “Your secretary Susan, and your butler, Tony.” So, I had to learn to govern without power, to enlist the voluntary interest of Fellows when there was a specific task to do, guide the College meetings to decrease friction and unneeded controversy, and spend much time doing it. Learning to lead without actual power came in good use in later years when (for example, at the NASA Astrobiology Institute, see below) I had considerable administrative power, but only rarely had need to use it.  Despite these responsibilities there was time for some science. Professor Raymond Dwek asked me to join the Glycobiology Institute, of which he was the Founder and Director; thus began a friendship and collaboration that has lasted since then. We established a program to study the glycosylation of the surface antigen of HBV) a little understood subject. The project quickly turned clinical when Timothy Block, a colleague and friend from Philadelphia came to work on the project during a sabbatical year. We studied the mechanism of the use of partially synthetic sugars to interfere with the glycosylation of the virus in the liver and *in vitro*. This appeared to hinder the intracellular assembly of the virus in addition to other mechanisms of action. The class of sugar therapies has possible application for the treatment of HBV, HCV, and other viruses that have a glycoprotein surface coating and has resulted in a whole new area of research.  Well, all things, even good things, come to an end and we left Balliol returning home around the world with extended visits in Australia and New Zealand. I served as a Visiting Professor in the Department of Biochemistry at the University of Otago investigating the presence of HBV homologous viral sequences in the human genome. (There are quite a few of them). While on the South Island, Jean and I hiked the Milford Track. It is billed as the most beautiful hike in the world; I agree. I have walked in many parts of Asia, Africa, Europe, and America, and Milford is the most engaging. There were five days of traversing deep glacial valleys, an alpine crossing, huge tree fern forests, and ending in the spectacular Milford Sound. It was a wonderful contrast with the urban life of Oxford and Europe.  The Nasa Astrobiology Institute After returning to Philadelphia I did not re-open my laboratory. In addition to several collaborative research projects I decided to spend some time teaching. In 1997 I was invited to the Program on Human Biology at Stanford University and offered courses in Medical Anthropology and Scientific Process.  Teaching students was pleasant, intellectually stimulating and rewarding because one could ease the access of young people into the life of science. But it was not as exciting as research. While at Stanford I was invited to attend the Astrobiology Roadmap Workshop at the National Aeronautics and Space Administration (NASA) Ames Research Center, at Moffett Field in nearby Mountain View, CA. (07.20.98). I was fascinated by the proceedings. NASA had recently established an astrobiology program and had invited several hundred scientists from the space science and general science communities to discuss and formulate a program for astrobiology. The mission statement for astrobiology is, “The study of the origin, distribution, evolution and future of life on earth and in the Universe”, no mean program. It addressed the heavy questions, “How did life start?” “Are we alone in the universe?” “What is the future of life on earth and elsewhere and what happens to life when it leaves its planet of origin?” Embodied in these questions is the issue of how does one define life, or, if a definition is impossible, what are the characteristics that can be used to identify life. An allied question is what constitutes death and how can you tell if something previously alive is no longer so. These are intriguing questions, of interest not only to scientists but to philosophers, the religious, ethicist, and many others. NASA proposed to study the issues using scientific process. The Workshop encouraged me to learn more about this emerging discipline.  A few months later I was asked to co-chair another roadmap workshop along with the Nobel laureate Richard Roberts; this was on “Genomic Studies on the International Space Station”. It was an exciting program and I met more of the NASA staff during the course of the meeting and its aftermath. Soon afterwards I was asked if I would agree to have my name put forward as the Director of the recently established NASA Astrobiology Institute. This was a surprise since I had not worked in this field before. However, apparently, NASA wanted to have an experienced scientist to take part in the initiation of this scientific program. After interviews with Daniel Goldin, the then Administrator of NASA, I was appointed the “Founding Director” of NAI.  The NAI is a virtual Institute with each of the research teams remaining in their home institutions. They are well funded by NASA and expected to take a part in the NAI activities using direct and electronic means to collaborate. Astrobiology included disciplines in which I did not have formal training; geology, paleontology, oceanography, astronomy, cosmology as well as the engineering that were needed to understand the technology that is a major part of any space mission. The Director had, theoretically, a large measure of control over the grantees’ research, but it was apparent that a top-down hierarchical model for management was inappropriate for the independent minded scientists the field attracted. I relied heavily on the Executive Council, made up of the principal investigators of each of the 11 teams that we funded. Although they were formally an advisory group, I nearly always took their advice, giving them *de facto* authority. I understood that my mandate was to establish a basic science organization that could discover and understand natural phenomenon that related to early life and to life elsewhere. At an introductory address to the members of the Institute I told them that I did not expect them to do exactly what they said they would do in their applications since, in a fast moving field, observations made after the application had been written could greatly change the path of research. This was greeted with cheers.  Fortunately, NAI attracted outstanding NASA professionals for the NAI staff located at our headquarters at Ames Research Center. This enabled us not only to maintain the efficient operation of the Institute, but also to innovate. There were major barriers to surmount to produce the “Culture of Collaboration” that we sought. These included collaboration between and across scientific disciplines, between different institutions, across geographic distances and different age groups, and between national groups. We developed techniques for realizing our goal of collaboration. These included: a) Modern videoconferencing capability at each of the teams. b) Frequent face to face meetings so that collaborators knew each other personally and could therefore relate better using electronic communication. c) Funding of field trips that included members of several teams. thus increasing the opportunity for people to learn about their colleagues scientific and other interests. d) A website that would bind the participants together and serve as a repository for mutually used data. e) Funding research fellows who could migrate from team to team to facilitate communication between the teams. f) Producing real-time interactive video lectures and conferences that could include members from many teams. The management structure was dispersed rather than command and control; we encouraged the teams to communicate and collaborate directly with each other without the need to go through NASA Central.  NAI has a strong emphasis on international cooperation. Space exploration has been a remarkably international event. Even during the depths of the Cold War Soviet and US astronauts, cosmonauts and space scientists collaborated on projects, as did their governments. We recognized that exploration of the solar system to look for life could not be exclusively a US activity. It is a human program in which nations who wish to collaborate, and can, should be encouraged to do so. Initially, several countries requested and received association or affiliation with NAI in part to demonstrate to their own governments that they had international recognition. Eventually, this was converted to a federal organization of national astrobiology institutes. This has resulted in rich and effective international programs.  The subject matter of astrobiology is fascinating. It includes physical cosmology, an understanding of the origin of elements and chemicals in the early universe; pre-biotic chemistry, that is, how simple organic molecules (many of which are found in space) can assemble to form the long chain molecules – proteins, DNA, RNA, long chain sugars and glycoproteins, fats – that are essential for life as we understand it. Mars and Earth had many similarities in their early days when the environment was much harsher than it currently is. Astrobiology includes the study of locations on contemporary Earth that have similarities to early Earth and, hence, early Mars. The locations include geothermal sites; locations deep under the sea at “black smokers” that form where a tectonic plate subducts under another; in deep ocean sediments and the sub-ocean floor; low and high temperatures; extremes of pH. These are exciting sites for the study of geology and geochemistry and also bacteria, archaea, viruses and multicellular organisms that flourish in what we consider to be harsh environments. I participated in field trips to several of these locations including: Death Valley, an area of high temperature, high salinity and scarce rainfall, Yellowstone National Park, the largest geothermal site in North America, Iron Mountain Mine in northern California whose outflow has a pH approaching zero, the Haughton Impact Crater on Devon Island in the Canadian Arctic Archipelago in the Territory of Nunavut, the salt ponds in Guerraro Negro, Baja California the home to large biomats that are common in contemporary extreme environments and were also common in the cretaceous, Mono Lake below the eastern slope of the Sierras of California where geothermal sites with low pH and high mineral concentrations are found. These made for very interesting trips in the company of a multidisciplinary team of scientists. I formed the NAI Virus Focus Group to study viruses and phage in these environments and we continue to have workshops and field trips.  During the time I directed the NAI I also served (for a year) as Senior Advisor for Biology to the Administrator of NASA at Headquarters in Washington, DC with a focus on Life Sciences. The tag line for the program was “Life beyond its planet of origin” that is, what happens when Earth life is brought into the space environment. In particular, it relates to the health of humans in low earth orbit, on the Moon and eventually on excursions to Mars. Working in Washington, in the shadow of Capitol Hill where the decisions where made on the priorities and funding of NASA was strange, stimulating and frustrating, often at the same time. The Administrator, Daniel Goldin, who I theoretically advised, was a dynamic and visionary leader with a forceful management style. I flew with him on “NASA One” on several occasions to the launches of the Space Shuttle at the Kennedy Space Center. It was a dramatic trip, along with participants in the launch activities in the ageing “G4” (Gulfstream 4 Jet) that was available to NASA. We landed on the rarely used Skid Strip, and, with a police escort proceeded to the Saturn building and then to the viewing platform for the mind-blowing launch. It was a big change from hanging out in a biochemistry laboratory.  I enjoyed my association with NASA over the course of more than five years. I had to learn a whole science that, on most days, found me at the edge of my intellectual capabilities, a happy challenge in my mid-70s. The people I interacted with were different from the medical and biological scientists that had peopled my previous scientific life; aviators, astronauts, astronomers, cosmologists, geologist, oceanographers, paleontologists, senior government and political figures. I enjoyed the outdoors life of California with wonderful walks in the Santa Cruz Mountains, backpack trips into the remote Trinity Mountains near Oregon, miles of walking on lonely beaches with the ocean on one side and shear cliffs on the other. Stanford and the NASA Research Center were in the middle of Silicon Valley and the enthusiasm, entrepreneurial spirit and optimism of the place were a source of stimulation and excitement.  Fox Chase Cancer Center Despite the joys of NASA I was happy to return to Philadelphia and to my activities at the Fox Chase Cancer Center where I had been employed, full or part time since 1964, even during the periods that I was away in Oxford and California. I published several papers on the general biology and ecology of HBV. There are strange interactions of HBV with humans in respect to gender. The response of parents to infection with HBV is related to the gender of their offspring. Parents who become persistent carriers of HBV have a higher ratio of boys to girls among their newborns than do parents who have developed antibody against the surface of the antigen. Uninfected parents have an intermediate ratio. The findings were the same in four populations that we studied and in two populations reported by others. The predicted demographic effect of HBV was very large. In addition, if our observations and inferences were correct, the vaccination program would significantly alter gender ratios in the impacted regions during the next few decades as the program coverage increases.  A measure of validation came from an unusual source. Emily Oster, then a graduate student in Economics in Boston read my book (see above), including the section on gender ratio, and proceeded to examine the issue at a population and economic level. She found a direct correlation between the prevalence of HBV carriers in a population and the ratio of males to females. She also found that in populations with a historic high prevalence of HBV carriers and where effective vaccination had been in place for about two decades, there was, as predicted, a decrease in the male to female gender ratios. If this and our other observations are confirmed it implies that HBV may have a causative role in determining gender ratios at birth.  The American Philosophical Society Well, life did not slow down appreciably after I stepped down from NASA employment. In 2005 I was elected the President of the American Philosophical Society. A word about the APS. It was founded in 1743 in Philadelphia by Benjamin Franklin and his colleagues. It is, probably, the oldest academic, scientific, or scholarly society in the United States. Its formation followed the publication by Franklin of *“A proposal for promoting Useful Knowledge among the British Plantations in America “* that advocated the encouragement of communication between “Men of Speculation, *Virtuosi*, Ingenious Men”. (Actually, women were included fairly early with the election of the Russian Princess Dashkova in 1789.) The members saw themselves as “Natural Philosophers”; they were active in the scientific revolution that was sweeping Europe at the time; the APS was one of the enlightenment’s North American centers. Among my predecessors as President were the Founder himself and Thomas Jefferson, who was simultaneously the President of the United States. Many of the Founding Fathers of the United States, for example, Washington, John Adams, John Q. Adams, and Alexander Hamilton, as a well as distinguished foreign members – Charles Darwin, Baron Alexander von Humboldt, Joseph Priestley, Antoine Lavoisier, Lord Kelvin (William Thomson) – were Members of the Society. The APS Library contains many important documents from the colonial period and the early days of the Republic including Jefferson’s hand-written draft of the Declaration of Independence, Franklin’s copy of the Constitution, and other icons of the birth of the United States. We also have a growing collection of the papers of contemporary (or recently contemporary) scientists particularly in the area of genetics. They include [Thomas Morgan](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1933/index.html), Ernst Mayr, Theodosius Dobzhansky, [Barbara McClintock](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1983/index.html), Sewell Wright, and many others. It is a major resource for the history of science of the 20th and 21st centuries.  In 2004 to commemorate the 200th anniversary of their epochal expedition, I helped to establish the Lewis and Clark Fund for Exploration and Field Research. The L & C provides funding for field studies by doctoral candidates and others. The amount is small, but sufficient to allow a field trip to most places in the world. We have funded geologists, paleontologists, field biologists, medical epidemiologists, archaeologists, anthropologists, etc. It has been wildly popular; we had over 520 applications by the second year of the program. Unfortunately we only have sufficient funds for a fraction of these. It is very gratifying to help young scientists undertake field work that could change the course of their scientific careers.  Conclusion Well, I have written far too much. The award of the Nobel Prize has provided many opportunities that would not have otherwise been available to me. In addition I have had the privilege of meeting many other laureates and their families over the years and attending the grand events held periodically in Stockholm and elsewhere. It has enriched my scientific life and the lives of my wife and family. Our four children have among them now produced nine grandchildren. We spend a great deal of time with them; they are our eyes into the future.  *Baruch S. Blumberg died on 5 April 2011.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0612** |
| Interview |  |
|  |  |
| ID | **0613** |
| Biographical | My scientific interests started before my school years, when as a boy of five years I wandered through gardens, fields and woods with my mother’s entomologist-sister, Tante Irene, as we overturned rocks and sought to find how many different plant and animal species of previously hidden life lay before us. We cut open galls to find the insects responsible for the tumors, and collected strange hardening gummy masses on twigs which hatched indoors to fill the curtains with tiny praying mantises, and discovered wasps with long ovipositors laying their eggs into the larvae of wood-boring beetles. In petri dishes we watched some leaf-eating insects succumb to insecticide poison while others survived, and on exciting excursions visited the laboratories and experimental greenhouses of the Boyce Thompson Institute for Plant Research in my hometown of Yonkers, New York, where my aunt, Irene Dobroscky, worked, studying in the 1920’s virus inclusions in the cells of leaf-hoppers.  In my first years at school I had problems with my teachers for carrying to school insect-killing jars, correctly labeled “Poison: potassium cyanide”. As a grade schoolboy, I met at the Boyce Thompson Institute laboratories the quiet, amused, watchful and guiding eyes of the mathematician and physical chemist, Dr. William J. Youden, who enjoyed letting me play with his hand cranked desk calculator, with his circular or cylindrical slide rules, and with models of crystal lattice structure, and on his laboratory bench where he taught me to prepare colloidal gold solution time color reactions and to manufacture mercuric thiocyanate snake-generating tablets. Before I was ten years old I knew that I wanted to be a scientist like my aunt and my quiet mathematician tutor. I rejected completely, as did my younger brother, Robert, who is now a poet and critic, the interests of our father and maternal grandfather in business, which had made our life style possible.  My life and outlook were greatly influenced by the polyglot immigrant Eastern European communities, adjacent and unwillingly interlaced, living in the carpet, elevator and copper wire manufacturing and sugar refining city of Yonkers, just upstream on the Hudson River from the New York megalopolis and possessing a schoolbook history of a Seventeenth Century Royal Dutch land grant of Indian land to Johng Heer (hence Yonkers) Adrian van der Donck. The cimbalon in our living room, beside the piano, Romanian and Hungarian gypsies who fiddled the *czardas* and *halgatos* at our family festivities and camped in the empty store adjacent to my father’s butcher shop, an uninterrupted flow of loud conversation in many tongues, rarely English, and kitchen odors of many Habsburg cuisines filling our crowded expanded-family-filled home, gave me an orthodox and optimistic view of America as a land of change and possibility which I never lost. Below our almost rural hilltop home – our family had “risen” – clustered the factories, churches, shops and two to four family houses of immigrant factory workers and tradesmen in the valleys of the almost obliterated Nepperhan and Tuckahoe Indian-named creeks. In this hollow stood Hungarian, Slovak and Polish Catholic and Russian Orthodox churches and a Presbyterian mission to the factory workers. (This exciting conglomeration of Eastern Europeans has been later displaced by Mediterranean and Caribbean and, still later, Black Americans, all similarly “melting”. )  My father, Karl Gajdusek, was a Slovak farm boy from a small village near Senica, who had left home as an adolescent youth to emigrate to America before World War I, alone and without speaking English, to become a butcher in the immigrant communities of Yonkers, where he met and married my mother, Ottilia Dobroczki. Her parents had also come, each alone, as youthful immigrants from Debrecen, Hungary to America. On my father’s side we were a family of farmers and tradesmen, vocations which never interested my brother or myself, but my father’s temperament for laughter and ribald fun, lust for life in work and play, music, song, dance and food, and above all, conversation; affected us strongly. On my mother’s side were the more somber academic and aesthetic aspirations of four university educated first generation American siblings and a heroic interest in fantasy and inquiry, in the classics and culture, nature, nurture and process. Because of my mother’s unquenchable interest in literature and folklore, my brother and I were reared listening to Homer, Hesiod, Sophocles, Plutarch and Virgil long before we learned to read.  I was born on September 9, 1923 in the family home we still own, while my maternal grandparents and my mother’s youngest sister shared the home. My brother arrived nineteen months later. He and I grew up closely together; for every move I made further into mathematics and the sciences, he moved further into poetry, music and the other arts. In 1930 we traveled to Europe to visit our relatives, mostly those of my father’s large family, which he had abandoned twenty years earlier. My brother and I were left for months in my father’s birthplace with his old father and the huge remaining family (the squire had sired some twenty five children), while our parents toured European capitals.  Back in America, my early school years were those of great happiness: I liked school and the enchanting family excursions up the Hudson valley were frequent. My Tante Irene was working on problems of economic entomology in the Philippines and South East Asia, and exotic artifacts and natural history specimens, particularly the beautiful giant leafhoppers clad in batiklike patterns, arrived to fascinate me. On her return from the Orient she took me on ever broader excursions to collect insects, to watch the emergence of the seventeen-year cicadas and to attend scientific meetings in the American Museum of Natural History. I became an early habitué of New York city’s museums, attending courses on Egyptology at the Metropolitan Museum of Art on schoolday afternoons after my fifth grade classes and at weekend and evening lectures on entomology, geology and botany at the Museum of Natural History.  Today, I and my large family of adopted sons from New Guinea and Micronesia still occupy, on our frequent visits to New York city, our family home in which I was born fifty-three years ago. Here, the boys recently discovered, while installing new attic insulation, daguerreotypes and tintypes of the family taken in towns east of the Danube and in turn-of-the-century New York city and also school notebooks which once belonged to my mother, her siblings, my brother, and myself. From this home, too, we buried both of my maternal grandparents, and my father and mother. On the occasion of my pagan mother’s death, the unavoidably close proximity of Slovak Catholic and Russian Orthodox churches, both named Holy Trinity, led to the confusion which resulted in burying her with ministrations of the wrong denomination, which she would have enjoyed, when I attempted to assuage, by asking the funeral director to call in the priest, the pious Roman Catholic relatives of my irreverent father, at whose earlier funeral the Slovak priest had declined to officiate.  I started to read seriously before puberty. Books by Scandinavian authors, Henrik Ibsen and [Sigrid Undset](https://www.nobelprize.org/nobel_prizes/literature/laureates/1928/index.html), were among the earlier works I read myself. I devoured enthusiastically three biographical works which must have had a profound effect on me: René Vallery-Radot’s biography of his father-in-law, Louis Pasteur; Eve Curie’s biography of her mother, [Marie Curie](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1911/index.html); and Paul de Kruif’s “Microbe Hunters.” I then stenciled the twelve names of microbiologists whom de Kruif had selected on the steps leading to my attic chemistry laboratory, where they remain today. At about this time, when I was about ten years old, I wrote an essay on why I planned to concentrate on chemistry, physics, and mathematics, rather than classical biology, in preparation for a career in medicine. Dr. Youden had succeeded in making it clear to me that education in mathematics, physics and chemistry was the basis for the biology of the future.  During the summers of my thirteenth to sixteenth years, I was often working at the Boyce Thompson Laboratories. Under Dr. John Arthur’s tutelage, I synthesized and characterized a large series of halogenated aryloxyacetic acids, many previously unsynthesized. The series of new compounds I derived from these failed to yield the fly-killing potency anticipated, but when they were tested several years later for their phytocidal capacity one of my new compounds, 2,4-dichlorophenoxyacetic acid, became the weed killer of commerce; and the Institute based its patent rights to royalties on my boyhood laboratory notebooks – the only venture I have had which involved commerce.  My experiences at the Boyce Thompson, especially with Youden, directed me towards physics at the University of Rochester, where I hoped to fulfill my plan, formulated in boyhood from my readings and teachings of my aunt and Youden, of studying mathematics, physics, and chemistry in preparation for a career in medical research.  From 1940 to 1943 I studied at the University of Rochester under Victor Weisskopf in physics; Curt Stern, Don Charles, David Goddard, Jim Goodwin, in biology; Vladimir Seidel in mathematics; and Ralph Helmkamp in chemistry. In the summer of 1941 I was inspired by the marine embryology course of Viktor Hamburger’s at Woods Hole Marine Biology Laboratories. In those years of my teens I learned to love mountaineering, hiking, canoeing and camping with a passion as great as that for science.  At nineteen to twenty-two years of age while at Harvard Medical School, I worked with John T. Edsall in the laboratory of protein physical chemistry, and with James L. Gamble in his laboratory of electrolyte balance at Boston Children’s Hospital. Thereafter, at ages of twenty-five and twenty-six, I worked at Caltech with [Linus Pauling](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1954/index.html) and John Kirkwood, where I was also greatly influenced by [Max Delbrück](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html), [George Beadle](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html), Walter Zechmeister and James Bonner. It was at Caltech that my peers – fellow postdoctoral students and young investigators (Gunther Stent, Jack Dunitz, Elie Wollman, Benoit Mandelbrot, David Shoemaker, John Cann, Harvey Itano, Aage Bohr, Ole Maaloe, Ted Harold, John Fincham, Reinhart Ruge, Arnold Mazur, Al Rich, and others) – had a profound effect on my intellectual development, goals and appreciation of quality in creative life, and on my career. This was the “Golden Age” at Caltech and the many close friends working in several different disciplines, as well as our mentors, have remained mutually stimulating coworkers in science and, above all, lasting personal friends for the past thirty years. With the group of students about Linus Pauling, John Kirkwood, Max Delbrück and George Beadle, I spent many days and evenings in wideranging discussions in the laboratories and at the Atheneum, and in even more protracted exchanges on camping and hiking trips to the deserts and mountains of the West, of Mexico and Canada. Max and Mannie Delbrück were often the hosts for our group at their home, and the prime organizers of many of our expeditions. This period of less than two years at Caltech has given me a group of friends who are interested critics of my work, who together with my major teachers in clinical and laboratory investigation, comprise, perhaps unwittingly, the jury whose judgements I most respect.  I had not counted on my captivation with clinical pediatrics. Children fascinated me, and their medical problems (complicated by the effect of variables of varying immaturity, growth, and maturation upon every clinical entity that beset them) seemed to offer more challenge than adult medicine. I lived and worked within the walls of Boston Children’s Hospital through much of medical school. Thereafter, I started my postgraduate specialty training in clinical pediatrics which I carried through to Specialty Board qualification, while also working in the laboratory of Michael Heidelberger at Columbia University College of Physicians and Surgeons, while at Caltech, and while with [John Enders](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html) on postgraduate work at Harvard. I have never abandoned my clinical interests, particularly in pediatrics and neurology, which were nurtured by a group of inspiring bedside teachers: Mark Altschuler, Louis K. Diamond, William Ladd, Frank Ingraham, Sidney Gellis, and Canon Ely at Harvard; Rustin McIntosh, Hattie Alexander, Dorothy Anderson, and Richard Day at Babies Hospital, Columbia Presbyterian Medical Center in New York; Katie Dodd, Ashley Weech, Joe Warkany, and Sam Rappaport at Cincinnati Children’s Hospital, and Ted Woodward of Baltimore.  In 1951 I was drafted to complete my military service from John Enders’ laboratory at Harvard to Walter Reed Army Medical Service Graduate School as a young research virologist, to where I was called by Dr. Joseph Smadel. I found that he responded to my over-ambitious projects and outlandish schemes with severity and metered encouragement, teaching me more about the methods of pursuing laboratory and field research, and presenting scientific results, than any further theoretical superstructure, which he assumed I already possessed.  From him and from Marcel Baltazard of the Institut Pasteur of Teheran, where I worked in 1952 and 1953 on rabies, plague, arbovirus infections, scurvy and other epidemic disease in Iran, Afghanistan and Turkey, I learned of the excitement and challenge offered by urgent opportunistic investigations of epidemiological problems in exotic and isolated populations. My quest for medical problems in primitive population isolates took me to valleys of the Hindu Kush, the jungles of South America, the coast and inland ranges of New Britain, and the swamps and high valleys of Papua New Guinea and Malaysia, but always with a base for quiet contemplation and exciting laboratory studies with John Enders in Boston, Joe Smadel in Washington, and [Frank Burnet](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1960/index.html) in Melbourne. To these teachers I am indebted for guidance and inspiration and for years of encouragement and friendship.  To Joe Smadel I also owe the debt of further sponsorship and encouragement, and recognition of my scientific potential for productive research which led him to create for me several years later a then unique position as an American visiting scientist at the National Institutes of Health, in the National Institute of Neurological Diseases and Blindness, under Dr. Richard Masland, wherein I could nurture my diverse interests in a selfstyled Study of Child Growth and Development and Disease Patterns in Primitive Cultures. Our Laboratory of Slow, Latent and Temperate Virus Infections grew out of the elucidation of one of our “disease patterns”, kuru, and blossomed into a new field of medicine. For about two decades I have enjoyed at the National Institutes of Health the base and haven for our diverse studies in remote parts of the world together with a small group of students and coworkers and many visiting colleagues who have formed the strong team of our endeavor. Here, Marion Poms, Joe Gibbs, Paul Brown, Vin Zigas, Michael Alpers, David Asher and Nancy Rogers have shared these adventures with me through almost two decades.  My boyhood reading, first in Homer, Virgil, and Plutarch, on which we were nurtured by our Classicist-Romanticist Hungarian mother, led, upon the instigation of my poet brother, to my more thorough return to the classics as a young, too-ardent scientist-cum-physician, and to the modern literature of European authors and philosophers, which I had missed in my university days devoted too exclusively to mathematics and the sciences. This reading changed greatly my way of thinking. Particularly, I would have to credit Dostoevsky, Chekhov and Tolstoy; Montaigne, Baudelaire, Rimbaud, Valery and [Gide](https://www.nobelprize.org/nobel_prizes/literature/laureates/1947/index.html); Shakespeare, Wordsworth, Yeats and Lawrence; Poe, Whitman and Melville; Ibsen; Goethe, Schiller, Kant, Nietzsche, Kafka and [Mann](https://www.nobelprize.org/nobel_prizes/literature/laureates/1929/index.html); Saadi and Hafiz.  In 1954 I took off for Australia to work as a visiting investigator with Frank Burnet at the Walter and Eliza Hall Institute of Medical Research in Melbourne from where, between periods of bench work in immunology and virology, I launched studies on child development and disease patterns with Australian aboriginal and New Guinean populations.  In eighteen volumes of some five thousand pages of published personal journals on my explorations and expeditions to primitive cultures, I have told far more about myself and my work since 1957, when I first saw kuru, under the guidance of Vincent Zigas, than one should in a lifetime … I do not see how I can précis that here.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1976*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1977  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *D. Carleton Gajdusek died on December 12, 2008.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0613** |
| Interview |  |
|  |  |
| ID | **0614** |
| Biographical | My interest in Biology began when I was a high school student and spent a summer at the Jackson Memorial Laboratory in Bar Harbor, Maine. There I first experienced research biology and saw research biologists at work; this experience led me to become a biology major in college.  I went on to Swarthmore College where I began as a major in biology but switched to chemistry later so that I could carry out a research thesis. Between my last two years at Swarthmore I spent a summer at the Cold Spring Harbor Laboratories working with Dr. George Streisinger, and the experience of working with and watching that great teacher led me to molecular biology.  I started graduate school at Massachusetts Institute of Technology in biophysics, but when I decided to work on animal viruses I left M.I.T. to study for a summer with Dr. Philip Marcus at the Albert Einstein Medical College and to take the animal virus course at Cold Spring Harbor, then taught by Dr. Richard Franklin and Dr. Edward Simon. I joined Dr. Franklin at the Rockefeller Institute to do my thesis work and then continued in animal virology as a postdoctoral fellow with Dr. James Darnell. I had already found that much could be learned by studying virus-specific enzymes, so I studied for a while with Dr. Jerard Hurwitz at the Albert Einstein College of Medicine to learn from someone who knew enzymology as a professional.  My first independent position was at the Salk Institute in La Jolla, California where I had the rare opportunity to work in association with Dr. [Renato Dulbecco](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html). After 2 1/2 years away from a university setting, I returned to M.I.T. in 1968 and have remained there. In 1974, I joined the staff of the M.I.T. Center for Cancer Research under the directorship of Dr. [Salvador Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) because I had found that my research interests, that previously had involved mainly the non-oncogenic RNA viruses, were more and more focused on the problems of cancer.   |  |  | | --- | --- | | Date and place of birth | | | March 7, 1938 in New York, New York | | |  | | | Education | | | 1956-1960 | Swarthmore College, Swarthmore, Pennsylvania B.A. with high honors in Chemistry, 1960 | | 1960-1961 | Massachusetts Institute of Technology, Cambridge Massachusetts, graduate courses toward Ph.D. | | 1961-1964 | Rockefeller University, New York, New York. Ph.D.  received in 1964 | |  |  | | Positions held | | | 1963-1964 | Postdoctoral Fellow, Massachusetts Institute of Technology, Cambridge, Mass. | | 1964-1965 | Postdoctoral Fellow, Albert Einstein College of Medicine, Bronx, New York | | 1965-1968 | Research Associate, Salk Institute for Biological Studies, La Jolla, California | | 1968-1972 | Associate Professor of Microbiology, Massachusetts Institute of Technology, Cambridge, Mass. | | 1972-present | Professor of Biology, Massachusetts Institute of Technology, Cambridge, Mass. | | 1973-present | American Cancer Society Professor of Microbiology |   From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1975*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1976  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1975 Addendum, May 2005 In 1975, when I received the Nobel Prize, I was already in New York on sabbatical, investigating the possibility of moving from virology into immunology. When I returned to MIT, I did reorient my laboratory and from then on I have pursued a mix of immunology and virology. Today that takes the form of an interest in using retrovirus vectors to modify the immune system.  Our most significant discovery in immunology was probably the identification of the protein pair that rearranges immunoglobulin genes, the so-called RAG proteins. This was actually done by two graduate students, David Schatz and Margie Oettinger. We turned to examining the transcription factors that modulate the development of B lymphocytes and discovered the key transcription factor, NF-KB.  We studied B lymphocyte development mainly using cells immortalized by the Abelson mouse leukemia virus. While examining the ability of this virus to cause cell transformation and cancer, we discovered that its oncoprotein was a tyrosine-specific protein kinase. This was a unique enzymatic activity at the time, also discovered by Tony Hunter. This observation led to the development of Gleevec, one of the most successful anti-cancer drugs and the first small molecule to target the activity of an oncoprotein.  While carrying out an active research program, I found myself drawn to administration of scientific institutions and I have maintained both interests to this day. My first foray into administration came about through an encounter with Mr. Jack Whitehead. He offered me the opportunity to start a small research institute, which he would fund. We founded the Whitehead Institute for Biomedical Research as an independent entity allied with MIT, devoted mainly to developmental biology. I was able to attract an amazing faculty and the Whitehead has continued as a great institution. One of its faculty, Eric Lander, was the driving force for the sequencing of the human genome and he has now generated an offspring of Whitehead, the Broad Institute.  I went from MIT and Whitehead to New York in 1990 to be President of the Rockefeller Institute, my graduate alma mater. I only stayed in that position through 1991 because a misconduct case against a collaborator of mine became a drag on my effectiveness. I returned to MIT in 1994 but was again taken away in 1997 to be President of the California Institute of Technology (Caltech). For the last eight years I have had the honor and challenge of running this great institution, described by my wife as the last ivory tower. As a student, I had learned about the physical sciences but as a biological research scientist I had had little interaction with the great advances in the field; coming to Caltech greatly broadened my appreciation for the remarkable advances being made across the board in science and technology. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0614** |
| Interview |  |
| Q1 | Dr Baltimore, you have been an active scientist for close to 40 years. How did it all started; how did you get into science? |
|  | I got into science really because of my mother. My mother was an experimental psychologist and she arranged, when I was in high school, for me to go to the Jackson Lab and Bar Harbor, Maine. I had the opportunity to do research for the summer in mass genetics and it was fabulous, and I never looked back so it was really after my junior year in high school that I was determined to be an experimental scientist, biologist, and through college and graduate school there was never any question that that was what I was going to do. |
| Q5 | Was there any teacher that inspired you? |
|  | It was really the people at Jackson Lab who inspired me. My high school teachers, bless their hearts, were terrible, particularly biology teacher was the worst. But the scientists there, Timmy Russell, Willy Silvers, Don Bailey, Charity Weymouth, were just fabulous people. Many of them were founders of contemporary mass genetics and for high school students to work with people like that is a very rare opportunity but they were so wonderful and made it so clear how exciting it was to do science. |
| Q3 | What happened after Jackson Laboratory, the summer experience? |
|  | I went back to high school and then I graduated and went to Swarthmore College and at Swarthmore there were many wonderful people but none of them were involved in what I would call contemporary research and so none of them were role models for me. I ended up teaching molecular biology when I was in college because I knew more than any in the faculty did, I just learned it from seminars. One summer programme I was at Cold Spring Harbor one summer and worked with George Streisinger. George was one of the central members of the Phage Group, very much of a sciency scientist, not well known outside of the field and a terrific man, superb man, and I worked experimentally with him for the summer and that was a great experience, and he was always somebody I looked up to. |
| Q11 | You got also in contact with Salvador Luria at an early stage. |
|  | At Cold Spring Harbour that summer, which was the summer after my junior year of college, a couple of people came, everybody used to come to Cold Spring Harbor for the summers, [Delbrück](https://www.nobelprize.org/prizes/medicine/1969/delbruck/facts/) and [Luria](https://www.nobelprize.org/prizes/medicine/1969/luria/facts/) and Leventhal and all the central people in the phage school.  These are in the late 1950s.  David Baltimore: This is now the summer of 1959, right, and Luria came and Leventhal. Both of them had recently become faculty members at MIT and they were starting one of the very first departments in molecular biology. In 1959 if you’d become interested in molecular biology, there were really only three places to go, to MIT, which was just starting out, to Rockefeller, which of course had been the centre of medical research in the United States for a long time, or Caltech, where Max Delbrück had the great school of molecular biology that generated the whole phage focus. The idea of going to Caltech oddly enough, never entered my head, the thought of going to California was just further away than I could imagine and although my previously good friend, already good friend, [Howard Temin](https://www.nobelprize.org/prizes/medicine/1975/temin/facts/) had done that, had left Swarthmore and gone to Caltech, but I couldn’t even think of that. So, I went to MIT, and it was really because I had met Luria that summer. He and Leventhal recognised that I was able to do these things pretty easily and that I had a good experimental sense and that I wanted to do the right things, so they asked me to come to MIT and that was the only place I had for graduate school so I went there. |
| Q23 | So rather than starting to work on phages, you decided to go in a totally different direction, that of the animal virus. |
|  | David Baltimore: That’s right.  What made you make this decision?  David Baltimore: I guess I had the feeling that the heyday of phage research was over, that phage had done for molecular biology what it was going to do and that in my career which after all wasn’t going to start as an independent investigator for another 5–10 years, that I should be looking somewhere else and I didn’t know where to look and so I took what was the most, the easiest sort of analogue or analogy. The analogy was if phage had been so important for working out the molecular biology of bacteria, animal viruses should be able to do the same thing for animal cells. I guess what that means is, although I didn’t think about it a lot, that I had already decided what I wanted to work on was the molecular biology of animal cells. I don’t know why, but I did and I saw animals viruses as a probe of that and so I went to Leventhal who I was doing some experiments with and I said, What do you think of that idea? and he said, You know, I’ve wondered that myself, he said. So that was helpful but didn’t get me anywhere so I went to Luria who was everybody’s greatest teacher and I said the same thing and he said, That’s an interesting question, why don’t you spend the summer investigating it. I’ll arrange for you to work with a young animal virus person, Phil Marcus at Albert Einstein [Medical College] and to take the animal virus course at Cold Spring Harbor.  I did that after my first year at graduate school and it was a revelation because there was just an enormous amount to be done and nobody was doing it. And so I came back particularly from the Cold Spring Harbor experience and said, Yes, this is what I want to do, but the man I want to do it with is Richard Franklin, who was the guy who was teaching the animal virus course that summer and he was at Rockefeller. So Luria arranged to help me transfer to Rockefeller which was a wonderful thing since he really had very few students at MIT in, as registered into microbiology because it just wasn’t something everybody was doing in 1960. And so, I transferred to Rockefeller and did my thesis in two years there and exactly what I suspected was true, was true. That is there was an enormous … to be done and every time you did an experiment you discovered something. I published lots of papers and had a very good time. |
| Q79 | The reason that one could start to address these questions for animal viruses was probably the development of the cell culturing techniques that made possible to make experimentations in the lab**.** |
|  | There were many different strains of development that lead to that moment being so opportune. One was cell culture. Harry Eagle developing a medium that you could use and learning how to manipulate healer cells and other cells. He was central and of course [Dulbecco](https://www.nobelprize.org/prizes/medicine/1975/dulbecco/facts/) invoked having developed a plaque assay for animal viruses so you could do quite a … of animal virology. Now that was only a couple of years before that the assays had been developed. That’s one of the things I discovered in Cold Spring Harbor was the plaque assays. Rubin and Temin’s work in the development of the quantity of assays for cell transformation, the focus-forming assays from the sarcoma virus that was also a very important strain, but for me, interested in molecular biology, one of the main things was biochemistry. It was the work of [Kornberg](https://www.nobelprize.org/prizes/medicine/1959/kornberg/facts/) with DNA polymerase basically and then lots of other people doing lots of other things, Ochoa with polynucleotide phosphorylase and whatever, but the DNA preliminaries was a key. It’s interesting, if you read what people were saying in the mid-50s about DNA when they were just trying to figure out whether DNA encodes proteins and how DNA replication occurs, they didn’t know what the precursors for DNA were. They really didn’t understand DNA synthesis, never mind the sort of geometry of replication, they didn’t understand the basic formation of the bond. Kornberg’s working out that the triphosphate was the precursor and that you could label with phosphate or with iridium the basis and getting corporation was a key.  One of the things that a lot of my thesis work was involved with was in vitro synthesis of poliovirus and Mengovirus RNA, an inhibition of RNA polymerase. Those things all followed on the models of Kornberg’s school basically, although the first … work was actually done by a guy in Chicago named Sam Wise. And then came radiography, radiography’s a very important tool at that point and Richard Franklin was one of the great exponents of that. That’s one of the things I had learned at Cold Spring Harbor and that showed us that viruses grew in the cytoplasm and cells made the RNA in the nucleus. You know, it wasn’t even clear then that all RNA was made in the nucleus, and I actually did some of the best experiments to show that using very rapid pulses in cells and autoradiography to show that all of the grains were in the nucleus. All the synthesis was going on in the nucleus, but if you did the same thing in a virus infected cell all the grains were in the cytoplasm. |
| Q33 | So rather than picking a DNA virus that was … DNA was the hot stuff in those days, you focused on the RNA virus, the Mengo- and the poliovirus and then followed the RNA dependent RNA polymerase. What did that mean to you? |
|  | Why did I do it that way? Really only because that’s what Richard Franklin worked on. It was not a conscious decision that RNA was more important or more interesting than DNA. In fact, in retrospect it was kind of stupid to do that although it worked out very well and got me in a new direction, but if I was really interested, I should have focused on DNA virus but then Richard didn’t do that, what he worked on was Mengo at the time and some with flu virus, most all, almost all RNA viruses. So that’s what I did, and I always figured I could do something else later if I wanted. |
| Q80 | At some point you moved to MIT and then, based on your experience with the picornaviruses the polio and the Mengo you also looked for RNA polymerases in other viruses. How do you come about to do that, to expand to other viruses? |
|  | It was not, it wasn’t a direct line, I had been doing work on the polio and Mengo polymerases at Rockefeller for my thesis and then when I left there and went to the Salk Institute I was actually involved more in protein synthesis and in showing the polyprotein was made and the important role of protein cleavage in the formation of viral proteins. When I came back to MIT in 1968, Alice Huang, then my post doc, later my wife, soon to be my wife, she was working on polio. She was trying to get some experience with the kinds of work that we had learned how to do over those years but she actually … Her first love was the vesicular stomatitis virus so she and I talked one day about what she was going to do in the future, and I said, Well, you know, it would be fun to work on a different virus. I’d been working on picornaviruses now for most of 10 years and that a lipid virus that had a whole different history would be interesting to start on. She of course knew how to deal with it and had wonderful stocks and worked out a lot of the biology interference which was necessary otherwise you’d spend your life studying interference, not the virus. We said, Let’s do that, and a student joined us, Martin Stanford, and we began to look at the virus.  At that point we were doing some hybridisation so we simply asked did the virus look like polio that is, did it have messenger RNA in the virus particle and quickly we were able to show that the RNA in the virus particle was not the messenger RNA, we didn’t find it on polysomes and what was the messenger RNA was the other strand and what the cell filled up with was the other strand, so these were clearly negative strained viruses. In fact we named them that because they had the anti-sense RNA not the sense RNA in the virus particle. But that then presented a puzzle because if a virus has within it anti-sense RNA, senseless RNA really, and that goes into the cell it can’t code for anything so there’s no way for the infection to get started. That puzzle lead me just wonder whether there wasn’t a polymerase in the virus particle that would get the whole infection started by copying the senseless strand and the anti-sense strand into sense RNA. Again I had all this background in biochemistry, looking for something like that was trivial for me, and so we just made some virus and opened them up with detergent and assayed it for RNA polymerase activity and it was … It went off the charts, that’s one of the easiest enzymes to assay that you can find. We were lucky we chose the right virus, I mean we were lucky that virus chose us, I guess. So that was fine and we published that.  And now we are in 1970.  David Baltimore: And now we are, yes, that was published in early 1970 I think, or maybe in the later, mid-1970, was finished in early 1970. And I started thinking about what other viruses you could study and find the same thing that is, you know ‘Hershey heaven’ – can I do the experiment over and over again and find new things. We tried viruses that looked like vesicular stomatitis virus, that is Newcastle disease virus and influenza virus. Newcastle disease virus, that was a polymerase, we published that with Mike Brett. Influenza virus, there was no polymerase activity, or there was just, I can’t remember, maybe there was a hint of activity but it was very low, and it was very hard to work with so we sort of gave up on it. I had been working on flu years before that, looking for … Showing that flu is acting on mice insensitive which is very strange, so flu was always a puzzle and now we know that flu is a puzzle, and we know why and it’s just much more difficult than these other viruses. |
| Q23 | So now the stage was set for the real discovery. |
|  | Now the stage was set. In the early 1970 one of the viruses I focused on was RNA tumour viruses, then called RNA tumour viruses. Rous sarcoma virus and murine leukaemia virus, very interesting viruses, very little known about them. They had RNA in them, very hard to grow, very hard to do any molecular biology and almost nothing known about them. I said, Well, let’s assay them, maybe they have a polymerase and of course I was very aware of the background of Howard Temin’s work for 10 years which had lead him to suggest that there was a DNA intermediate in the growth of these RNA viruses and that was an intriguing idea but it’s not that there was no support for it, there was almost anti-support for it. The experiments that had been done to test it were really very poor and came out of it, great poorly, didn’t work well. I was aware of that and said, Well, maybe there’s DNA polymerase in those viruses and that of course would explain everything Howard had been talking about and be very dramatic, wonderful. To do that I got in touch with some friends of mine who worked on these viruses and said, Is there any way I can get some material, because I wasn’t going to try to grow them, they were impossible to think about for me at that point.  Two people were helpful, Peter Vogt, who sent me a preparation of Rous sarcoma virus and George Todaro, who put me in touch with a group at NIH that was storing away enormous amounts of virus and they didn’t know why. They’d had a contract to do it and somebody thought it was a good idea to have it, it was in the freezer, and I called them and I said, Would you send me some, they said, We’d love to send you some. I don’t know that they’d ever had a request before for any of this material, How much would you like? I said, I don’t know, what kind of units do you measure it in? and they said, Millilitres. How many millilitres would you like? I said, What’s in a millilitre? They said, We don’t know. They didn’t have a biological measure, they didn’t have a chemical measure, they just had a protocol and it made millilitres and they froze those away and it was a contract firm, they didn’t know what was in there. But they said, It’s worth a lot of money. I said, Why don’t you send me … I don’t know, I can’t remember what I said … 100 millilitres? They said, Oh fine, we’ll do that, shall we send it by courier? I said, Is it frozen isn’t it, why don’t you just pack it up and send it? They said, It’s worth a lot of money. I never found out how much money it was supposed to be worth, but this contract was a very rich contract. They were spending millions of dollars on this stuff so this was certainly tens of thousands dollars worth of virus. But Vogt’s virus came first and the Rous sarcoma virus. I said, I’m going to do the likely experiment, so I looked for the same kind of RNA polymerase that I’d discovered previously in VSV and elsewhere and there was nothing there.  It was a good clean experiment and that was good virus and I knew the experiment didn’t work. But I had very little left after that because he hadn’t sent me much, so I left that frozen away and the virus came from NIH and there was these little millilitres of milky stuff. I put some in a test tube and now I said, I’ll assay for DNA polymerase and again I knew how to do that, I actually had been a post doc working on DNA polymerase, so I’d purified the polymerase, I knew all about them. And I got a hint of activity. One of these things that’s just enough to keep you doing experiments, but not enough so you know if it’s real or not. I just did something very simple which I took it and I centrifuged it for a while and took the pellet and re-suspended it in ten-fold concentrated and put that in the test tube the next day and it went off scale and I knew I had it. And then it was a matter of doing some control experiments showing it was rather nucleus sensitive, acting on mice and resistant and things like that, that indicated that it was RNA being copied, sorry, it was DNA being copied from RNA, not from DNA, not from anywhere else and we published it. |
| Q11 | At the same time without your knowing I guess, Howard Temin was having exactly the same problem in Wisconsin and you published the papers back to back. How did you get to know about each other? |
|  | He had a post doc, Mr Towney, who was working … Howard himself was definitely not a biochemist but Mr Towney was, and Mr Towney was working on this virus, Rous sarcoma virus, and I didn’t know that, I’d never heard of Mr Towney. I had not been in contact with Howard for a number of years, just hadn’t run into him, but I knew he’d be interested, so the moment that I had the data and was in the process of writing it up I called him to tell him, because I just knew he’d be interested. He then told me that he was working on the same thing and he also had data. I said, Well, let’s publish it together. I had already, I think maybe I had submitted the paper that day, so he quickly got his stuff together and submitted it about 10 days later and *Nature* did not take long to publish it. |
| Q81 | Although for you the discovery of reverse transcriptase did not come as a real big surprise because you had anticipated that and that … to also for Howard Temin. The rest of the world were taken not by surprise, but even it was shocking news, because the centre of dogma at the time was that genetic information could only flow from DNA via RNA to protein, and now you went through against the central dogma. Was that immediately accepted by the scientific community? |
|  | It was accepted and it was accepted largely because two of us had made the discovery, I think if one of us had made the discovery it would have taken a lot longer before people took it seriously and because Saul Spielman upon hearing about this went back to the laboratory and immediately got his people doing the experiment because he had wanted to find something like this but hadn’t really done the right experiment and he was able to reproduce it in no time at all. I don’t think there was anybody within a week or two, I don’t think there was anybody who doubted that the experiments were reproducible and correct. People could have worried about the meaning of the experiment because we had not really demonstrated what people thought we had demonstrated. And we said that. What we had demonstrated was that there was a polymerase in the virion in the virus particle that could copy RNA into DNA. If you set up the Kornberg polymerase correctly it will copy RNA to DNA. It could have been a DNA polymerase that usually copies DNA but that happened to copy RNA was a contaminant of the virus particle. That’s one of many hypotheses, because we had no genetic evidence that this was critical, we didn’t even know it was encoded by the virus at the time, there’s no way to know that. We certainly didn’t know that the DNA that was being made, although hybridised to the RNA so we knew it was a real copy, we didn’t know it had biologic abilities, that it was a real intermediate in the growth of the virus.  On the other hand, I must say everybody accepted our evidence as saying that and it’s a very interesting story in the sort of history of ideas, why a certain kind of experiment captures the community’s fancy and they believe it and believe all it’s implications right away even though, and the investigators may understand, should understand the limitations of it, people won’t think about it. Other kinds of experiments for one reason or another, all everybody thinks about is the limitations and they never think about … They won’t take this as the answer. I can think of two examples like that, one was the Avery experiments that showed that DNA was the genetic material, that was 1944 and yet most of the scientific community didn’t believe that until 1952 when [Hershey](https://www.nobelprize.org/prizes/medicine/1969/hershey/facts/) and Chase did an experiment that was certainly no better and arguably a lot worse than the Avery experiment. Why was one experiment accepted and not the other, is the time, is the idea right, or was it the nature of the experiment? I think it’s the nature of the experiment and I could talk about what it is, but I don’t really know what the nature is that’s so important.  Another example was, and that may have been pure stubbornness, when the [Watson](https://www.nobelprize.org/prizes/medicine/1962/watson/facts/)–[Crick](https://www.nobelprize.org/prizes/medicine/1962/crick/facts/) model was published. The Watson-Crick model implied that these intertwined strands of DNA colour pairing are duplicated and the best minds of the scientific community, Allbrook, Leventhal, others at the time, focused on the difficulty of imagining that you could unwind the strands, that was the big question. There are many many papers published about the difficulty of unwinding the strands and actually Leventhal published the only sensible article about it in which he said it’s not a big difficulty, because he actually calculated the forces involved. But that was the generation of the Meselson-Stahl experiments. The Meselson-Stahl experiment … There’s a whole book about this that I’ve just been reading. Meselson was very careful to say that his work only showed that the nitrogen in DNA was semiconservatively distributed during DNA synthesis, but the scientific community immediately said that the unwinding problem is not a big problem, clearly that’s how DNA works, done. It was the years later before it was really proven that that’s how it worked. Why was the Meselson-Stahl experiment so influential and yet really limited in what it said. I don’t know. Anyway, our experiment was very influential and the world was very comfortable right away, but it was really hill and hell over. A pair of Czech scientists who a number of years later showed that the DNA intermediate that you can get from cells were infectious DNA that proved that there was a DNA intermediate. We didn’t prove it. |
| Q23 | … and you were awarded the prize say just five years afterwards, in 1975, together with Howard Temin for the discovery of a reverse transcriptase. That’s an unusually short period for the assembly to be convinced of the impact of the discovery. Could you comment on the downstream effects of your discovery, the role of reverse transcriptase in biomedical research after that. |
|  | I think the Nobel assembly was responding to one thing which was that our discovery of reverse transcriptase, whatever it said about the biology of the virus, provided the technology for working with retro viruses and turned an intractable viral system into an easy manipulable viral system because you had available of biochemistry to use. You could find out what the genes were, you could find out how the replication worked, you could uncover all of its secrets and ultimately because you could then find oncogenes using the copies of the RNA as probes. I think by 1975 that was eminently clear and probably, well certainly rarely in history have there been so many papers published that followed from an initial observation as there were published in the cancer research literature following our discovery. Cancer is the thing that frightens people most in the whole medical world and was at that point a virtually intractable disease, it’s still a very difficult disease, so a major step forward in cancer research was something that, in a sense it’s not surprising that the Nobel Assembly responded and responded to quickly and it was real. I don’t take credit for the fact that our observations lead to that, it was just that that turned out to be the bottle neck and then suddenly everything opened up. I think that’s what they were responding to.  Two other things happened soon thereafter but they weren’t clear in 1975. One was that we had also opened up biotechnology and we didn’t know that, but a year or two after we discovered the polymerase, we learned how to make enough of it, we learned how to assay it with exogenous templates, not just what was in the virus, turned out it purified easily. Then /- – -/ working in my laboratory as well as somebody working with Phil Leder showed that you could copy globin messenger RNA with it and that was in terms of bio technology one of the most important discoveries that was made, because it opened up the whole ability to capture the information in messenger RNAs as DNA and allowed you to use what then became cloning technology but of course that was only after 1974, 1975. You could use cloning technology to insert genes and detectors and to manipulate them and so that was a really central technology. But it wasn’t so obvious by -75 that that was true.  The third thing was obviously only done in 1982-83 and that was the discovery of HIV, because HIV is a retro virus like the ones we’d been working on and was in fact discovered by its reverse transcriptase activity, that was a tremendous downstream advantage. Had HIV been discovered in 1970 rather than 1980, nobody would have known how to look for it, because we wouldn’t have had that information. If it were discovered in 1960, ten years before reverse transcriptase. The world would have been a terrible place for that because it was already getting to be a terrible place by 1982 because of fear. It’s the kind of thing we now see with mad cow disease, when you don’t know the biology of a situation people get terrified about where the disease might come from and how it might affect them and they stop eating meat even though the meat of the animals probably doesn’t have any chance to hurt them. This stopped sex and dealt with a transmission of a basically sexual disease. It was a terrible time for two or three years there when we didn’t know it was a virus and every hypothesis you could imagine was being suggested. It was an immune response to semen, was a classic thought. It never occurred to me but some other people, so yes, the discovery had lots of downstream impact and that was enormously gratifying. It continues to be, we just sequenced the genome, the human genome, and it turns out to be on the order of 50% of the human genome comes about by reverse transcription so it’s not exactly a small mechanism in biology. |
| Q6 | And you were 37 when you got the prize. The general idea is that once you get the Nobel Prize your scientific career is almost over and it’s deleterious for your future research. How did the prize affect you? |
|  | It affected me in lots of ways, I became a sort of semi-public figure, but I tried hard not to live up to the prize, that is to somehow change the way I lived because I was a Nobel Prize winner, and most of the time I could manage to live without thinking about it. I just continued to do science the way I wanted to do science and have done so since. The year I won the prize, 1075, I was on sabbatical in New York with a clear desire to change the orientation of the science I was doing. The reason for that goes right back to where we began this, that cloning technology had come along and it was now clear that we were going to be able to do with animal cells what we had previously only been able to do with viruses or with bacterial cells, because we could take out the genes one by one and clone them and characterise them and put them in bacteria and deal with them that way. I said to myself this is the time to move to a mammalian cell system that would enable me to look at genes in mammalian cells rather than genes of viruses. The system that I really wanted to work on was the immune system and I should have gone to a laboratory where I could do that, but most of the laboratories where I could do that were either far away or I didn’t want to be there. I instead went to Jim Darnell’s laboratory in New York at Rockefeller, partly because it was comfortable for me, partly because my parents were in New York and partly because the important thing was to get away. The Nobel Prize followed me and so I didn’t have the nice quiet year that I expected to have, but I did manage one way or another to learn enough and think enough and talk to enough people to decide that I could move into immunology and use the background that I had effectively in immunology. I’d always had immunology in my sights ever since I was at the Salk Institute because at the Salk Institute I’d become very friendly with a number of immunologists particularly Martin Weigert and Mel Cohn and they were extremely clear thinkers and they had oriented my thinking about immunology in a very, what turned out to be very productive and what seemed to be then a very precise way and it was a focus on, again the molecular mechanisms on, gene rearrangements on somatic mutation and … so that’s in fact what I did. |
| Q34 | This time in the mid 1970s was also a very critical time for the development of recombinant DNA technology, I think -75 was a critical year. You together with some prominent scientists raised the warning finger and you convened a meeting in Asilomar to discuss what the implications of the new recombinant DNA technology could be and the risks involved. That also led to a moratorium of gene cloning or recombinant DNA work in Cambridge, Harvard and MIT. Could you tell a little about why you took that step and whether that was a thing you would re-do if you would re-live it. |
|  | There was a presentation at a Gordon conference in the summer of 197-, I think it’s -74 it may be -73, that Maxine Singer had been involved, I think she’d organised the meeting and she wrote a letter to the National Academy of Sciences along with the other co-organiser of the meeting Dieter Söll saying that at this meeting it had been announced that it was possible to put together pieces of DNA from different sources and re-insert them into bacteria and get them to be maintained and that was the start of recombinant DNA technology. Anybody could look downstream and see that this was going to be a dominant technology of molecular biology from then on. But there were a lot of concerns and there were some very particular ones that made sense to me. One was that you could spread animal viruses if you tried to put the whole copy of an animal virus into a bacterium, because the bacteria could be a source of the virus and that this was a sort of unnatural system of spread. Same thing was that you could spread antibiotic resistance because you could put genes for antibiotic resistance into bacteria in the lab in this cloning way and then they would spread to other places. And there were some other concerns that we had that were, I think, pretty precisely focused. Then there was some very vague general concern about whether we really knew what we were doing if we were going to put genes from any source into any other animal or plant or bacteria.  We didn’t know how to respond to this concern so the first thing we did was that a small group of senior people got together to talk about it. Actually, the letter was sent to the National Academy, the National Academy called [Paul Berg](https://www.nobelprize.org/prizes/chemistry/1980/berg/facts/) and said, Paul, help, what do we do about this? Paul called me and I said, Let’s have a meeting. We all got together at MIT actually, in the cancer centre, on the fifth-floor conference room in the cancer centre and talked for a day about this. In the end we decided that first of all this is a problem that, this is a situation that if it became a real problem was going to get out of hand very rapidly. Unless we stopped what people were doing and had a breather and thought about it for a while, we were just going to march ahead without thinking, so we said this is a situation which we needed to monitor. We called this form moratorium in the sign of the community, we didn’t have any status to do this, but we did it and we wrote a letter that was published in PNAS and in Science magazine signed by Paul Berg and me and Jim Watson and Norton Zinder and a whole group of people. We brought that letter to the National Academy as a response to their concern, and it was adopted by the National Academy as an appropriate action. As far as I know it was absolutely observed by everybody in the community and it said, Let’s not do certain kinds of experiments – and it was the kinds that I talked about, antibiotic resistance, genes and virus genomes and that sort of thing – and let’s get up some kind of regulatory framework around this.  The big question that none of us knew enough about, it was partly because of the people who were there, was what’s the natural history of virus, of bacteria that we grow in the laboratory. Some of us felt that probably anything you grow in the laboratory is so feeble as an organism and is so full of genes that you put in there and mutations you put in there that it couldn’t possibly grow in nature. But other people said, How do you know that’s true? and we didn’t and How do you know that it couldn’t share it’s genetic material with some other organism in nature and so maybe it can’t grow but it can transform another or make with another organism? and we didn’t know. We felt there were a lot of questions there and there were some people who knew about this, who had worked more on unnatural situations. We said, Let’s all get together and have a meeting and talk about the science that underlies the kinds of issues that concerned us, and ask ourselves are these issues? We put together an international meeting which was held the next year at Asilomar, known as Asilomar 2, because we had all been together concerned about another set of biological safety issues and we had Asilomar 1 a couple of years before that. The recommendations that came out of Asilomar 2 was that we should keep the moratorium in place effectively – we didn’t like the word moratorium but that’s what it was – but find a way of dealing with the question serially and reducing the kinds of containment that were necessary to do these experiments or establishment containment and then reduce over time, which meant two things. We needed a national panel to oversee this on a continuing basis and that was established as the recombinant DNA advisory committee of the NIH and that we had at all costs avoid legislation because as soon as there was legislation, and there was a lot of public interest at that time, it was going to be frozen in stone and almost impossible to reverse because once you put in some regulatory framework and legislation, getting it out of there is politically very difficult. |
| Q82 | Let me go back two steps here. The molecular analyses of animal viruses lead to the discovery of the reverse transcriptase that lead to the unravelling of the mechanism how retroviruses or congenic viruses replicate. That in turn took you to gene therapy, HIV, to the oncogenes and so forth and so on. You have covered very broad areas during your 40 year’s career. Could you tell me … In retrospect everything looks very logical, you go from A to B to C, could you tell how your science evolved, was it a logic rational approach to new problems or does it only look like that from retrospect? |
|  | There was certainly never any logic in prospect. That is, I never said to myself in 1960 that if I start working on animals viruses I can go to cancer and that I can go to the immune system and development. It was little steps. I started working on picornaviruses and then I saw a little opportunity and I moved into other kinds of viruses and found the reverse transcriptase and that lead me to think about cancer and so I started some systems based in cancer viruses. Then one of those turned out to transform B lymphocytes so that was an attractive notion to go into immunology. And then, as I described to you, I also had other reasons to think immunology was interesting, so it was as if lightening had struck twice and was telling me something. I worked on Abelson virus and Abelson virus turned out to transform the B lymphocytes and I was interested in /- – -/ transfer which turned out to be a key determinant of gene arrangement, somatic mutation in lymphocytes. It sounded like I ought to work more seriously in that area so I moved into that area, did more work in that area. So, there was always a reason and always a connection between the past and the future but I was never consciously directing myself so that I would end up somewhere. I was just following my nose and then not being afraid to take a step to the side or a step in a new direction when that opportunity seemed to be ripe. |
| Q82 | And this was showed that basic science is unpredictable, you never know where you actually go. |
|  | Careers are unpredictable, at least productive careers are unpredictable. It’s not so much that basic science is unpredictable, although it is, it certainly is, and you never do know where the exciting things are going to come from. But then you have to be sensitive to them and willing to respond to them and I think a lot of people aren’t, spend their life mining just that area that they started out in without branching out into other areas and it’s a shame. |
| Q34 | We live in a very exciting time in science today with genome projects, we have gone from viruses to bacteria to simple organism, now we have the human genome to attend to. Could you predict what this will mean for the scientific development and the implications of the human genome? |
|  | There are two implications of the human genome that I find very powerful. One of them is that we have come to closure on the question of what genes there are in humans, or in mice or in other animals for that matter, plants even. Closure means that now when I do an experiment, I never have to say maybe there’s something out there I don’t know about which is causing that effect. Maybe I don’t know what’s causing the effect, but I know where to find it, it’s in that catalogue. I may not know how to read the catalogue, I mean don’t know where to look, but I know what my problem is, my problem is where in that catalogue is it all coming from, not is there something out there I’ve never seen before, nobody’s ever seen before. That’s a different way to do science. It’s a closed system rather than an open system. The other big thing and that’s really affecting how I’m doing work today is that we can scan the whole genome for its response to a given situation, just take as an example, I infect a cell with a virus. Up until now, I looked at the cell and said what was different about it by looking at specific proteins or specific cytology or specific something or other, because that’s what I was interested in, but I was never able to say what are all the changes in this cell that are going on.  Today, at least at the level of gene expression, I can say what are all the things that are going on and measure them all and that’s what these gene chips do for you, the ability to scan the genome. Again, it’s a different kind of science. At a certain stage it’s not even hypothesis driven, it’s just let’s have a look, but then all sorts of hypotheses come out of that so it’s just observational science for a moment like back in the days when Harvey first opened the body and looked inside that lead to lots of hypotheses. And that’s incredibly exciting and just nails you to do things, so having closure and having the ability to scan the whole system all at once are two things that are just going to make science different. |
| ID | **0615** |
| Biographical | I was born in Catanzaro, Italy, from a Calabrese mother and a Ligurian father. I stayed in that city for a short time; my father was called into the army (World War I) and we moved to the north, Cuneo and Torino. At the end of the war my father, who was in the “Genio Civile”, was sent to Imperia, Liguria, where we stayed for many years. The life I remember begins at Imperia, where I went to school, including the Ginnasio-Liceo “De Amicis”. What I remember most of that period, besides my family and the few friends, was the rocky beach where I spent most of my time during the summer holiday, and a small meteorological observatory, where I used to spend lots of my free time throughout the year. There I developed a strong liking for physics, which I put to good use by building an electronic seismograph, probably one of the first of its kind, which actually worked.  I graduated from high school at 16 (1930) and went to the University in Torino. Although I liked especially physics and mathematics for which I had considerable talent, I decided to study medicine. This profession had for me a strong emotional appeal, which was reinforced by having an uncle who was an excellent surgeon.  In Torino I was a very successful student, but I soon realized that I was interested in biology more than in applied medicine. So I went to work with Giuseppe Levi, the professor of Anatomy, where I learned Histology and the rudiments of cell culture. For my degree, however, I went to morbid anatomy and pathology. In Levi’s laboratory I met two students who later had a strong influence on my life: [Salvador Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) and [Rita Levi-Montalcini](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1986/index.html).  All through the student years I was at the top of my class although I was two years younger than everybody else.  After taking my MD degree in 1936 I was called up for military service as a medical officer. In 1938 I was discharged and returned to pathology. A year later, however, I was called up again because of the Second World War. I was sent briefly to the French front, and a year later to Russia. There I had a narrow escape on the front of the Don during a major Russian offensive in 1942: I was hospitalized for several months and sent home. When Mussolini’s government collapsed and Italy was taken over by the German army I hid in a small village in Piemonte and joined the Resistance, as physician of the local partisan units. I continued to visit the Institute of Morbid Anatomy in Torino where I joined in underground political activities together with Giacomo Mottura, a senior colleague. I was part of the “Committee for National Liberation” of the city of Torino, and became a councillor of that city in the first postwar city council. However, the life of routine politics was not for me and within months I left that position to return to the laboratory. I also went back to school, enrolling in regular courses in physics, which I pursued for the next two years.  I moved back to Levi’s Institute and worked together with Levi-Montalcini, who encouraged me to go to the USA to work in modern biology. My dream was to work in genetics of some very simple organism, possibly using radiations. This dream became a reality after Luria, who had been in the USA since the beginning of the war, and was working in this very field, came in the summer of 1946 to Torino. He encouraged me and offered me a small salary for working in his group. I was urged in this direction by Rita Levi-Montalcini, who was herself preparing to go to another laboratory in USA. So in the autumn 1947 we both embarked for the US.  I went to work with Luria in Bloomington, Indiana, where I shared with him a small laboratory under the roof, to be soon joined by [Jim Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html). Within a year I had made two good pieces of work, using my mathematical knowledge, and discovered photoreactivation of phage inactivated by ultraviolet light. This attracted the interest of [Max Delbrück](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html), who offered me a job in his group at Caltech.  I moved to Caltech in the summer 1949. I remember that memorable trip from Indiana to California with my family in an old car, with our limited possessions in a small trailer behind. I was fascinated by the beauty and immensity of the USA and the kindness of its people. Reaching the Pacific Ocean in Oregon was like arriving at a new world, an impression that continued and increased as we made our way south to Pasadena. I resolved at that time that I would not like to live anywhere else in the world – a resolution that I changed only some twenty-three years later.  At Caltech I continued to work with phages for a few years. One day I was told by Delbrück that a rich citizen had given Caltech a fund for work in the animal virus field. He asked me whether I was interested. My medical background and the experience gained in Levi’s laboratory came back to me and I accepted. After visiting the major centers of animal virus work in the US I set out to discover the way to assay animal viruses by a plaque technique, similar to that used for phages, using cell cultures. Within less than a year, I worked out such a method, which opened up animal virology to quantitative work. I used the technique for studying the biological properties of poliovirus. These successes brought me an appointment first to associate professor, then to full professor at Caltech.  In the late fifties I had as a student [Howard Temin](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html), who, together with Harry Rubin, then a postdoctoral fellow in my laboratory, worked on the Rous Sarcoma Virus. Their work started my interest in the tumor virus fields. I myself started working on an oncogenic virus, polyoma virus, in 1958, and continued until now. This work has led to discovering many aspects of the interaction of this virus (and of SV40) with the host cells in lytic infection and transformation.  I moved from Caltech to the Salk Institute in 1962, and in 1972 to the Imperial Cancer Research Fund Laboratories in London. One of the reasons for the latter move was the opportunity to work in the field of human cancer.  My work throughout the years has been strongly influenced by my associates. Giuseppe Levi taught me the essential value of criticism in scientific work, Rita Levi-Montalcini helped me to determine my goals at an early stage; Salvador Luria introduced me to viruses; [Herman Muller](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1946/index.html), at the University of Indiana taught me the significance of Genetics; Max Delbrück helped me understand the scientific method and the goals of biology, and Marguerite Vogt contributed to my knowledge of animal cell cultures. Perhaps more important than all this, the daily interaction through the years with a continuously changing group of young investigators shaped my work. For although I had general goals, the actual path followed by my research was pragmatically determined by what could be done at any given time, and my young collaborators were an essential part of this process. I always did as much as possible of the experimental work with my own hands, but in the later part of my research career this became progressively less feasible, both because the demand on my time increased and because the increasing technical sophistication and complexities of the experiments demanded a great deal of specialized skills.  Since 1962 my scientific life has had the support of my second wife, Maureen, who for some years helped in my experiments. Without her affectionate encouragement and sound advice I doubt whether I would have been able to accomplish what I have done.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1975*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1976  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1975 Addendum, August 2005 After I received the Nobel Prize my research interest shifted to the study of naturally occurring cancers. I concentrated on a model system, mammary cancers induced in rats, and I spent some time learning how to work with them. In 1977 I returned to the Salk Institute, where I continued, with some collaborators, in the new direction, concentrating on the normal development of the gland. Using monoclonal antibodies against our cells we could identify several different types of cells, and proposed a role for them in the development of the gland.  During this work I became aware of the major difficulty in trying to identify cell types and their roles in both development and carcinogenesis. It became obvious to me that some major effort had to be made to gain knowledge of the genes active in cells; the determination of the genes present in a given species would be the starting point. I thus suggested the starting of a genome project in two lectures I gave in 1985 and 1986. These suggestions remained without consequences. Thus I wrote a paper to the same effect in *Science* in 1986. The paper had enormous resonance, at first mostly negative, but very soon converted into positive. In the end it helped the emergence of the genome project.  In 1988 I was asked to act as temporary president of the Salk Institute, and soon I was promoted to regular president, a position I held until 1992. During this time I gave up my lab, in order to concentrate on the needs of the Institute, which was going through a very difficult period. In 1992 I was asked by the Italian National Research Council to organize an Italian Genome Project. For this purpose I spent, in the following years, about half of my time in Italy. The Italian Project produced some results, but was handicapped by the isolation of the researchers and the limitation of facilities and financing. It came to an end after five yeas, and was not renewed.  During these years I collaborated with investigators of the National Research Council and of the National Cancer Institute in Milan. We continued the study of mammary development, using a tissue culture system in which differentiation occurs in vitro. We identified several genes controlling the process, some in a positive, others in a negative way. We also started investigating the changes in gene expression in human breast cancer, using two new approaches for improving the results: one was the isolation of pure cancer cells in order to avoid contamination with genes expressed by various types of normal cells present in a cancer; the other was to adopt the SAGE approach to measure gene expression, in order to avoid the complications of the microarray technology. The results can be interpreted as implicating the mammary stem cells in the origin of the cancer.  At the beginning of 2006, when I will reach 92 years of age, I will give up the Italian connections, and will retire at La Jolla, to follow the work going on at the Salk Institute, and to play the piano.  *Renato Dulbecco died on 19 February 2012.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0615** |
| Interview |  |
|  |  |
| ID | **0616** |
| Biographical | I was born on December 10, 1934 in Philadelphia, Pennsylvania, United States of America, the second of three sons of Annette and Henry Temin. My father was an attorney, and my mother has been continually active in civic affairs, especially educational ones. My older brother, Michael, is also an attorney in Philadelphia, and my younger brother, Peter, is a Professor of Economics at the Massachusetts Institute of Technology, Cambridge, Mass.  I received my elementary and high school education in the public schools of Philadelphia. My specific interest in biological research was focused by summers (1949-1952) spent in a program for high school students at the Jackson Laboratory in Bar Harbor, Maine, and a summer (1953) spent at the Institute for Cancer Research in Philadelphia. I attended Swarthmore College from 1951 to 1955, majoring and minoring in biology in the honors program. After another summer (1955) at the Jackson Laboratory, I became a graduate student in biology at the California Institute of Technology in Pasadena, California, majoring in experimental embryology. After a year and a half, I changed my major to animal virology, becoming a graduate student in the laboratory of Professor [Renato Dulbecco](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html). My doctoral thesis was on Rous sarcoma virus. Much of my early work on this virus was carried out with the dose collaboration of Dr. Harry Rubin, then a postdoctoral fellow in Professor Dulbecco’s laboratory. At Cal Tech, I was also greatly influenced by Professor [Max Delbrück](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) and by Dr. Matthew Meselson. After finishing my Ph.D. degree in 1959, I remained for an additional year in Professor Dulbecco’s laboratory as a postdoctoral fellow. In that year, I performed the experiments that led to the formulation in the same year of the provirus hypothesis for Rous sarcoma virus.  In 1960, I moved to Madison as an Assistant Professor in the McArdle Laboratory for Cancer Research, which is also the Department of Oncology, in the Medical School, The University of Wisconsin-Madison. My first laboratory was in the basement, with a sump in my tissue culture lab and with steam pipes for the entire building in my biochemistry lab. Here I performed the experiments that led in 1964 to my formulating the DNA provirus hypothesis. In the fall of 1964, the entire department moved to a new building. I became successively Associate Professor, Full Professor, Wisconsin Alumni Research Foundation Professor of Cancer Research, and, in 1974, American Cancer Society Professor of Viral Oncology and Cell Biology. From 1964 to 1974, I also held a Research Career Development Award from the National Cancer Institute.  During my first years at Wisconsin, I worked with only two technicians. My first postdoctoral fellow joined me in 1963, and my first graduate student, in 1965. I had no more than two or three postdoctoral fellows and graduate students at one time until about 1968.  During the late 1960’s, about half of my time was spent in studying the control of multiplication of uninfected and Rous sarcoma virus-infected cells in culture. This work led to my appreciation of the role of specific serum factors in the control of cell multiplication and the demonstration that a multiplication-stimulating factor in calf serum for chicken fibroblasts was the same as somatomedin.  I serve on the editorial boards of several journals, including the *Journal of Cellular Physiology,* the *Journal of Virology,* and the *Proceedings of the National Academy of Sciences U.S.A*. I have also been a member of the Virology Study Section of the National Institutes of Health. In addition, I do much other paper and grant reviewing.  Since the general acceptance of the DNA provirus hypothesis in 1970, I have received many honors, including the Warren Triennial Prize (with [David Baltimore](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1975/index.html)); the Pap Award of the Papanicolaou Institute, Miami, Florida; the Bertner Award, M. D. Anderson Hospital and Tumor Institute, Houston, Texas; the U. S. Steel Foundation Award in Molecular Biology, National Academy of Sciences U.S.A.; the American Chemical Society Award in Enzyme Chemistry; the Griffuel Prize, Association Developpment Recherche Cancer, Villejuif, France; the G.H.A. Clowes Award, American Association for Cancer Research; the Gairdner International Award (with David Baltimore); the Albert Lasker Award in Basic Medical Research; and honorary degrees from Swarthmore College and New York Medical College. I have also presented several honorary lectures. I am a fellow of the American Academy of Arts and Sciences and a member of the National Academy of Sciences, U.S.A.  In 1962 I married Rayla Greenberg of Brooklyn, New York, a population geneticist. She has been a constant source of support and warmth. We have two daughters, Sarah Beth and Miriam. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | **0617** |
| Biographical | I was born in Belgium, in 1899. Longlier, my birthplace, is located in a high point of the Belgian Ardennes, atop the rising spur of an eroded remnant of the foot of the Alps, next to a deep valley. In the Middle Ages, it had been a fortified place, of the Francs and Carolegian dynasties. Pepin le Bref, crowned King of the Francs in 751 spent in Longlier two winters, from October to Easter, in the years 750 and 763. His son Charlemagne who by then had become Emperor of the Occident called a High Court of Justice of the Empire to meet in Longlier: the diploma, still preserved, was signed by him there in 771. In the year 1050, the Charlemagne Villa became a Monastery, and renamed later “Ferme Charlemagne”. In the 17th-18th century, it was adorned with a high sloping roof “à la mansarde”, whereas the round towers, standing high at the wall corners, matched the roof with elegant, bell-shaped tops, a situation which remained unchanged until 1914.  The landscape of the Longlier region is covered with remnants of the primeval forest of oak trees, progressively invaded by evergreens. The bluegreen color of the pines, which blends with the blue-grey color of the massif of slate rocks emerging through a meager soil gives the countryside an aspect, severe, but also of serene beauty, and even more, when the pure coat of the snow covers it during the long and cold winters.  The population was sparse, at least at the time I was a boy. Our agglomeration was made of scattered small farms, regrouped into hamlets which, with the village, amounted to about 800 inhabitants in all. Rarely, because the people were few, a funeral procession was climbing slowly from the valley, back of our house, and to the old church next to the Charlemagne farm, with the cemetery between them.  The unique school of the Longlier region was built at the outskirt, a kilometer from my home, and about equal distance from the surrounding hamlets, so that the children could leave their home, and reach the school at about the same time. Actually, this school was just a single room with high windows, and a central stove, fed with coal and wood, by the teacher himself. As I remember, there was a set of 5 benches at either side of the stove, with a common sitting board which could accommodate 5 children, in all 50 seats, for an average population, from year to year, of 40 pupils, at the most. The sexes and grades were mixed, and the ages, from 6 to 11 years old. All the courses were taught at the same time, in the same room, by the same and unique teacher. Under this highly pluralistic system, the school was running smoothly, and the results, as remembered over the years, turned out to be, in every respect, excellent.  As usual for the time, the roads were not lighted at night, and no water distribution was available, nor in prospect. Due to the elevation of the site, we had to rely on rainwater, collected from the roofs, and on the clear water, filtering and running from the bare rocks, to the river and the streams below.  In the Ardennes, the washed soil is poor, and the configuration rugged. When the spring and summer came, the heat of the sun brought life and beauty to the land. The farmers, however, rose early and worked late, each on their farm, relatively far apart, without the occasion, or the need, to communicate between themselves. Even more than in the cold of the winter, there was a strange stillness, in the heat of the afternoon.  After supper, and when the daily work was over, we did not light the kerosene lamp, nor the makeshift carbide lamp we used, when the war came upon us, but sat outdoors, in the silence and the darkness of the night. As many have done before us, since the early rise of mankind, I reclined on the sloping back of a chair, and gazed intensely, and for hours, at the quivering milky way, and watched the coming of falling stars.  When I became old enough, I took my turn in getting up early, and ringing the church bells (there were two of them) calling for the daily mass, at six o’clock in the morning. The ropes of the bells were hanging freely down the hollow shaft of the church tower, so that we could seize them and pull them from the ground, with the bells seen overhead. When the bells were in full swing, we used to grasp the rope firmly and let ourselves be lifted, just when the hammer hit the roaring bronze. This little familiarity had created an affectionate and reciprocal understanding between us and the Bells. One night, during a heavy storm, we were awakened by a crash. The Pepin le Bref tower, as it was called, which had stood there for many centuries had collapsed, bringing down, with it, the church bells. A few years later, in 1914, the madness of war reached our peaceful shores; the Charlemagne Villa, and part of the village, next to our home, was burnt. I was 15 years old, and starting to become an adult. For us, and for the dying Europe, and the thousands years of its past, it was a new World, and the end of an Era.  My grandfather was born in 1830, just the year the Flemish and French speaking Catholics decided to secede from the Lutheran Dutch people of the low lands, governed by the House of Orange. His place of birth was not Longlier. For a number of generations tracing back to the 17th century, his ancestors had been active in maintaining a Relay, or Stagecoach stop, providing horses, food and lodging for travellers, and wagons for the conveyance of goods. The site of this undertaking was a small plateau, about the locality of Offaing, rising from the opposite side of the Longlier valley, away and higher up from the Charlemagne Villa. From this rather ancient time, I have a witness helping me to imagine and recreate the past. It is a chest of heavy oak with a secret lock, and a slit with a receptacle underneath, in which the hostess, my great-grandmother, would drop the coins she received from the customers, in payment for their expenditure at the inn. This chest, for the past twenty years, has been in my bedroom, next to my bed, supporting a lamp and a clock.  My great-grandfather, Godfroid, born on the heights of Offaing in 1800, or about, had five or six sons, including my grandfather, and a similar number of daughters, most of them promised to live well over ninety. In this healthy, no doubt dynamic, but crowded environment, my grandfather may have felt the pressure of competition, but most likely happened to the most adventurous and most farsighted: he decided to move and settle on his own.  Following the Belgian revolution of 1830 the new nation decided to give itself a King, the choice being Léopold, Prince of Saxe-Cobourg and recent widower of the heir of the throne of England, with the crowning in 1831. Léopold the First was a man of high character and wisdom. It is to his knowledge of the industry of England and to his own initiative that Belgium owed to have had the first railroad lines on the Continent, the first one connecting Bruxelles with Antwerp and its harbor. The next undertaking was much more ambitious. This second line was to be transcontinental, starting from Brussels, through Namur, Luxembourg, Vienna, and further on.  The Longlier valley gap, however, which happened to stand exactly across the projected direction of the new railroad line, would have to be bridged. In addition to this technical difficulty, it was found that the Devonian synclinal, which is the geologic substructure of the region was disturbed by a tectonic anomaly in the form of a narrow band, less than one kilometer in width, which had become deflected in front of the Longlier valley, passing just under the terminal point where the construction of the railroad had stopped. The problems were such that the construction of the line was postponed, for an undetermined length of time. My grandfather saw the opportunity and moved to Longlier. Apparently, he was not without means. Within a relatively short time he built a hotel, next to the freight depot of the railroad terminus. From the commissioned Agency handling the freight traffic for the line, the “Messageries Van Gent”, he obtained some agreement whereby he would be responsible for the freight that landed at the Terminal, for its distribution outside the railroad areas. Very soon, he had horses and wagons distributing goods and wares in various directions, as far as the north of France, especially Sedan and Bazeilles, where we had some relatives. His business prospered rapidly, and he became relatively wealthy.  For me, this story of railroads and of a diligent grandfather, which I have recalled, has been more meaningful than the effect of a tectonic anomaly on a Devonian synclinal. Without the decision of my grandfather to move to Longlier, my mother would have been someone else, and there would have been no tales of ringing bells in a medieval church tower, and no ailing uncle to take care of. It was a question of being, or not being. Once the first step taken, what remains to deal with are the important but universal problems of the individual, versus his environment. My mother, Glaudice Watriquant, was 45 years old when I was born, and my father 43. I was the youngest of four, two brothers and one sister, with a gap of 9 years with the oldest. As it happened, most of my early years were spent in the company of old, or very old people, each having their problems and ailments, but never complaining. This created a pervading feeling of tolerance, kindness, and stoic strength which made me happy and feel secure.  For a while, my father worked for my grandfather. As a child eight years old he was already accompanying the driver, not much older than himself, returning by night bringing back fresh vegetables and labile goods from the renowned French market-garden of Fonds-de-Givonne. They took turn to rest, although the traffic was rare at night, especially in the long forest roads; moreover, the horses knew the way and kept on driving even if both drivers fell asleep, as occurred more than once. It was pleasant for youngsters to wake up at the songs of the birds, in a mellow summer night. I would have enjoyed it as they did. My father was gentle, and romantic, in tune with his century. He liked to memorize poetry, from Lamartine, and especially Victor Hugo, whom he admired the most. When he returned from his work and we were very young, we asked him to recite verses to us or sing a lieder, quite well, of the same vein. When he came of age, my father chose to become a baker and pastry maker, perhaps as a complement to the hotel, and for which he spent three years of training in Paris. He was there the year the poet Hugo died. On the Champs Elysées early, he found his way on the top of a gas lamp-post from where he watched pass the funeral procession of hundreds of thousands, for hours. It was in 1885, and my father was 29. It was also his last year of training. His first residence when married, two years later, was in the right wing of the Charlemagne Farm, next to the round tower, and my eldest brother was born there. The second residence, with the bakery and a store, where my second brother and my sister were born, was next to the railroad station. By the time of my birth, my father had taken over a former property of my grandfather, remodeled it and added a large building to serve as a kind of general store. During my time, the local work was already done by hired bakers, my father being away all day, taking care of orders and deliveries.  Two or 3 years after I was born, my mother developed a carcinoma of the breast which appeared shortly after she hurt herself in a fall. She died when I was 7. Too young to go to school, and my elder brothers away in the high school in the town nearby, I was with her most of the time. She suffered, but calmly. I was careful not to make demands on her, and tried to help her when I could. Neighbours and acquaintances came to visit her, sometimes two or three at a time. They didn’t pay attention to me; on their way out I followed them to the door, and heard them describe, in their own way, the future course of the disease. I was sad but kept it to myself. Not to leave me alone at home, she took me with her when visiting some healer that had been recommended to her. For one of them, in Marbehan, we had to take the train. Living close to her and partaking of her pain, I felt more and more being as a little nurse at her side. But like the grown-ups of that time, I could not help.  The death of our mother made a big change in the family. After a few years of increasing difficulties (there was a pre-war depression going-on), the decision was made to move to Athus, a prosperous steel mills region bordering both France and the Grand Duchy of Luxembourg. A couple of years before we left, my eldest brother Léon, student at the high school was sitting, one day, at the kitchen table with a book flat beside him. Cautiously, I approached him and said, pointing the right hand page to him: what is this? I remember that, in order to see the page, I had to stand on the tip of my toes, and stretch my head forward. What I saw was the simple outline of a retord, drawn in a square, marginal indentation of the text. My brother did not turn me but began to explain, molding his words with his hands. I did not remember what he said, and could not understand their technical meaning, but as he was speaking I felt my chest, my heart, and the roots of my soul expand. It was a revelation, never to be forgotten. How beautiful this world within the book. I intensely wished to see and know more. In the innocence of my age, I did not doubt that I could. I was 8 1/2 years old. The kitchen table of our youth followed in Athus, an is now in Brussels, in the kitchen of our home.  My attendance at the Longlier primary school was curtailed more than a year before the moving. When we arrived in Athus, we found ourselves in an essentially German speaking community. In the church, the hymns and prayers were said in German, and German was spoken in the school where I was received. Every day at 4 PM, each pupil in turn had to read aloud a chapter of the bible. The bible in use, and of which I had a copy, was printed in gothic characters of the oldest type. I may have practiced the sound of them at home, orduring the long, idle hours in the school: when my turn came, I succeeded in reading my part aloud without knowing the words. Again, as before in the world of the aged people I had lived in, I was made to observe my environment from without, in an abstract way, as visitors in an aquarium.  After a year or two, I was asked to return to Longlier to help in the care of an uncle who had suffered a major cerebral hemorrhage. His right side was paralyzed and he had lost the use of his speech. He was tall and heavy, and my aunt was in her 60th year, and ailing. Soon, I took over all the care of my uncle, day and night, and later, progressively the responsibility of the management and the routine work of the household. I was about 13 years old, and more duties and problems of other sorts were added when the war came. My only outside contacts then were the frequent visits of the doctor, who came regularly, or when we called for him in case of emergencies. He came driving himself his horse and cab which he used also when making the rounds of his patients in the country. To me, he looked old, but must have been less than 60. He had experience and common sense, and never seemed in a hurry. I reported to him about my uncle, and listened to his comments and advices. Finally, we conversed about other subjects and the news of the day. This familiarity with a respected physician and my appreciation of his work, or the tragedy I experienced with the long, tormented agony and death of my mother might have influenced me in wanting to study medicine. It was not the case. As far as I remember, even younger than eight, I have always been guided by reason. Not cold reason, but that which leads to the truth, to the real, and to sane Justice. When I went to the University, the medical school was the only place where one could hope to find the means to study life, its nature, its origins, and its ills.  Summarized Civic and Academic Status  Albert Claude was born in Longlier, Belgium, August 24, 1899, and obtained his medical degree from the Université de Liège, Belgium, in 1928.  He spent the winter of 1928-29 in Berlin, first at the Institute für Krebsforschung, and then at the Kaiser Wilhelm Institute, Dahlem, in the laboratory of tissues culture of Prof. Albert Fischer.  He joined the Rockefeller Institute (now the Rockefeller University), in the summer of 1929, and has been connected with this Institution, in different degrees, ever since.  He is Director emeritus of the Jules Bordet Institute for Cancer Researche and treatment, and Professor emeritus, the Faculty of Medicine, at the University of Brussels, Belgium.  He is now Professor, at the Rockefeller University, New York, N.Y., and Professor, at the Université Catholique de Louvain, Louvain, Belgium.  He is Director of the “Laboratoire de Biologie Cellulaire et Cancérologie”, at the Université Catholique de Louvain, Louvain-la-Neuve, Belgium. |
| Autobiographical |  |
| Podcast |  |
| Telephone interview | **0617** |
| Interview |  |
|  |  |
| ID | **0618** |
| Biographical | I was born on October 2nd 1917, in Thames-Ditton, near London. My parents, of Belgian-German extraction, were Belgian nationals who had taken refuge in England during the war. They returned to Belgium in 1920, and I grew up in the cosmopolitan harbour city of Antwerp, at a time when education in the Flemish part of the country was still half French and half Flemish. Due to these various circumstances, when I entered the Catholic University of Louvain in 1934, I had already travelled in a number of European countries and spoke four languages fairly fluently. This turned out to be a valuable asset in my subsequent career as a scientist.  That I would embrace such a career was, however, very far from my mind. My education, according to the tradition of the jesuit school which I attended, had been centered on the “ancient humanities”, and I was strongly attracted to the more literary branches. I nevertheless decided to study medicine, largely because of the appeal of medical practice as an occupation. Medical studies left a fair amount of free time in those days, and there was a tradition at the university that the better students joined a research laboratory. So it was that I entered the physiology laboratory of Professor J. P. Bouckaert, whose rigorous analytical mind exerted a strong influence on my intellectual development. I was attached to a group investigating the effect of insulin on glucose uptake. By the time when I graduated as an MD in 1941, I had abandoned all thought of a medical career, and had only one ambition: to elucidate the mechanism of action of insulin.  In the meantime, war had broken out. After a brief interval in the army and a temporary stay in a prisoners’ camp, from which I promptly escaped thanks to the general confusion which followed the disastrous defeat of the allies, I had returned to Louvain to complete my studies. I had become convinced that the problem of insulin action needed to be approached by means of biochemical methods. Since research activities were almost paralysed due to lack of essential supplies, I embarked an another four-year curriculum, to gain the degree of “Licencié en Sciences Chimiques”. I combined these studies with a clinical internship in the Cancer Institute, with as much experimental work as war circumstances allowed, and with extensive reading of the earlier literature on insulin.  As a medical student, I had been rather relaxed, but I worked really hard during those four years. Still I could not have achieved what I did without the support of my clinical chief, Professor Joseph Maisin, who enthusiastically approved of my plans and gave me a great deal of free time. By 1945, I had presented a thesis on the mechanism of action of insulin, which earned me the degree of “Agrégé de l’Enseignement Supérieur”, written a 400-page book entitled “Glucose, Insuline et Diabète”, and prepared a number of research articles for publication.  By that time, the war had ended and I felt a great need of further training in biochemistry. In 1946-1947, I had the good fortune of spending 18 months at [the Medical Nobel Institute](http://www.nobelprizemedicine.org/) in Stockholm, in the laboratory of [Hugo Theorell](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1955/index.html), who was awarded the Nobel Prize in 1955. I then spent 6 months as a Rockefeller Foundation fellow at Washington University, under [Carl and Gerty Cori](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html) who jointly received the Nobel Prize while I was there. In St. Louis, I collaborated with [Earl Sutherland](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1971/index.html), Nobel laureate in 1971. Indeed, I have been very fortunate in the choice of my mentors, all sticklers for technical excellence and intellectual rigour, those prerequisites of good scientific work.  I returned to Louvain in March 1947 to take over the teaching of physiological chemistry at the medical faculty, becoming full professor in 1951. I started a small research laboratory, where I was joined by a young physician, Gery Hers, who had already worked with me during the war, and by an increasing number of first class students, including Jacques Berthet, Henri Beaufay, Robert Wattiaux, Pierre Jacques and Pierre Baudhuin. All have since carved distinguished careers for themselves.  Insulin, together with glucagon which I had helped rediscover, was still my main focus of interest, and our first investigations were accordingly directed on certain enzymatic aspects of carbohydrate metabolism in liver, which were expected to throw light on the broader problem of insulin action. But fate had a surprise in store for me, in the form of a chance observation, the so-called “latency” of acid phosphatase. It was essentially irrelevant to the object of our research but it was most intriguing. My curiosity got the better of me, and as a result I never elucidated the mechanism of action of insulin. I pursued my accidental finding instead, drawing most of my collaborators along with me.  Our investigations were very fruitful. They led to the discovery of a new cell part, the lysosome, which received its name in 1955, and later of yet another organelle, the peroxisome. At the same time, we were prompted to develop progressively improved instrumental, technical and conceptual tools in relation to the separation and analysis of cell components, and to apply them to an increasing variety of problems of biological and also medical interest.  In 1962, I was appointed a professor at the Rockefeller Institute in New York, now the Rockefeller University, the institution where [Albert Claude](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/index.html) had made his pioneering studies between 1929 and 1949, and where [George Palade](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/index.html) had been working since 1946. I retained my position in Louvain and have since shared my time more or less equally between the two universities. In New York, I was able to develop a second flourishing group, which follows the same general lines of research as the Belgian group, but with a program of its own. The two laboratories work closely together and complement each other in many respects.  Recently, with a number of colleagues, I have created a new institute, the International Institute of Cellular and Molecular Pathology, or ICP, located on the new site of the Louvain Medical School in Brussels. The aim of the ICP is to accelerate the translation of basic knowledge in cellular and molecular biology into useful practical applications.  In September 1943, I married the former Janine Herman, the daughter of a physician. We have four children, three of whom are married, and two grandchildren.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1974*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1975  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1974 Addendum, December 1997 Since the writing of this note, our fourth child has married and the number or our grand-children has risen to 7. I still share my time between Belgium and New York, but my professional duties have slowly come to an end. I became emeritus at the University of Louvain in 1985 and at the Rockefeller University in 1988. My duties as president of the ICP ended in 1991, but I still remain on the board of this institute, as Founder-Administrator.  Much of my time and effort have been devoted to the ICP, where some 270 investigators and technicians work on a variety of problems of basic science and on the application of their findings to medical progress. About one-third of the institute is occupied by the Brussels branch of the Ludwig Institute for Cancer Research. The head of this branch, Professor Thiery Boon, is also my successor as director of the ICP.  In the last few years, I have become increasingly interested in the origin and evolution of life. I have written three books, which have been translated in a number of languages: *A Guided Tour of the Living Cell* (New York: Scientific American Books, 1984); *Blueprint for a Cell* (Burlington, NC: Neil Patterson Publishers, 1991); and *Vital Dust* (New York: Basic Books, 1995). I plan to devote my remaining years to further probing what, if anything, our growing understanding of life and mind can tell us about the structure and meaning of the universe.  *Christian de Duve died on 4 May 2013.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0618** |
| Interview |  |
| Q23 | Why don’t we start and say that this interview is in the Insel Halle during the Lindau meeting and I’m Sten Orrenius. And I have the pleasure of carrying out this discussion with Professor Christian de Duve who received the Nobel Prize in 1974 for discoveries concerning the structural and functional organisation of the cell together with Albert Claude and George Palade. And my first question is perhaps a banal one, but I would like you to comment briefly on how it all started. |
|  | I won’t give you the whole history of my life, but basically when I entered university I wanted to become a physician. That was my goal. But then when I was in medical school I had some free time and spent it in a physiology laboratory doing some research under a professor there and I was so enthusiastic about research that I found it difficult to finish my medical studies, because I didn’t want to waste time getting a clinical training, but anyway, I finished. By that time the war had started in Belgium and I was interested at that time in insulin, the mechanism and action of insulin. I decided that I could not solve this problem with the kind of techniques that I was using in this rather traditional physiology laboratory. I decided I needed biochemistry. Since I had time on my hands, I went back to school and studied chemistry and got a degree in chemistry, doing many other things at the same time, including being an assistant in a cancer hospital, at least to get the food and lodging.  Anyway, the war was ended and then I decided now I know medicine and biology, I know chemistry, it’s time to become a biochemist. There were really not very good biochemists in my university, and also I want to take advantage of newly gained freedom, get out of the country and find the training I needed elsewhere. I had been, before the war already, I had been to Sweden and to Norway, I knew the countries and I loved them very much, and since Sweden had not known occupation, I thought well let me try and find something in Sweden. I had known a Swedish girl, she was really Hungarian, who was a chemist, and she worked with [Hans von Euler](https://www.nobelprize.org/prizes/chemistry/1929/euler-chelpin/facts/) and I decided I would go and work with von Euler. I wrote to her, I hadn’t seen her for five years of course, and I wrote to her and she said Hans von Euler is passé, you should go to [Hugo Theorell](https://www.nobelprize.org/prizes/medicine/1955/theorell/facts/), he is the coming man in Stockholm. I wrote to Theorell, I wrote a letter in which I explained all this. I said I don’t know anything about biochemistry. I want to become a biochemist. I would work on any problem you give me.  Amazingly, he accepted me. I still don’t understand why he accepted me because, I had a thesis, but on insulin. So anyway, that’s how I spent 18 months at the Medicinska Nobelinstitutet, Hantverkargatan 3 in Stockholm. Those were fantastic months, I really enjoyed them. But when I came there, I will tell you, I said to Theorell: I know nothing about biochemistry, you’ll just have to give me a problem, any problem, which was crystallising human myoglobin, that’s the problem he gave me, so that I can learn the techniques. He sent me to a fantastic man, who’s dead now, you may have known him, Åkesson, who was his first technician, but who eventually became a PhD and a professor at the end of his years. Åke Åkesson was a fantastic teacher, he really taught me to pipette, to measure pH, to precipitate proteins with amino, and so on and so on. I learned the trade from Åke Åkesson. I learned many other things from Theo, as we all called him, Hugo Theorell, who was a wonderful man. Also I met a number of very interesting people because that laboratory had become world famous, and so by the time I was there, after I arrived, I was about the first one to come, there were a number of Americans, Breton Charles arrived, and John Buchanan, there was Ralph Holman, there Chris Athenson arrived the day I left, so it had become a major laboratory. And I will always remember those times which were really wonderful and of course I got to learn the Sweden and there are many other stories, including Nobel stories, that I could tell, but there isn’t time and it’s not important here.  Then after Theorell, I went for six months to work with [Carl](https://www.nobelprize.org/prizes/medicine/1947/cori-cf/facts/) and [Gerty Cori](https://www.nobelprize.org/prizes/medicine/1947/cori-gt/facts/) in Washington University in St Louis because I wanted to get back to my main problem which was insulin, and of course they worked on that. There I was able to work for five months with [Earl Sutherland](https://www.nobelprize.org/prizes/medicine/1971/sutherland/facts/), in fact, together we established that glucagon is made by the alpha cells of the pancreatic islet. Finally at the beginning of 1948 I came back to Belgium to start my own laboratory. You can see I’ve been very, very lucky because Hugo Theorell got the Nobel Prize in Medicine in 1955, Carl and Gerty Cori got it in 1947, just while I was there, and Earl Sutherland got it in 1971, so chance has it that all my mentors were … Even my Belgian mentors were not Nobel Laureates but had worked with Nobel Laureates. They always ask whether the Nobel Prizes are hereditary and not genetically I think, although there are a couple of father and son pairs. But I think science, and this is really a rather important message, I think science, especially the art, the craft of scientific research, is not learned in books. The only way you can learn to do good science is to work under a good or several good scientists. |
| Q8 | I wondered because we have just heard a panel discussion on creative milieus in science and certain things were brought up there, among those differences between Europe and America. I would like to come back to this and ask you the question: if you compare the creativity and the milieus in the Theorell laboratory when you came as a post-doc, with the Cori laboratory and your time in America, at that time were there obvious differences? Was one more European and the other more American? Or were they pretty similar would you say? |
|  | The Cori’s came from Europe, and their laboratory was much more the hierarch kind of, European, they were very autocratic. We all did what we wanted but it was all very, you know, their door was not open all the time. Whereas Hugo Theorell, Theo, he was available all the time. He would be in the lab, he would talk with people, he would sing, he would walk on his hands, because he had polio and had a problem walking on his legs, so he would be walking on his hands, singing. I would have lunch with him every day. That was a privilege, I don’t know why. Anyway we would try to talk French, he liked to use me to speak French. We never spoke of science. Mostly we spoke of music because Theo, as you know, was a very good violinist and Margit, his wife, she was a concert pianist and a harpsichord player. We spoke of music, we spoke of many things but rarely of science. |
| Q43 | Would you say that from that aspect that the Theorell laboratory at the time was a pretty unusual or uncommon European laboratory? |
|  | I’ve never known in my life a laboratory that had a very strong boss and a hierarchical organisation. Wherever I went there was a tremendous conviviality and collaboration and lack of formalism between professor and students. I think perhaps the better scientists are probably less … insist less of being on top of the mountain and looking down on those students and so on, because I think you have to feel insecure to want to put this distance between you and the other people. But good scientists are not insecure. |
| Q34 | There are several other interesting aspects I would like to bring up in this interview, and that is when you returned to Belgium from the United States, you returned to go back to your work, maybe you had gone back to your insulin work already at the time, and you had pursued that very actively for a long period of time. You went back to Belgium and then during the late 1950s you changed your direction of research. |
|  | No, it started much earlier. To try to make it very short, all these 12 years that I had devoted to my personal training had as a final goal to elucidate the mechanism of action of insulin on liver, that’s what I wanted to do. As soon as I had my own lab and a small group of collaborators, I decided that I would study some of the biochemical aspects, enzymatic aspects of liver to try and find out what made it so difficult to demonstrate this action of insulin in vitro on liver. Then I chose an enzyme that had in fact been discovered by the Cori’s, but not characterised by them, because I thought it might be a very critical enzyme in this whole mechanism because it exists in liver and not in muscle and that may be a big difference. That was glucose 6-phosphatase.  Our first work was to characterise, trying to purify glucose 6-phosphatase. Now it turned out that, I’ll try not to go into details, but when we tried to purify this enzyme by standard techniques we came to the conclusion that it must be bound to some structure. The main conclusion was that at pH5 the enzyme would be precipitated and then it would remain precipitated, even at the external, so it was not isoelectric precipitation, it was some kind of agglutination. Claude had just described his techniques for fractionation and so I said – it was a difficult decision – let’s find out what structure by using Claude’s technique. We did that first, we developed our first system for centrifugal fractionation following published techniques and quickly demonstrated that glucose 6-phosphatase is basically a microsomal enzyme. It’s bound to microsomes, now we know it’s bound to membranes of the endoplasmic reticulum. That was that. We knew about that and at the same time we had proved something, namely that microsomes correspond to a special cell, but which was not yet clear at that time. It so happened that at the same time we had been studying another phosphatase, acid phosphatase. Not because we were interested in it, but because when we purified the glucose 6-phosphatase we had to separate it from the acid phosphatase. We also measured the acid phosphatase on the fractions. And run into this – now it’s a well-known observation, at that time it was very surprising – namely that in our fractions the enzyme had disappeared. We could not find it or very small amounts. I thought at first that we’d made a mistake and five days later, we kept the fractions in the refrigerator, and we re-assayed them and there the enzyme was. One thing leading to another, I thought that was a mystery, the missing enzyme and so on, why is it missing, why is it not?  One thing leading to another, I left insulin on the back burner to find out why acid phosphatase did not show its normal activity. When you know the answer it was because it was inside a little bag and as long as the membrane of that bag was intact, the enzyme would not be able to act on an external substrate. You open the membrane, it comes out. it acts on the substrate, that was a fascinating observation. I left insulin on the back burner for a little longer and went after that, because there were a couple of other enzymes that were possible candidates for this kind of behaviour, beta-glucuronidase and cathepsin D, indeed they did behave in the same way. Then two others were found to behave in the same way, acid ribonuclease and acid dioxygenase, and by 1955 we had published already six tissue fractionation papers. And the number six has in it the word lysosol, that’s when the word lysosome was invented, so you see by 1955 I was already very much immersed in this kind of work. Although in the lab many people were still working, and are still working today, on carbohydrate metabolism. And so peroxysomes followed lysosomes in fractionation and so we discovered the peroxysomes. And that is basically how I became a cell biologist. I never used an electron microscope in my life. In fact, we did not even have a microscope when we did all this work. All this work was strictly biochemical. I discovered, if you like, tried isolated those two new cell paths, lysosomes and peroxysomes using strictly the approachable biochemist when he purifies a protein using fractionation techniques of one sort of another, chemical measurements to follow my enzyme. |
| Q23 | The latency of the acid phosphatase led to the work on lysosomes and the discovery and characterisation of the lysosome. Was there a similar observation that led to the peroxysomes? |
|  | No, it turned out that when you fractionate using the classical technique then the lysosomal enzymes sediment about two thirds with the mitochondrial fraction, one third with the microsomal fraction. We devised a technique with an additional very small intermediate fraction between the mitochondria and the microsomes in which those enzymes were highly concentrated so that they are associated with particles that are a little smaller than mitochondria but bigger than microsomes and so they sediment in between. From working the literature in particular, some work that was done by Alex Novikoff, who became as you know the electron microscopist most interested in lysosomes and peroxysomes. I included in our measurements an enzyme that might be a candidate for the lysosomes and that was urate oxidase, uricase. It behaved the same way but it was not latent. It had an alkaline pH optimum where all the others have an acid pH optimum. We said, well that looks like maybe something different, and so we followed, we found other enzymes, diamino acid oxidase, catalase, lactic acid oxidase, behaving in the same way and not being latent, except catalase for some special reason. We developed new techniques based on density gradient centrifugation, in which we were able to separate those two groups, lysosomes on one hand and the non-hydrolytic enzymes which were mostly oxydasers plus catalase. And that was the peroxysomes, which we now know of course to be very complex organelles in some plants and in some lower animals and so on. |
| Q83 | When you had gone back to Belgium and developed your career and became professor at the University of Louvain you continued to build the group and to do your research. Then, a bit later you also were recruited as a professor to the Rockefeller University as it was at the time, and from my early time in research, I remember you having passes to major research institutions or research groups, both contributing enormously to the cell biology field. How did that come about and how important were these two appointments, the two milieus? |
|  | That is one of the many lucky accidents in my life. Belgium, I had a wonderful group, you know their names: Berthet, Beaufay … They were really excellent people, but it was a very, very hard job for me because I had to do all the teaching of biochemistry for the medical students, to take all of the examinations which took me two months. I had administration, I had to find funds for this group and so on, and to direct a group that was getting bigger and bigger. It was a very, very big load and I found it a little difficult. And one day I visited George Palade, I was travelling in the United States and I was in his office and I said, My God, you are really fortunate, I wish I could work here. Just like that. George looked at me and he said, Do you mean this? I said, Yes George, I mean it. Six months later Detlev Bronk, the President of the Rockefeller University offered me a job.  Then came the complications because I wanted to work there and at the same time when the opportunity came, there was the problem of family, I could’ve taken my family with me, I had four children by that time, but there was also the problem of what would happen to my Belgian lab and so on. Bronk came to Louvain, talked to the director and finally they agreed, because suddenly the director of Louvain had discovered some qualities in me. I was relieved of most of my academic duties in Louvain and I was accepted by both, to share about 50% of my time between the two, that’s how I was able to start a new lab at Rockefeller. But this was supposed to be for five years and I’m still commuting today. It became permanent. But it was a crazy business, I mean to run two labs on each side of the Atlantic, nobody would say that’s a good way of doing science. But I had so many good co-workers that it was possible. I would always take one of my Belgian co-workers with me to New York. When I went back to Belgium he would keep on. We were able to do in New York, thanks to the Rockefeller, a large amount of work that I would not ever have been able to do. Now perhaps since you were talking about my career, perhaps I should add one more thing, if you don’t mind. Namely that I changed again, I’ve changed my field twice since. In 1975 I opened this new institute in Brussels, the ICP, which is a small biomedical research institute more or less copied on Rockefeller but on a much smaller scale. I went back to medicine, finally to medical research through that institute. Then in the last 10-15 years I have found new interest with origin of life and evolution. |
| ㅃ5 | I think it’s very important that you say so. I was going to more or less end my questioning by coming back to your fantastic career and that you have developed world renowned laboratories, at least three of them, and also recruited so many internationally very well-known scientists and followers. Would you have some final comment on creativity or how as a teacher and a mentor should you be in order to achieve what you have achieved? |
|  | I think it’s been said today already, namely that it’s extremely important to collaborate, to communicate, to be open to the ideas of others. I think it’s extremely important to give young people freedom. I think they should be allowed freedom. The important thing in life is to recruit the best, that’s the most difficult thing, find the best. Give them an environment in which they are able to develop their own potential, the best that is. Not only the instruments, the techniques, but the colleagues, the atmosphere, there must be some kind of environment in which creativity is fostered, in which freedom is fostered. I think basically that is the important thing. The secret of creativity, I would not know, it’s a very complex cocktail. Certainly to be a first class scientist, it is not sufficient to be intelligent. In fact, I’ve known some of my co-workers who were very much, and I’m not being modest, much more intelligent than I am, but they never achieved perhaps the same kind of science that I achieved because they lacked something which is I think extremely important for this cocktail, and that’s imagination. And that is where science and art get together. Namely, imagination is a quality common to both and essential to both. |
| Q6 | Has the Nobel Prize changed your career in some way to the better or the worse? |
|  | I would be completely dishonest if I said it had not changed my career. First of all, it was a tremendous pleasure when I got it, a tremendous encouragement. We all like recognition and we all know that we’ve done some good work and that we may be candidates, but as you know very well, there’s a big distance between being a candidate and being a laureate. And there is an element of chance there also. Sometimes I tell people, I think I won the big lottery. They say no, you’re being much too modest. I say but the tickets are very expensive. Anyway, to get back to your question, it has changed my life in many ways. I think it has made a number of things easier, at least in Belgium it has made it easier for me to get some funding and support for my new institute which was opened just the day I came back from Stockholm, so that was very helpful. It certainly has given me personally a certain amount of visibility which one may or may not enjoy. Certainly it has given me opportunities to do things, like being invited to conferences and symposium and so on. All that I would say was rather positive.  The negative aspects, in the United States for instance, I had a feeling it was more difficult to get financial support for some wild reasons that I don’t know, but anyway I had some problems. Maybe my science was not so good anymore. Then of course one wastes a lot of time because of all these things like being interviewed for television, things like that. I would say that perhaps what I would consider the most negative aspect about Nobel Prizes, and now I’m being really very serious, is that within the scientific community it establishes a distance between individuals that is not deserved. Within the scientific community there are many scientists who I consider just as good, if not better than me. I know many who could’ve shared the prize with me and did not share it. As you know some of the people, the unlucky candidates, who do not become laureates can suffer very much. I think it’s a pity within the scientific community to create this kind of super class of scientists who have this little Nobel badge and are greeted everywhere like being very special, although they are just the same as all the others. I think that’s dangerous. Since we’re talking about the Nobel Foundation here, I think there is a redeeming aspect to this. Namely, within the scientific community, maybe it’s a pity that something like the Nobel Prize exists, but for the relationship of the scientific community in the outside world, I think the Nobel Prizes have been tremendous because somehow they have caught the collective imagination of the world. The respect for Nobel Prize winners, which is not deserved, anyway becomes translated in the general public into some kind of respect for science. I think in this way the Nobel Foundation, by giving those high prestige prizes, have probably done an enormous amount of good for the visibility of science within the general community, for the appreciation by every people, not enough perhaps, but to some extent of the importance and the significance of science. |
| ID | **0619** |
| Biographical | I was born in November 1912 in Jassy (Iasi), the old capital of Moldavia, the eastern province of Romania. My education was started in that city and was continued through a baccalaureate (continental style) at the “Al Hasdeu” Lyceum in Buzau. My father, Emil Palade, was professor of philosophy and my mother, Constanta Cantemir-Palade, was a teacher. The family environment explains why I acquired early in life great respect for books, scholars and education.  My father had hoped I was going to study philosophy at the University, like himself, but I preferred to deal with tangibles and specifics, and – influenced by relatives much closer to my age than he was – I entered the School of Medicine of the University of Bucharest (Romania) in 1930.  Early in my student years I developed a strong interest in basic biomedical sciences by listening to, and speaking with, Francisc Rainer and André Boivin, professors of Anatomy and Biochemistry, respectively. As a result, I started working in the Anatomy laboratory while still in medical school. I went, nonetheless, through six years of hospital training, mostly in internal medicine, but I did the work for my doctorate thesis in microscopic anatomy on a rather unusual topic (for an M.D.): the nephron of the cetacean *Delphinus delphi.* It was an attempt to understand its structure in terms of the functional adaptation of a mammal to marine life.  I graduated in 1940 and, after a short period as an assistant in internal medicine, I went back to Anatomy, since the discrepancy between knowledge possessed by, and expected from, the medical practitioners of that time made me rather uneasy.  During the second world war, I served in the medical corps of the Romanian Army, and after the war – encouraged by Grigore Popa, Rainer’s successor – I came to the United States in 1946 for further studies. I worked for a few months in the Biology Laboratory of Robert Chambers at New York University and, while there, I met [Albert Claude](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1974/index.html) who had come to give a seminar on his work in electron microscopy. I was fascinated by the perspectives opened by his findings and extremely happy when, after a short discussion following his seminar, he asked me to come to work with him at The Rockefeller Institute for Medical Research in the fall of the same year. This was truly a timely development, since Chambers was retiring that summer.  At The Rockefeller Institute, Claude was working in the department of Pathology of James Murphy with George Hogeboom and Walter Schneider as direct collaborators; Keith Porter was in the same department but had developed his own line of research on the electron microscopy of cultured animal cells. At the beginning, I worked primarily on cell fractionation procedures, and I developed with Hogeboom and Schneider the “sucrose method” for the homogenization and fractionation of liver tissue. This first “Rockefeller group” had a rather short existence: Schneider returned to the University of Wisconsin, Hogeboom moved to the National Cancer Institute, and Claude went back to Belgium in 1949 to assume the directorship of the Jules Bordet Institute. Only Porter and I remained at The Rockefeller Institute; two years later, upon Murphy’s retirement, we became “orphans” and were adopted by [Herbert Gasser](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1944/index.html) then the director of the Institute, since none of us had the rank required to head a laboratory.  Around that time, I started working in electron microscopy with the general aim of developing preparation procedures applicable to organized tissue. This line of research had been tackled before by a few investigators, Claude included, but there was still ample room for improvement. Taking advantage of whatever techniques were already available, Porter and I worked out enough improvements in microtomy and tissue fixation to obtain preparations which, at least for a while, appeared satisfactory and gratifying. A period of intense activity and great excitement followed since the new layer of biological structure revealed by electron microscopy proved to be unexpectedly rich and surprisingly uniform for practically all eukaryotic cells. Singly, or in collaboration with others, I did my share in exploring the newly open territory and, in the process, I defined the fine structure of mitochondria, and described the small particulate component of the cytoplasm (later called ribosomes); with Porter, I investigated the local differentiations of the endoplasmic reticulum and with Sanford Palay I worked out the fine structure of chemical synapses. With all this activity, our laboratory became reasonably well known and started functioning as a training center for biological electron microscopy. The circumstances that permitted this development were unusually favorable: we didn’t have to worry about research funds (since we were well supported by Herbert Gasser), we had practically complete freedom in selecting our targets, strong competitors who kept us alert, and excellent collaborators who helped us in maintaining our advance.  In the middle 1950’s, I felt that the time was ripe for going back to cell fractionation as a means of defining the chemical composition and the functional role of the newly discovered subcellular components. The intent was to use electron microscopy for monitoring cell fractionation. I was starting from structural findings and morphological criteria seemed appropriate for assessing the degree of homogeneity (or heterogeneity) of the cell fractions. Philip Siekevitz joined our laboratory in 1955 and together we showed that Claude’s microsomes were fragments of the endoplasmic reticulum (as postulated by Claude in 1948) and that the ribosomes were ribonucleoprotein particles. To find out more about the function of the endoplasmic reticulum and of the attached ribosomes, we started an integrated morphological and biochemical analysis of the secretory process in the guinea pig pancreas.  In 1961, Keith Porter who had been the head of our group since 1953 joined the Biological Laboratories of Harvard University and, with his departure, the history of the second “Rockefeller group” came to an end. It was during this period that cell biology became a recognized field of research in biological sciences and that the Journal of Cell Biology and the American Society for Cell Biology were founded. Our group participated actively in each of these developments.  In the 1960’s, I continued the work on the secretory process using in parallel or in succession two different approaches. The first relied exclusively on cell fractionation, and was developed in collaboration with Philip Siekevitz, Lewis Greene, Colvin Redman, David Sabatini and Yutaka Tashiro; it led to the characterization of the zymogen granules and to the discovery of the segregation of secretory products in the cisternal space of the endoplasmic reticulum. The second approach relied primarily on radioautography, and involved experiments on intact animals or pancreatic slices which were carried out in collaboration with Lucien Caro and especially James Jamieson. This series of investigations produced a good part of our current ideas on the synthesis and intracellular processing of proteins for export. A critical review of this line of research is presented in the Nobel Lecture.  In parallel with the work on the secretory process in the pancreatic exocrine cell, I maintained an interest in the structural aspects of capillary permeability, that goes back to the early 1950’s when I found a large population of plasmalemmal vesicles in the endothelial cells of blood capillaries. Along this line of research, Marilyn Farquhar and I investigated the capillaries of the renal glomeruli and recognized that, in their case, the basement membrane is the filtration barrier for molecules of 100A diameter or larger; a byproduct of this work was the definition of junctional complexes in a variety of epithelia. Visceral (fenestrated) capillaries were investigated with Francesco Clementi, and muscular capillaries with Romaine Bruns and Nicolae and Maia Simionescu.  The capillary work has relied primarily on the use of “probe” molecules of known dimensions detected individually or in mass (after cytochemical reactions) by electron microscopy. It led to the identification of the passageways followed by large water-soluble molecules in both types of capillaries and by small molecules in visceral capillaries. The pathway followed by small, watersoluble molecules in muscular capillaries is still under investigation.  In the middle of the 1960’s our laboratory began a series of investigations on membrane biogenesis in eukaryotic cells using as model objects either the endoplasmic reticulum of mammalian hepatocytes (with P. Siekevitz, Gustav Dallner and Andrea Leskes), or the thylakoid membranes of a green alga (*Chlamydomonas reinhardtii*) (With P. Siekevitz, Kenneth Hoober and Itzhak Ohad). These studies showed that “new” membrane is produced by expansion of “old” preexisting membrane (there is no *de novo* membrane assembly), and that new molecules are asynchronously inserted, and randomly distributed throughout the expanding membrane. Asynchrony also applies to the turnover of membrane proteins in the endoplasmic reticulum as shown by work down with P. Siekevitz, Tsuneo Omura and Walter Bock.  In 1973, I left the Rockefeller University to join the Yale University Medical School. The main reason for the move was my belief that the time had come for fruitful interactions between the new discipline of Cell Biology and the traditional fields of interest of medical schools, namely Pathology and Clinical Medicine. Besides, my work at the Rockefeller University was done: when I left there were at least five other laboratories working in different sectors of cell biology.  At present I am investigating, together with my collaborators, the interactions which occur among the membranes of the various compartments of the secretory pathway, namely the endoplasmic reticulum, the Golgi complex, the secretion granules, and the plasmalemma.  I have been a member of the National Academy of Sciences (U.S.A.) since 1961, and I have received in the past a number of awards and prizes for my scientific work, among them: the Lasker Award (1966), the Gairdner Special Award (1967), and the Hurwitz Prize – shared with Albert Claude and Keith Porter (1970).  Since my high school years I have been interested in history, especially in Roman history, a topic on which I have read rather extensively. The Latin that goes with this kind of interest proved useful when I had to generate a few terms and names for cell biology.  I have a daughter, Georgia Palade Van Duzen, and a son Philip Palade from a first marriage with Irina Malaxa, now deceased. In 1970 I married Marilyn Gist Farquhar who is a cell biologist like myself. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0619** |
| Interview |  |
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| ID | **0620** |
| Biographical | I was born on 20 November 1886 in Vienna, the son of university professor Anton Ritter von Frisch and his wife Marie, *née* Exner. I studied at a grammar school and later at the University of Vienna in the Faculty of Medicine. After the first exams, I switched to the Faculty of Philosophy and studied Zoology in Munich and Vienna. I received my doctorate from the University of Vienna in 1910. In the same year I became assistant to Richard Hertwig at the Zoological Institute at the University of Munich. There I gained my University Teaching Certificate in Zoology and Comparative Anatomy.  In 1921 I went to the University of Rostock as Professor and Director at the Zoology Faculty; in 1923 I moved to Breslau and in 1925 I succeeded my former teacher Richard Hertwig in Munich. With support from the Rockefeller Foundation I oversaw the building of a new Zoological Institute with the best facilities available. After the destruction of the latter during the Second World War, I went to Graz in 1946, but returned to Munich in 1950 after the Institute had been reopened. I have been a Professor Emeritus since 1958, and have continued my scientific studies. Of my published papers the following are the most important:  Der Farben und Formensinn der Bienen: Zoologische Jarbücher (Physiologie) 35, 1-188, (1914-15). (*The bee’s sense of colour and shape.*)  Über den Geruchssinn der Bienen und seine blütenbiologische Bedeutung: Zoologische Jahrbücher (Physiologie) 37, 1-238 (1919). (*The bee’s sense of smell and its significance during blooming.*)  Über die “Sprache” der Bienen. Eine tierpsychologische Untersuchung: Zoologischer Jahrbücher (Physiologie) 40, 1-186 (1923). (*Bee’s ‘language’- an examination of animal psychology.*)  Untersuchung über den Sitz des Gehörsinnes bei der Elritze: Zeitschrift für vergleichende Physiologie 17, 686-801 (1932), with R. Stetter. (*Examination into the position of the sense of hearing in the minnow.*)  Über den Geschmachsinn der Bienen: Zeitschrift für vergleichende Physiologie 21, 1-156 (1934). (*The bee’s sense of taste.*)  Über einen Schreckstoff der Fischhaut und seine biologische Bedeutung: Zeitschrift für vergleichende Physiologie 29, 46-145 (1941). (*On the repellant substance on fish skin and its biological significance.*)  Die Tänze der Bienen: Österreichische Zoologische Zeitschrift 1, 1-48 (1946). (*The bee’s dances.*)  Die Polarisation des Himmelslichtes als orientierender Faktor bei den Tänzen der Bienen: Experientia (Basel) 5, 142-148 (1949). (*The polarisation of skylight as a means of orientation during the bee’s dances.*)  Die Sonne als Kompaß im Leben der Bienen: Experientia (Basel) 6, 210-221 (1950). (*The sun as compass in the life of bees.*)  Tanzsprache und Orientierung der Bienen, Springer Verlag Berlin-Heidelberg-New York (1965). (*The Dance Language and Orientation of Bees,* Harvard University Press, 1967.)  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1971-1980*, Editor Jan Lindsten, World Scientific Publishing Co., Singapore, 1992  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Karl von Frisch died on June 12, 1982.* |
| Autobiographical |  |
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| Telephone  interview | **0620** |
| Interview |  |
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| ID | **0621** |
| Biographical | I consider early childhood events as most essential to a man’s scientific and philosophical development. I grew up in the large house and the larger garden of my parents in Altenberg. They were supremely tolerant of my inordinate love for animals. My nurse, Resi Führinger, was the daughter of an old patrician peasant family. She possessed a “green thumb” for rearing animals. When my father brought me, from a walk in the Vienna Woods, a spotted salamander, with the injunction to liberate it after 5 days, my luck was in: the salamander gave birth to 44 larvae of which we, that is to say Resi, reared 12 to metamorphosis. This success alone might have sufficed to determine my further career; however, another important factor came in: [Selma Lagerlöf](https://www.nobelprize.org/nobel_prizes/literature/laureates/1909/index.html)‘s Nils Holgersson was read to me – I could not yet read at that time. From then on, I yearned to become a wild goose and, on realizing that this was impossible, I desperately wanted to *have* one and, when this also proved impossible, I settled for having domestic ducks. In the process of getting some, I discovered imprinting and was imprinted myself. From a neighbour, I got a one day old duckling and found, to my intense joy, that it transferred its following response to my person. At the same time my interest became irreversibly fixated on water fowl, and I became an expert on their behaviour even as a child.  When I was about ten, I discovered evolution by reading a book by Wilhelm Bölsche and seeing a picture of Archaeopteryx. Even before that I had struggled with the problem whether or not an earthworm was in insect. My father had explained that the word “insect” was derived from the notches, the “incisions” between the segments. The notches between the worm’s metameres clearly were of the same nature. Was it, therefore, an insect? Evolution gave me the answer: if reptiles, via the Archaeopteryx, could become birds, annelid worms, so I deduced, could develop into insects. I then decided to become a paleontologist.  At school, I met one important teacher, Philip Heberdey, and one important friend, Bernhard Hellmann. Heberdey, a Benedictine monk, freely taught us Darwin’s theory of evolution and natural selection. Freedom of thought was, and to a certain extent still is, characteristic of Austria. Bernhard and I were first drawn together by both being aquarists. Fishing for Daphnia and other “live food” for our fishes, we discovered the richness of all that lives in a pond. We both were attracted by Crustacea, particularly by Cladocera. We concentrated on this group during the ontogenetic phase of collecting through which apparently every true zoologist must pass, repeating the history of his science. Later, studying the larval development of the brine shrimp, we discovered the ressemblance between the Euphyllopod larva and adult Cladocera, both in respect to movement and to structure. We concluded that this group was derived from Euphyllopod ancestors by becoming neotenic. At the time, this was not yet generally accepted by science. The most important discovery was made by Bernhard Hellmann while breeding the aggressive Cichlid Geophagus: a male that had been isolated for some time, would kill any conspecific at sight, irrespective of sex. However, after Bernhard had presented the fish with a mirror causing it to fight its image to exhaustion, the fish would, immediately afterwards, be ready to court a female. In other words, Bernhard discovered, at 17, that “action specific potentiality” can be “dammed up” as well as exhausted.  On finishing high school, I was still obsessed with evolution and wanted to study zoology and paleontology. However, I obeyed my father who wanted me to study medicine. It proved to be my good luck to do so. The teacher of anatomy, Ferdinand Hochstetter, was a brilliant comparative anatomist and embryologist. He also was a dedicated teacher of the comparative method. I was quick to realize not only that comparative anatomy and embryology offered a better access to the problems of evolution than paleontology did, but also that the comparative method was as applicable to behaviour patterns as it was to anatomical structure. Even before I got my medical doctor’s degree, I became first instructor and later assistant at Hochstetter’s department. Also, I had begun to study zoology at the zoological institute of Prof. Jan Versluys. At the same time I participated in the psychological seminars of Prof. Karl Bühler who took a lively interest in my attempt to apply comparative methods to the study of behaviour. He drew my attention to the fact that my findings contradicted, with equal violence, the opinions held by the vitalistic or “instinctivistic” school of MacDougall and those of the mechanistic or behavioristic school of Watson. Bühler made me read the most important books of both schools, thereby inflicting upon me a shattering disillusionment: none of these people *knew* animals, none of them was an expert. I felt crushed by the amount of work still undone and obviously devolving on a new branch of science which, I felt, was my responsibility.  Karl Bühler and his assistant Egon Brunswick made me realize that theory of knowledge was indispensable to the observer of living creatures, if he were to fulfill his task of scientific objectivation. My interest in the psychology of perception, which is so closely linked to epistemology, stems from the influence of these two men.  Working as an assistant at the anatomical institute, I continued keeping birds and animals in Altenberg. Among them the jackdaws soon became most important. At the very moment when I got my first jackdaw, Bernhard Hellmann gave me Oskar Heinroth’s book “Die Vögel Mitteleuropas”. I realized in a flash that this man knew everything about animal behaviour that both, MacDougall and Watson, ignored and that I had believed to be the only one to know. Here, at last, was a scientist who also was an expert! It is hard to assess the influence which Heinroth exerted on the development of my ideas. His classical comparative paper on Anatidae encouraged me to regard the comparative study of behaviour as my chief task in life. Hochstetter generously considered my ethological work as being comparative anatomy of sorts and permitted me to work on it while on duty in his department. Otherwise the papers I produced between 1927 and 1936 would never have been published.  During that period I came to know Wallace Craig. The American Ornitologist Margaret Morse Nice knew about his work and mine and energetically put us into contact. I owe her undying gratitude. Next to Hochstetter and Heinroth, Wallace Craig became my most influential teacher. He criticized my firmly-held opinion that instinctive activities were based on chain reflexes. I myself had demonstrated that long absence of releasing stimuli tends to lower their threshold, even to the point of the activity’s eruption in vacuo. Craig pointed out that in the same situation the organism began actively to seek for the releasing stimulus situation. It is obviously nonsense, wrote Craig, to speak of a re-action to a stimulus not yet received. The reason why in spite of the obvious spontaneity of instinctive behaviour, I still clung to the reflex theory, lay in my belief, that any deviation from Sherringtonian reflexology meant a concession to vitalism. So, in the lecture I gave in February 1936 in the Harnackhaus in Berlin, I still defended the reflex theory of instinct. It was the last time I did so.  During that lecture, my wife was sitting behind a young man who obviously agreed with what I said about spontaneity, murmuring all the time: “It all fits in, it all fits in.” When, at the end of my lecture, I said that I regarded instinctive motor patterns as chain reflexes after all, he hid his face in his hands and moaned: “Idiot, idiot”. That man was Erich von Holst. After the lecture, in the commons of the Harnackhaus, it took him but a few minutes to convince me of the untenability of the reflex theory. The lowering thresholds, the eruption of vacuum activities, the independence of motor patterns of external stimulation, in short all the phenomena I was struggling with, not only could be explained, but actually were to be postulated on the assumption that they were based not on chains of reflexes but on the processes of endogenous generation of stimuli and of central coordination, which had been discovered and demonstrated by Erich von Holst. I regard as the most important break-through of all our attempts to understand animal and human behaviour the recognition of the following fact: the elemental neural organisation underlying behaviour does not consist of a receptor, an afferent neuron stimulating a motor cell and of an effector activated by the latter. Holst’s hypothesis which we confidently can make our own, says that the basic central nervous organisation consists of a cell permanently producing endogenous stimulation, but prevented from activating its effector by another cell which, also producing endogenous stimulation, exerts an inhibiting effect. It is this inhibiting cell which is influenced by the receptor and ceases its inhibitory activity at the biologically “right” moment. This hypothesis appeared so promising that the Kaiser-Wilhelmsgesellschaft, now renamed Max-Planck-Gesellschaft, decided to found an institute for the physiology of behavior for Erich von Holst and myself. I am convinced that if he were still alive, he would be here in Stockholm now. At the time, the war interrupted our plans.  When, in autumn 1936, Prof. van der Klaauw convoked a symposium called “Instinctus” in Leiden in Holland, I read a paper on instinct built up on the theories of Erich von Holst. At this symposium I met [Niko Tinbergen](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/index.html) and this was certainly the event which, in the course of that meeting, brought the most important consequences to myself. Our views coincided to an amazing degree but I quickly realized that he was my superior in regard to analytical thought as well as to the faculty of devising simple and telling experiments. We discussed the relationship between spatially orienting responses (taxes in the sense of Alfred Kühn) and releasing mechanism on one hand, and the spontaneous endogenous motor patterns on the other. In these discussions some conceptualisations took form which later proved fruitful to ethological research. None of us knows who said what first, but it is highly probable that the conceptual separation of taxes, innate releasing mechanisms and fixed motor patterns was Tinbergen’s contribution. He certainly was the driving force in a series of experiments which we conducted on the egg-rolling response of the Greylag goose when he stayed with us in Altenberg for several months in the summer of 1937.  The same individual geese on which we conducted these experiments, first aroused my interest in the process of domestication. They were F1 hybrids of wild Greylags and domestic geese and they showed surprising deviations from the normal social and sexual behaviour of the wild birds. I realised that an overpowering increase in the drives of feeding as well as of copulation and a waning of more differentiated social instincts is characteristic of very many domestic animals. I was frightened – as I still am – by the thought that analogous genetical processes of deterioration may be at work with civilized humanity. Moved by this fear, I did a very ill-advised thing soon after the Germans had invaded Austria: I wrote about the dangers of domestication and, in order to be understood, I couched my writing in the worst of nazi-terminology. I do not want to extenuate this action. I did, indeed, believe that some good might come of the new rulers. The precedent narrow-minded catholic regime in Austria induced better and more intelligent men than I was to cherish this naive hope. Practically all my friends and teachers did so, including my own father who certainly was a kindly and humane man. None of us as much as suspected that the word “selection”, when used by these rulers, meant murder. I regret those writings not so much for the undeniable discredit they reflect on my person as for their effect of hampering the future recognition of the dangers of domestication.  In 1939 I was appointed to the Chair of Psychology in Köningsberg and this appointment came about through the unlikely coincidence that Erich von Holst happened to play the viola in a quartette which met in Göttingen and in which Eduard Baumgarten played the first violin. Baumgarten had been professor of philosophy in Madison, Wisconsin. Being a pupil of John Dewey and hence a representative of the pragmatist school of philosophy, Baumgarten had some doubts about accepting the chair of philosophy in Köningsberg – Immanuel Kant’s chair – which had just been offered to him. As he knew that the chair of psychology was also vacant in Köningsberg, he casually asked Erich von Holst whether he knew a biologically oriented psychologist who was, at the same time, interested in theory of knowledge. Holst knew that I represented exactly this rather rare combination of interests and proposed me to Baumgarten who, together with the biologist Otto Koehler and the botanist Kurt Mothes – now president of the Academia Leopoldina in Halle – persuaded the philosophical faculty in Köningsberg of putting me, a zoologist, in the psychological chair. I doubt whether perhaps the faculty later regretted this choice, I myself, at any rate, gained enormously by the discussions at the meetings of the Kant-Gesellschaft which regularly extended late into the night. My most brilliant and instructive opponents in my battle against idealism were the physiologist H. H. Weber, now of the Max-Planck-Gesellschaft, and Otto Koehler’s late first wife Annemarie. It is to them that I really owe my understanding of Kantian philosophy – as far as it goes. The outcome of these discussions was my paper on Kant’s theory of the à priori in the view of Darwinian biology. [Max Planck](https://www.nobelprize.org/nobel_prizes/physics/laureates/1918/index.html) himself wrote a letter to me in which he stated that he thoroughly shared my views on the relationship between the phenomenonal and the real world. Reading that letter gave me the same sort of feeling as hearing that the Nobel Prize had been awarded to me. Years later that paper appeared in the Systems Year Book translated into English by my friend Donald Campbell.  In autumn 1941 I was recruited into the German army as a medical man. I was lucky to find an appointment in the department of neurology and psychiatry of the hospital in Posen. Though I had never practised medicine, I knew enough about the anatomy of the nervous system and about psychiatry to fill my post. Again I was lucky in meeting with a good teacher, Dr. Herbert Weigel, one of the few psychiatrists of the time who took psychoanalysis seriously. I had the opportunity to get some first-hand knowledge about neurosis, particularly hysteria, and about psychosis, particularly schizophrenia.  In spring 1942 I was sent to the front near Witebsk and two months later taken prisoner by the Russians. At first I worked in a hospital in Chalturin where I was put in charge of a department with 600 beds, occupied almost exclusively by cases of so-called field polyneuritis, a form of general inflammation of nervous tissues caused by the combined effects of stress, overexertion, cold and lack of vitamins. Surprisingly, the Russian physicians did not know this syndrome and believed in the effects of diphteria – an illness which also causes a failing of all reflexes. When this hospital was broken up I became a camp doctor, first in Oritschi and later in a number of successive camps in Armenia. I became tolerably fluent in Russian and got quite friendly with some Russians, mostly doctors. I had the occasion to observe the striking parallels between the psychological effects of nazi and of marxist education. It was then that I began to realize the nature of indoctrination as such.  As a doctor in small camps in Armenia I had some time on my hand and I started to write a book on epistemology, since that was the only subject for which I needed no library. The manuscript was mainly written with potassium permanganate solution on cement sacking cut to pieces and ironed out. The Soviet authorities encouraged my writing, but, just when it was about finished, transferred me to a camp in Krasnogorsk near Moscow, with the injunction to type the manuscript and send a copy to the censor. They promised I should be permitted to take a copy home on being repatriated. The prospective date for repatriation of Austrians was approaching and I had cause to fear that I should be kept back because of my book. One day, however, the commander of the camp had me called to his office, asked me, on my word of honor, whether my manuscript really contained nothing but unpolitical science. When I assured him that this was indeed the case, he shook hands with me and forthwith wrote out a “propusk”, an order, which said that I was allowed to take my manuscript and my tame starling home with me. By word of mouth he told the convoy officer to tell the next to tell the next and so on, that I should not be searched. So I arrived in Altenberg with manuscript and bird intact. I do not think that I ever experienced a comparable example of a man trusting another man’s word. With a few additions and changes the book written in Russia was published under the title “Die Rückseite des Spiegels”. This title had been suggested by a fellow prisoner of war in Erivan, by name of Zimmer.  On coming home to Austria in February 1948, I was out of a job and there was no promise of a chair becoming vacant. However, friends rallied from all sides. Otto Storch, professor of zoology, did his utmost and had done so for my wife even before I came back. Otto König and his “Biologische Station Wilhelminenberg”, received me like a longlost brother and Wilhelm Marinelli, the second zoologist, gave me the opportunity to lecture at his “Institut für Wissenschaft und Kunst”. The Austrian Academy of Sciences financed a small research station in Altenberg with the money donated for that purpose by the English poet and writer J. B. Priestley. We had money to support our animals, no salaries but plenty of enthusiasm and enough to eat, as my wife had given up her medical practice and was running her farm near Tulln. Some remarkable young people were ready to join forces with us under these circumstances. The first was Wolfgang Schleidt, now professor at Garden University [1](https://www.nobelprize.org/prizes/medicine/1973/lorenz/biographical/#note1) near Washington. He built his first amplifier for supersonic utterances of rodents from radio-receivers found on refuse dumps and his first terrarium out of an old bedstead of the same provenance. I remember his carting it home on a wheel-barrow. Next came Ilse and Heinz Prechtl, now professor in Groningen, then Irenäus and Eleonore Eibl-Eibesfeldt, both lady doctors of zoology and good scientists in their own right.  Very soon the international contact of ethologists began to get re-established. In autumn 1948 we had the visit of Professor W. H. Thorpe of Cambridge who had demonstrated true imprinting in parasitic wasps and was interested in our work. He predicted, as Tinbergen did at that time, that I should find it impossible to get an appointment in Austria. He asked me in confidence whether I would consider taking on a lectureship in England. I said that I preferred, for the present, to stick in Austria. I changed my mind soon afterwards: [Karl von Frisch](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/index.html) who left his chair in Graz, Austria, to go back to Munich, proposed me for his successor and the faculty of Graz unanimously concurred. When the Austrian Ministry of Education which was strictly Catholic again at this time, flatly refused Frisch’s and the faculty’s proposal, I wrote two letters to Tinbergen and to Thorpe, that I was now ready to leave home. Within an amazingly short time the University of Bristol asked me whether I would consider a lectureship there, with the additional task of doing ethological research on the water-fowl collection of the Severn Wildfowl Trust at Slimbridge. So my friend Peter Scott also must have had a hand in this. I replied in the affirmative, but, before anything was settled, the Max-Planck-Gesellschaft intervened offering me a research station adjunct to Erich von Holst’s department. It was a hard decision to take; finally I was swayed by the consideration that, with Max Planck, I could take Schleidt, Prechtl and Eibl with me. Soon afterwards, my research station in Buldern in Westfalia was officially joined to Erich von Holst’s department in a newly-founded ” Max-Planck-Institut für Verhaltensphysiologie”. Erich von Holst convoked the international meeting of ethologists in 1949. With the second of these symposia, Erich von Holst and I celebrated the coming-true of our dream in Buldern in autumn 1950.  Returning to my research work, I at first confined myself to pure observation of waterfowl and of fish in order to get in touch again with real nature from which I had been separated so long. Gradually, I began to concentrate on the problems of aggressivity, of its survival function and on the mechanisms counteracting its dangerous effects. Fighting behaviour in fish and bonding behaviour in wild geese soon became the main objects of my research. Looking again at these things with a fresh eye, I realized how much more detailed a knowledge was necessary, just as my great co-laureate Karl von Frisch found new and interesting phenomena in his bees after knowing them for several decades, so, I felt, the observation of my animals should reveal new and interesting facts. I found good co-workers and we all are still busy with the same never-ending quest.  A major advance in ethological theory was triggered in 1953 by a violent critique by Daniel D. Lehrmann who impugned the validity of the ethological concept of the innate. As Tinbergen described it, the community of ethologists was humming like a disturbed bee-hive. At a discussion arranged by Professor Grassé in Paris, I said that Lehrmann, in trying to avoid the assumption of innate knowledge, was inadvertently postulating the existence of an “innate school-marm”. This was meant at a reduction to the absurd and shows my own error: it took me years to realize that this error was identical with that committed by Lehrmann and consisted in conceiving of the “innate” and of the “learned” as of disjunctive contradictory concepts. I came to realize that, of course, the problem why learning produces adaptive behaviour, rests exclusively with the “innate school-marm”, in other words with the phylogenetically programmed teaching mechanism. Lehrmann came to realize the same and on this realisation we became friends. In 1961 I published a paper “Phylogenetische Anpassung und adaptive Modifikation des Verhaltens”, which I later expanded into a book called “Evolution and Modification of Behaviour” (Harvard University Press, 1961).  Until late in my life I was not interested in human behaviour and less in human culture. It was probably my medical background that aroused my awareness of the dangers threatening civilized humanity. It is sound strategy for the scientist not to talk about anything which one does not know with certainty. The medical man, however, is under the obligation to give warning whenever he sees a danger even if he only suspects its existence. Surprisingly late, I got involved with the danger of man’s destruction of his natural environment and of the devastating vicious circle of commercial competition and economical growth. Regarding culture as a living system and considering its disturbances in the light of illnesses led me to the opinion that the main threat to humanity’s further existence lies in that which may well be called mass neurosis. One might also say that the main problems with which humanity is faced, are moral and ethical problems.  Todate I have just retired from my directorship at the Max-Planck-Institut für Verhaltensphysiologie in Seewiesen, Germany, and am at work building up a department of animal sociology pertaining to the Institut für Vergleichende Verhaltensforschung of the Austrian Academy of Science.  [1.](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/) According to Professor Wolfgang Schleidt, on July 22 1998, there is no Garden University. He was professor at the University of Maryland, College Park Campus from 1965 to 1985.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1973*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1974  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Konrad Lorenz died on February 27, 1989.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0621** |
| Interview |  |
|  |  |
| ID | **0622** |
| Biographical | I was born in The Hague, Netherlands, on 15th April 1907, the third of five children of Dirk C. Tinbergen and Jeannette van Eek. We were a happy and harmonious family. My mother was a warm, impulsive person; my father – a grammar school master in Dutch language and history – was devoted to his family, a very hard worker, and an intellectually stimulating man, full of fine, quiet humour and *joie de vivre.*  I was not much interested in school, and both at secondary school and at University, I only just scraped through, with as little effort as I judged possible without failing. Wise teachers, including my University Professors in Leiden, H. Boschma and the late C. J. van der Klaauw, allowed me plenty of freedom to engage in my hobbies of camping, bird watching, skating and games, of which playing left-wing in grass hockey teams gave me free rein for my almost boundless youthful energies.  Throughout my life, Fortune has smiled on me. Holland’s then unparalleled natural riches – its vast sandy shores, its magnificent coastal dunes, the abundant wildlife in its ubiquitous inland waters, all within an hour’s walk of our urban home – delighted me, and I was greatly privileged in having access to the numerous stimulating writings of the two quite exceptional Dutch naturalists, E. Heimans and Jac P. Thijsse – still household names in the Netherlands.  As a boy, I had two small aquaria in our backyard, in which I watched, each spring, the nest building and other fascinating behaviours of Sticklebacks. My natural history master at our High School, Dr. A. Schierbeek, put some of us in charge of the three seawater aquaria in the classroom, rightly arguing to the Head Master that I got plenty of fresh air, so that no one needed to worry about my spending the morning break indoors.  Having been frightened off by what I had been told of academic Biology as it was then taught in Leiden, I was at first disinclined to go to University. But a friend of the family, Professor Paul Ehrenfest, and Dr. Schierbeek urged my father to send me, in 1925, to Professor J. Thienemann, the founder of the famous ‘Vogelwarte Rossitten’, and the initiator of bird ringing. While Thienemann did not quite know what to do with this awkward youth, the photographer Rudy Steinert and his wife Lucy took me along on their walks along the uniquely rich shores and dunes of the *Kurische Nehrung,* where I saw the massive autumn migration of birds, the wild Moose, and the famous *Wanderdünen.* Upon my return to Holland, Christmas 1925, I had decided to read Biology at Leiden University after all. Here I had the good fortune to be befriended by Holland’s most gifted naturalist Dr. Jan Verwey, who instilled in me, by his example, a professional interest in animal behaviour (he also beat me, much to my humiliation, in an *impromptu* running match along the deserted *Noordwijk* seashore – two exuberant Naked Apes!). I owe my interest in seagulls to early imprinting on a small protected Herring Gull colony not far from the Hague, and to the example of two fatherly friends, the late G. J. Tijmstra and Dr. h. c. A. F. J. Portielje.  Having scraped through my finals without much honour, I became engaged to Elisabeth Rutten, whose family I had often joined on skating trips on the Zuiderzee; this made me realise that some day I would have to earn a living. Influenced by the work of [Karl von Frisch](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/index.html), and by J.-H. Fabre’s writings on insects, I decided to use the chance discovery of a colony of Beewolves (*Philanthus* – a digger wasp) for a study of their remarkable homing abilities. This led to an admittedly skimpy but still quite interesting little thesis, which (as I was told later) the Leiden Faculty passed only after grave doubts; 32 pages of print were not impressive enough. But I was itching to get this milestone behind me, for, through the generosity of Sidney Van den Bergh, I had been offered the opportunity of joining the Netherlands’ small contingent for the International Polar Year 1932-33, which was to have its base in Angmagssalik, the homeland of a small, isolated Eskimo tribe. My wife and I lived with these fascinating people for two summers and a winter just before they were westernised. Our first-hand experience of life among this primitive community of hunter-gatherers stood us in good stead forty years laters when I tried to reconstruct the most likely way of life of ancestral Man.  Upon our return to Holland, I was given a minor instructor’s job at Leiden University, where in 1935 Professor C. J. van der Klaauw, who knew how to stretch his young staff members, told me to teach comparative anatomy and to organise a teaching course in animal behaviour for undergraduates. I was also allowed to take my first research graduates into the field and so could extend my official 12-day annual holiday to an annual two months’ period of field work. This we used for further studies of the homing of Beewolves and behaviour studies of other insects and birds.  In 1936 Van der Klaauw invited [Konrad Lorenz](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1973/index.html) to Leiden for a small symposium on ‘Instinct’, and it was then that Konrad and I first met. We ‘clicked’ at once. The Lorenzes invited us, with our small son, for a fourmonths’ stay in their parental home in Altenberg near Vienna, where I became Lorenz’ second pupil (the first being Dr. Alfred Seitz, of the *Seitz’s Reizsummenregel*). But from the start ‘pupil’ and ‘master’ influenced each other. Konrad’s extraordinary vision and enthusiasm were supplemented and fertilised by my critical sense, my inclination to think his ideas through, and my irrepressible urge to check our ‘hunches’ by experimentation – a gift for which he had an almost childish admiration. Throughout this we often burst into bouts of hilarious fun – in Konrad’s words, in *Lausbuberei.*  These months were decisive for our future collaboration and our lifelong friendship. On the way back to Holland, I shyly wrote to the great Von Frisch asking whether I could call at his already famous Rockefeller-built laboratory in Munich. My recollection of that visit is a mixture of delight with the man Von Frisch, and an anxiety on his behalf when I saw that he refused to reply to a student’s aggressive *Heil Hitler* by anything but a quiet *Grüss Gott.*  In 1938 the Netherlands-America Foundation gave me free passage to and from New York, which I used for a four months’ stay, eked out by fees for lectures given in halting English, by living for one dollar a day in YMCAs (40 c for a room, 50 c for a day’s food, and 2 nickels for the subway), and travelling by Greyhound. During that visit I met Ernst Mayr, Frank A. Beach, Ted Schneirla, Robert M. Yerkes (who offered me hospitality both in Yale and Orange Park, Florida) and many others. I was frankly bewildered by what I saw of American Psychology. I sailed for home shortly after the Munich crisis, bracing myself for the dark years that we knew were lying ahead.  There followed a year of intense work, and of lively correspondence with Lorenz, which was broken off by the outbreak of war. Both of us saw this as a catastrophe. *Wir hätten soviel Gutes vor,* wrote Lorenz before the evil forces of nazism descended on Holland.  In the war I spent two years in a German hostage camp while my wife saw our family through the difficult times; Lorenz was conscripted as an Army doctor and disappeared during the battle of Witebsk; he did not emerge from Russian prison camps until 1947. Our reunion, in 1949, in the hospitable home of W. H. Thorpe in Cambridge, was to both of us a deeply moving occasion.  Soon after the war I was once again invited to the United States, and to Britain, to lecture on our work on animal behaviour. Lasting friendships with Ernst Mayr and David Lack proved decisive for my later interest in evolution and ecology. The lectures in the U.S. were worked out to a book ‘The Study of Instinct’ (1951); and my visit to Oxford, where David Lack had just taken over the newly founded Edward Grey Institute of Field Ornithology, ultimately led to our accepting the invitation of Sir Alister Hardy to settle in Oxford.  Apart from establishing, as Hardy had asked me, a centre of research and teaching in animal behaviour, I spent my Oxford years in seeing our newly founded journal Behaviour through its early years, in helping to develop contact with American psychology (of which we were perhaps excessively critical), and in fostering international cooperation. This work would not have been possible without the active help, behind the scenes, of [Sir Peter Medawar](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1960/index.html) (who urged the Nuffield Foundation to finance our little research group through its first ten years) and of E. M. Nicholson, who allocated generous funds from the Nature Conservancy which, with hardly any strings, was to last until my retirement. When Professor J. W. S. Pringle succeeded Alister Hardy as Head of the Department of Zoology in Oxford, he not only supported and encouraged our group, but also interested us in bridging the gap (so much wider than we had realised) between ethology and neuro-physiology. By founding the new inter-disciplinary Oxford School of Human Sciences he stimulated my still dormant desire to make ethology apply its methods to human behaviour.  Our research group was offered unique opportunities for ecologically oriented field work when Dr. h. c. J. S. Owen, the then Director of Tanzania’s National Parks, asked me to help him in founding the Serengeti Research Institute. A number of my pupils have since helped to establish this Institute’s world fame; and the scientific ties with it have remained strong ever since.  Our work received recognition by various proofs of acceptance by the scientific community, among which I value most my election as a Fellow of the Royal Society in 1962; as a Foreign Member of the *Koninklijke Nederlandse Akademie van Wetenschappen* in 1964; the conferment, in 1973, of the honorary degree of D. Sc. by Edinburgh University; and the awarding of the Jan Swammerdam medal of the *Genootschap voor Natuur-, Genees-, en Heelkunde* of Amsterdam in 1973.  In recent years I have, with my wife, concentrated my own research on the socially important question of Early Childhood Autism. This and other work on the development of children has recently brought us in contact with Professor Jerome S. Bruner, whose invigorating influence is already being felt throughout Britain. My only regret is that I am not ten years younger, so that I could more actively join him in developing his centre of child ethology in Oxford.  Among my publications the following are representative of my contributions to the growth of ethology:   |  |  | | --- | --- | | 1951 | The Study of Instinct – Oxford, Clarendon Press | | 1953 | The Herring Gull’s World – London, Collins | | 1958 | Curious Naturalists – London, Country Life | | 1972 | The Animal in its World Vol. 1. – London, Allen & Unwin; Harvard University Press | | 1973 | The Animal in its World Vol. 2. – London, Allen & Unwin; Harvard University Press | | 1972 | (together with E. A. Tinbergen) Early Childhood Autism – an Ethological Approach – Berlin, Parey |   From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1973*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1974  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Nikolaas Tinbergen died on December 21, 1988.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0622** |
| Interview |  |
|  |  |
| ID | **0623** |
| Biographical | Dr. Gerald M. Edelman was born on July 1, 1929 in New York City to Edward Edelman and Anna Freedman Edelman. His father is a practicing physician in New York.  After his education in New York public schools, Edelman attended Ursinus College in Pennsylvania and received the B.S. degree, magna cum laude, in 1950. He then attended the Medical School of the University of Pennsylvania where he received the M.D. degree in 1954. In the succeeding year, he was a Medical House Officer at the Massachusetts General Hospital. He became a Captain in the U.S. Army Medical Corps in 1955 and practiced general medicine at a Station Hospital connected with the American Hospital in Paris, France. In 1957, he joined the Rockefeller Institute as a graduate fellow in the laboratory of Dr. Henry G. Kunkel.  After receiving the Ph.D. degree in 1960, he remained at the Rockefeller Institute as Assistant Dean of Graduate Studies and started work in his own laboratory. In 1963, he became Associate Dean of Graduate Studies, a position from which he retired in 1966. From that time to the present, he has been a Professor of the Rockefeller University.  Edelman is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the American Society of Biological Chemists and the American Association of Immunologists, as well as a number of other scientific societies. He was a member of the Biophysics and Biophysical Chemistry Study Section of the National Institutes of Health from 1964 to 1967. Presently, he is an Associate of the Neurosciences Research Program at Massachusetts Institute of Technology, a member of the Board of Governors of the Weizmann Institute of Science and a member of the Advisory Board of the Basel Institute for Immunology.  He has given the Carter-Wallace Lectures at Princeton University in 1965, the National Institutes of Health Biophysics and Bioorganic Chemistry Lectureship at Cornell University in 1971, and delivered the Darwin Centennial Lectures at the Rockefeller University in 1971. In 1972, he was the first Felton Bequest Visiting Professor at the Walter and Eliza Hall Institute for Medical Research in Melbourne, Australia.  Edelman has received the Spencer Morris Award of the University of Pennsylvania in 1954, the Eli Lilly Award in Biological Chemistry given by the American Chemical Society in 1965, and the Annual Alumni Award of Ursinus College in 1969. In addition to his studies of antibody structure, his research interests have included the application of fluorescence spectroscopy and fluorescent probes to the study of proteins and the development of new methods of fractionation of both molecules and cells. His present research interests include work on the primary and three-dimensional structures of proteins, experiments on the structure and function of plant mitogens and studies of the cell surface.  In 1950, Edelman married Maxine M. Morrison. They have two sons, Eric and David and one daughter, Judith.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1972*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1973  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  Copyright © The Nobel Foundation 1972 Addendum, May 2005 Dr. Edelman is Director of The Neurosciences Institute and President of Neurosciences Research Foundation, the publicly supported not-for-profit organization that is the Institute’s parent. Separately, he is Professor at The Scripps Research Institute and Chairman of the Department of Neurobiology at that institution.  Dr. Edelman has made significant research contributions in biophysics, protein chemistry, immunology, cell biology, and neurobiology. His early studies on the structure and diversity of antibodies led to the Nobel Prize for Physiology or Medicine in 1972. He then began research into the mechanisms involved in the regulation of primary cellular processes, particularly the control of cell growth and the development of multicellular organisms. He has focused on cell-cell interactions in early embryonic development and in the formation and function of the nervous system. These studies led to the discovery of cell adhesion molecules (CAMs), which have been found to guide the fundamental processes by which an animal achieves its shape and form, and by which nervous systems are built. One of the most significant insights provided by this work is that the precursor gene for the neural cell adhesion molecule gave rise in evolution to the entire molecular system of adaptive immunity.  Most recently, he and his colleagues have been studying the fundamental cellular processes of transcription and translation in eukaryotic cells. They have developed a method to construct synthetic promoters and have also been able to enhance translation efficiency by constructing internal ribosomal entry sites of a modular composition. These findings have rich implications for the fields of genomics and proteomics.  Dr. Edelman has formulated a detailed theory to explain the development and organization of higher brain functions in terms of a process known as neuronal group selection. This theory was presented in his 1987 volume *Neural Darwinism*, a widely known work. Dr. Edelman’s continuing work in theoretical neuroscience includes designing new kinds of machines, called recognition automata, that are capable of carrying out tests of the self-consistency of the theory of neuronal group selection and promise to shed new light on the fundamental workings of the human brain. A new, biologically based theory of consciousness extending the theory of neuronal group selection is presented in his 1989 volume *The Remembered Present*. A subsequent book, *Bright Air, Brilliant Fire*, published in 1992, continues to explore the implications of neuronal group selection and neural evolution for a modern understanding of the mind and the brain. His book published with Giulio Tononi, entitled *A Universe of Consciousness: How Matter Becomes Imagination*, presents exciting new data on the neural correlates of conscious experience. In his latest book, published this year, entitled *Wider than the Sky: The Phenomenal Gift of Consciousness*, Dr. Edelman offers a model of the biology of consciousness.  Dr. Edelman was born in New York City in 1929. He earned his B.S. degree at Ursinus College and an M.D. at the University of Pennsylvania. He spent a year at the Johnson Foundation of Medical Physics, and after a medical house officership at the Massachusetts General Hospital, he served as a captain in the Army Medical Corps. In 1960 he earned his Ph.D. at The Rockefeller Institute (now University). In addition to the Nobel Prize, Dr. Edelman has been the recipient of numerous awards and honors, including many honorary degrees. He is a member of the National Academy of Sciences, the American Philosophical Society, and several foreign societies, including the Academy of Sciences, Institute of France. He is author of over 500 research publications.  *Gerald M. Edelman died on 17 May 2014.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0623** |
| Interview |  |
|  |  |
| ID | **0624** |
| Biographical | Rodney Robert Porter born 8 October 1917 at Newton-le-Willows, Lancashire, England.  He was educated at the Ashton-in-Makerfield Grammar School taking his Hons.B.Sc. (Biochemistry) in 1939 at the University of Liverpool and his Ph.D. at the University of Cambridge in 1948.  After one year’s postdoctoral work at Cambridge, Professor Porter joined the scientific staff of the National Institute of Medical Research in 1949 and was there until 1960 when he joined St. Mary’s Hospital Medical School, London University as the first Pfizer Professor of Immunology.  In 1967, he was appointed Whitley Professor of Biochemistry in the University of Oxford and Fellow of Trinity College, Oxford.  Amongst his awards are those of:  Fellow of the Royal Society, 1964 Gairdner Foundation Award of Merit, 1966 Ciba Medal (Biochemical Society), 1967 Karl Landsteiner Memorial Award from the American Association of Blood Banks, 1968 National Academy of Sciences, U.S.A., Foreign Member 1972  He took his Ph.D. at Cambridge under the supervision of Dr. [F. Sanger](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1958/index.html) investigating protein chemistry. In 1948 Professor Porter started to investigate the structure of antibodies, but on moving to Mill Hill he worked on methods of protein fractionation collaborating with Dr. [A. J. P. Martin](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1952/index.html). The particular interest was in chromatographic methods of fractionation.  He returned to the study of the chemical structure of antibodies leading to the finding of the three fragments produced by splitting with papain in 1958-59. He continued this work at St. Mary’s Hospital Medical School and put forward the peptide chain structure of antibodies in 1962.  Since moving to Oxford he has been concerned with the structure of antibody combining site, of the genetic markers of immunoglobulins and recently in the chemical structure of some of the early complement components.  During the war years 1940-46 Professor Porter was in the army serving with the R.A., R.E., and R.A.S.C., finishing with the rank of Major. He was with the First Army in 1942 in the invasion of Algeria and with the 8th Army during the invasion of Silicy and then Italy. He remained with the Central Mediterranean Forces in Italy, Austria, Greece and Crete until January 1946.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1972*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1973  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Rodney R. Porter died on September 6, 1985.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0624** |
| Interview |  |
|  |  |
| ID | **0625** |
| Biographical | Born: Burlingame, Kansas, November 19, 1915  Married: 1963  Children: 2 sons, 2 daughters    Education  B.S. Washburn College, 1937  M.D. Washington University, School of Medicine 1942, St. Louis    Professional Experience  Interneship, Barnes Hospital, 1942  Assistant in Pharmacology, School of Medicine, Washington University 1940-42  Instructor in Pharmacology, School of Medicine, Washington University 1945-46  Instructor in Biochemistry, School of Medicine, Washington University 1946-50  Assistant Professor of Biochemistry, School of Medicine, Washington University 1950-52  Associate Professor of Biochemistry, School of Medicine, Washington University 1952-53  Professor Pharmacology and Director of the Department, School of Medicine, Western Reserve University, Cleveland, Ohio, 1953-63  Professor of Physiology, Vanderbilt University, School of Medicine, Nashville, Tenn., 1963- present  Career Investigator – American Heart Association 1967    Memberships  American Society of Biological Chemists  American Chemical Society  American Society for Pharmacology and Experimental Therapeutics  AAAS  Sigma Xi  Alpha Omega Alpha  National Academy of Sciences    Editorial Board  Biochemical Preparations, 1951-56  Journal of Pharmacology and Experimental Therapeutics, 1957-58  Panel of Metabolism, Section on Biochemistry of the Committee on Growth (Nat. Res. Council) 1953-54  Study Section (Pharmacology and Experimental Therapeutics) Public Health Service, 1954-58  Member, National Institutes of Health Pharmacology Training Committee 1958-62, 1963-65  Member, National Institutes of Health Arthritis and Metabolic Disease Program Committee 1966- |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0625** |
| Interview |  |
|  |  |
| ID | **0626** |
| Biographical | Bernard Katz was born on March 26th, 1911, in Leipzig, Germany, of Russian Jewish origin, only son of Max Katz and Eugenie Rabinowitz. His school education was at the Albert Gymnasium in Leipzig (1921-1929). He studied Medicine at the University of Leipzig, 1929-1934; received the Siegfried Garten Prize for physiological research in 1933 and obtained his M.D. in 1934.  He left Germany in February 1935 and was accepted as a Ph. D. student by Professor [A.V. Hill](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html) at University College, London. Katz worked in A.V. Hill’s laboratory until August 1939. He received a Ph.D. (London University) and a Beit Memorial Research Fellowship in 1938. In 1942, he was awarded the degree of Doctor of Science (London University).  In 1939, Bernard Katz joined [J. C. Eccles](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/index.html)‘ laboratory at Sydney Hospital, Australia, as a Carnegie Research Fellow. He collaborated with J. C. Eccles and S. W. Kuffler in neuromuscular research.  In 1942, after naturalization in 1941, he joined the Royal Australian Air Force, and served as a Radar Officer in the South West Pacific until the end of the war.  In 1946, returning from Australia to University College, London, Katz rejoined A.V. Hill’s research unit as Assistant Director of Research and Henry Head Research Fellow (appointed by the Royal Society). He was appointed Reader in Physiology in 1950; since 1952 he holds the post of Professor of Biophysics at University College, London.  Professor Katz was elected Fellow of the Royal Society in 1952; Fellow of the Royal College of Physicians in 1968. He is a Foreign Member of the Royal Danish Academy of Sciences and Letters (1968), Accademia Nazionale Lincei (1969); American Academy of Arts and Sciences (1969). Fellow of University College, London (1961). Feldberg Foundation Award (1965); Baly Medal, Royal College of Physicians, and Copley Medal, Royal Society (1967). He was knighted in 1969. He is a member of the Agricultural Research Council since 1967; Biological Secretary of the Royal Society since 1968.  The major fields of research of Professor Katz include: studies of nerve and muscle, especially of the physico-chemical mechanism of neuromuscular transmission.  In 1945, Bernard Katz married Marguerite Penly, of Cremorne, New South Wales. They have two children: David (born 1947), studying Pharmacology and Medicine in London, and Jonathan (born 1950), studying Classics at Pembroke College, Oxford.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Sir Bernard Katz died on April 20, 2003.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0626** |
| Interview |  |
|  |  |
| ID | **0627** |
| Biographical | Ulf S. von Euler was born in Stockholm on February 7th, 1905, as the second son of [Hans von Euler-Chelpin](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1929/index.html) and Astrid Cleve. His father was born in Augsburg, Germany, as the only son of general Rigas von Euler-Chelpin. Hans von Euler-Chelpin received the Nobel Prize for Chemistry in 1929. Ulf’s mother was the daughter of Per Teodor Cleve, who was Professor of Chemistry in Uppsala, and the discoverer of the elements thulium and holmium. Astrid Cleve received her Ph. D. in botany and later devoted most of her scientific activities to diatomes and to geology and obtained the title of professor in 1955.  After school years in Stockholm and in Karlstad, Ulf von Euler entered the [Karolinska Institute](http://www.ki.se/) as a medical student in 1922. The scientific atmosphere at home and the regular opportunities to meet scientists – [Svante Arrhenius](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1903/index.html) (Nobel Prize for Chemistry in 1903) was his godfather – had, no doubt, a great part in his growing interest in research. This was facilitated but never enforced upon him by his parents. After a period of study with Robin Fåhraeus (a pioneer in blood sedimentation and rheology) von Euler began some research work on his own and he was much encouraged by a prize given for a study on vasoconstrictor properties of fever blood.  From 1926 he worked as assistant in G. Liljestrand’s Department of Pharmacology, where he produced his thesis in 1930, followed by an appointment as Assistant Professor in Pharmacology in the same year.  Aided by the continuous support of Liljestrand, von Euler had the good fortune of obtaining a Rockefeller Fellowship for studies abroad (1930-1931) with [H. H. Dale](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1936/index.html) in London, I. de Burgh Daly in Birmingham, [C. Heymans](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1938/index.html) in Ghent and G. Embden in Frankfurt. This period of diversified studies in Physiology and Pharmacology provided an invaluable basis for further research. Having had the good luck of discovering an active biological factor in intestinal extracts («Substance P»), further developed with J. H. Gaddum in Dale’s laboratory, von Euler’s interest, soon after his return home, turned in that direction and led subsequently to the findings of prostaglandin and vesiglandin (1935), piperidine (1942) and noradrenaline (1946).  In [A. V. Hill](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html)‘s laboratory in London, von Euler obtained some insight into problems and methodology of biophysics (1934). Expert teaching in the subjects of neuromuscular transmission was given by G. L. Brown in London (1938). Various aspects of endocrinology and experimental renal hypertension were later studied with E. Braun-Menéndez in [B. A. Houssay](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html)‘s laboratory in Buenos Aires in 1946-1947.  After a period from 1930 to 1939 as Assistant Professor, von Euler was appointed Professor of Physiology at the Karolinska Institute, a post which he has held until 1971. Conditions for work were improved by the transfer from the old site of the Karolinska Institute to modern laboratories in the new premises just outside Stockholm. Experimental work was greatly facilitated by generous support from the Medical Research Council (after 1950) but also from private funds and the pharmaceutical industry, as well as from research funds in the United States of America.  After the identification of noradrenaline as the adrenergic neurotransmitter in 1946, most of von Euler’s research work has been devoted to this subject. Its distribution in nerves and organs, its excretion during various physiological and pathological conditions and its quantitation have been studied in his laboratory. The finding that the transmitter was stored in subcellular particles (with his late colleague N-Å. Hillarp) gave a new direction to the research, and problems concerning uptake, storage and release from nerve granules as well as the neurotransmission process have been the main research subject since 1958. A large number of students, research assistants and research associates have taken part in these studies.  During the years 1953 to 1960 Ulf von Euler was a Member of the [Nobel Committee for Physiology or Medicine](http://www.nobelprizemedicine.org/?page_id=326) and from 1961 to 1965 he served as Secretary of the Committee. In 1965 Professor von Euler was appointed Chairman of the Board of the Nobel Foundation.  From 1965 to 1971 he served as Vice-President of the International Union of Physiological Sciences.  Professor von Euler was awarded the Gairdner Prize (Canada) in 1961, the Jahre Prize (Norway) 1965, the Stouffer Prize (U.S.A.) in 1967, Carl Ludwig Medaille (Germany) 1953, Schmiedeberg Plaquette (Germany) 1969, La Madonnina (Italy) 1970.  Professor von Euler is a Member of the [Royal Academies of Sciences in Stockholm](http://www.kva.se/) and in Copenhagen, the Leopoldina Academy (Halle), Real Academia de Medicina in Barcelona and The American Philosophical Society. Honorary Member of The American College of Physicians, Council on Clinical Cardiology of the American Heart Association, Swedish College of Physicians, Italian Pharmacological Society, Swedish Endocrinological Society, and the Aeromedical Society.  He is Dr. h. c. at the Universities of Umeå, Rio de Janeiro, Dijon, Ghent, Tübingen, Buenos Aires, Edinburgh, Madrid, Gustavus Adolphus College.  From 1930 to 1957, Ulf von Euler was married to Jane Sodenstierna, they had four children: Hans Leo, scientist administrator at the National Institutes of Health, Bethesda, U.S.A.; Johan Christopher, anesthesiologist, Serafimer Hospital, Stockholm; Ursula Katarina, B. A. Assistant in the Department of History of Arts, University of Stockholm; and Marie Jane, Chemical Engineer, Melbourne, Australia.  Since 1958 Ulf von Euler is married to countess Dagmar Cronstedt.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Ulf von Euler died on March 9, 1983.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0627** |
| Interview |  |
|  |  |
| ID | **0628** |
| Biographical | Julius Axelrod was born on May 30th, 1912, in New York City. He obtained his B. Sc. in 1933 at the College of the City of New York, M. A. in 1941 at New York University, and Ph. D. in 1955 from the George Washington University.  From 1933 to 1935 he was Laboratory Assistant at the Department of Bacteriology of New York University Medical School; from 1935-1946 he was Chemist at the Laboratory of Industrial Hygiene; 1946-1949, Research Associate, Third New York University Research Division, Goldwater Memorial Hospital; 1949-1950, Associate Chemist, Section on Chemical Pharmacology, National Heart Institute, NIH; 1950-1953, Chemist, National Heart Institute, NIH, where he became Senior Chemist in 1953, and was appointed Chief of the Section on Pharmacology, Laboratory of Clinical Science, National Institute of Mental Health, Health Services and Mental Health Administration, Department of Health, Education and Welfare in 1955.  The following honors and awards were granted to Dr. Axelrod: National Science Foundation Travel Award, 1958; Corresponding Member of the German Pharmacological Society, 1959; International Physiological Union Travel Award, 1961; Otto Loewi Memorial Lecture, New York University Medical School, 1964; Distinguished Research Award, Assoc. Res. Nerv. Mental Diseases, 1965; Karl E. Paschkis Memorial Lecture, Philadelphia Endocrine Society, 1966; Honorary Sc.D., University of Chicago, 1966; The Gairdner Foundation Award, 1967; National Institutes of Health Lecture, 1967; Nathanson Memorial Lecture, University of Southern California, 1968; Distinguished Achievement Award, George Washington University, 1968; Superior Service Award, DHEW, 1968; Claude Bernard Professorship, University of Montreal, 1969; Distinguished Service Award, DHEW, 1970; Distinguished Service Award, Modern Medicine Magazine, 1970.  Dr. Axelrod is a Member of Sigma Xi, International Brain Research Organization, American Chemical Society, American Society of Pharmacology and Experimental Therapeutics, American Society of Biological Chemists, American Association for the Advancement of Science, and a Fellow of the American College of Neuropsychopharmacology, 1961 (Member of the Council, 1966-1969).  Dr. Axelrod is a Member of the editorial boards and committees of a number of journals, among which: *Journal of Pharmacology and Experimental Therapeutics, Journal of Medicinal Chemistry, Life Sciences, Circulation Research, Journal of Neurobiology, Pharmacological Research Communications, Journal of Neurochemistry, International Journal of Psychobiology.*  In 1970 he beame a Member of the Psychopharmacology Study Section, National Institute of Mental Health.  Julius Axelrod married Sally Taub in 1938; they have two children. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0628** |
| Interview |  |
|  |  |
| ID | **0629** |
| Biographical | Max Delbrück was born on September 4th, 1906, in Berlin, Germany, the youngest of seven children. His father, Hans Delbrück, Professor of History at the University of Berlin, was for many years editor and political columnist of the *Preussische Jahrbücher.* His mother was a granddaughter of the chemist, Justus von Liebig.  Max Delbrück grew up in a suburb of Berlin (Grunewald) populated by moderately affluent members of the academic, professional, and merchant community, many of them with large families. The period of affluence and lively hospitality before 1914 was followed by the war years with hunger, cold, and death, and the postwar period of revolution, inflation, and impoverishment.  His interest in science dates back to boyhood and was directed first towards astronomy, which he seized upon as a means of finding an identity in an environment of strong personalities. All senior to him, many with high accomplishments, none was in the sciences. The one exception, the oldest boy in the Bonhoeffer family, Karl Friedrich (his father Karl Bonhoeffer was Professor of Psychiatry), eight years older than Max Delbrück, was a physical chemist of high distinction, and became the mentor and lifelong friend of Delbrück. The shift to theoretical physics during the latter part of his graduate studies in Göttingen was an easy one from astrophysics and a natural one in the late twenties, just after the breakthrough of quantum mechanics, for which Göttingen was one of the centers.  Among his friendships during the later student years, the most intense and influential one was with Werner Brock, now emeritus Professor of Philosophy, Freiburg.  There followed three postdoctoral years (1929-1932) abroad, in England, Switzerland, and Denmark. The stay in England, with its immersion into a new language and a new culture, had a vast effect on widening his outlook on life. In Switzerland and Denmark the associations with [Wolfgang Pauli](https://www.nobelprize.org/nobel_prizes/physics/laureates/1945/index.html) and [Niels Bohr](https://www.nobelprize.org/nobel_prizes/physics/laureates/1922/index.html) shaped his attitude toward the pursuit of truth in science.  Delbrück’s interest in biology was first aroused by Bohr, in connection with his speculations that the complementarity argument of quantum mechanics might have wide applications to other fields of scientific endeavor and especially in regard to the relations between physics and biology. A move to Berlin in 1932, as assistant to Lise Meitner, was largely motivated by the hope that the proximity of the various Kaiser Wilhelm Institutes to each other would facilitate the beginning of an acquaintance with the problems of biology. Paradoxically, this good intention was helped by the rise of Nazism which made official seminars less interesting. A small group of physicists and biologists began to meet privately beginning about 1934. To this group belonged N. W. Timofeeff-Ressovsky (genetics). Out of these meetings grew a paper by Timofeeff, Zimmer, and Delbrück on mutagenesis. A popularization of this paper of 1935 in [Schroedinger](https://www.nobelprize.org/nobel_prizes/physics/laureates/1933/index.html)‘s little book «*What is Life?*» (1945) had a curiously strong influence on the development of molecular biology in the late 1940’s.  The move to the United States in 1937 was made possible by a second fellowship of the Rockefeller Foundation, permitting Delbrück to pursue with greater freedom and effectiveness his interests in biology. He chose Caltech because of its strength in *Drosophila* genetics, and to some extent because of its distance from the impending perils at home. Although his job in Germany seemed reasonably secure, it was clear that political reasons would bar him from advancement.  At Caltech he soon teamed up with E. L. Ellis doing phage research. The fellowship of the Rockefeller Foundation ran out in September 1939. World War II had started and Delbrück elected to stay in the United States. He accepted an instructorship in the Physics Department at Vanderbilt University in Nashville, Tennessee. The years at Vanderbilt were the war years. Both [Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html) (at Bloomington, Indiana) and Delbrück (at Vanderbilt) were technically enemy aliens, a status affording them the privacy to concentrate on science.  In 1941 Delbrück married Mary Bruce. She has given his life the harmony needed for its fulfillment. They have four children – a first set, Jonathan and Nicola, born in 1947 and 1949, and, since these turned out so happily, a second set, Tobias and Ludina, born in 1960 and 1962.  Since the early 1950’s Delbrück’s research interests have shifted from molecular genetics to sensory physiology and especially to the idea of introducing here, too, a microorganism of suitable simplicity. He turned to the sporangiophores of *Phycomyces* as a model system for the study of stimulus transductions. The goal of clarifying the molecular nature of the primary transducer processes of sense organs in general and of *Phycomyces* in particular has held his attention since then, with one interruption.  This interruption was the setting up of an institute of molecular genetics at the University of Cologne. Delbrück’s goal was to demonstrate the feasibility of modern interdisciplinary research and of the «department system» (with several professors in one institute) within a German university setup, and to boost molecular genetics in Germany.  The Institut für Genetik der Universität Köln was formally dedicated on June 22nd, 1962, with Niels Bohr as the principal speaker. His lecture entitled «Light and Life – Revisited» commented on his original one of 1933, which had been the starting point of Delbrück’s interest in biology. It was to be Bohr’s last formal lecture. He died before completing the preparation of the manuscript of this lecture for publication.  Since 1964 the experimental work on *Phycomyces* is once more being pursued with full force, together with theoretical studies on related systems.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Max Delbrück died on March 9, 1981.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0629** |
| Interview |  |
|  |  |
| ID | **0630** |
| Biographical | Alfred Day Hershey was born on December 4th, 1908, in Owosso, Michigan. He studied at the Michigan State College, where he obtained B.S. in 1930, and Ph.D. in 1934. In 1967 he got an honorary D.Sc. at the University of Chicago.  From 1934 till 1950 he was engaged in teaching and research, at the Department of Bacteriology, Washington University School of Medicine. In 1950 he became a Staff Member, at the Department of Genetics, Carnegie Institution of Washington, Cold Spring Harbor, New York; in 1962 he was appointed Director of the Genetics Research Unit of the same institution.  Alfred Hershey married Harriet Davidson in 1945, they have one son, Peter.  Alfred Hershey is a Member of the American Society for Microbiology, the National Academy of Sciences, and the American Academy of Arts and Sciences. Hershey is Recipient of the Kimber Genetics Award of the National Academy of Sciences, 1965. Michigan State University honored him with an M.D.h.c. in 1970.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Alfred D. Hershey died on May 22, 1997.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0630** |
| Interview |  |
|  |  |
| ID | **0631** |
| Biographical | Salvador Edward Luria was born on August 13th, 1912, in Torino, Italy. He has been a naturalized citizen of the U.S.A. since January 1947.  In 1929 he started his studies in Medicine at the University of Torino, where he obtained his M. D. *summa cum laude* in 1935. From 1938 to 1940 he was Research Fellow at the Institute of Radium in Paris; 1940-1942, Research Assistant in Surgical Bacteriology at Columbia University; from 1943 to 1950 he was Instructor, Assistant Professor, and Associate Professor of Bacteriology at Indiana University; in 1950 he was appointed Professor of Microbiology at the University of Illinois; from 1959-1964 he has been Professor of Microbiology at the Massachusetts Institute of Technology; in 1964 he became Sedgwick Professor of Biology at the M. I. T. and in 1965, non-resident Fellow at the Salk Institute for Biological Studies. In 1970 Luria was appointed Institute Professor at the Department of Biology of the M.I.T.  Professor Luria was honoured with the following awards: 1935, Lepetit Prize; 1965, Lenghi Prize, Accademia dei Lincei; 1969, Louisa Gross Horwitz Prize, Columbia University.  He was Guggenheim Fellow, 1942-1943 at Vanderbilt and Princeton; during the year 1963-1964 he worked again in Paris, this time at the Institut Pasteur. He is, or has been, Editor or Member of the Editorial Board of the following journals: *Journal of Bacteriology, Virology, Experimental Cell Research, Journal of Molecular Biology, Photochemistry and Photobiology, American Naturalist, Proceedings of the National Academy of Sciences, Annual Review of Genetics.*  Professor Luria is a Member of the National Academy of Sciences, American Academy of Arts and Sciences, American Philosophical Society, American Academy of Microbiology, American Society for Microbiology (President, 1967-1968), American Society of Biological Chemists, Society for General Microbiology, Genetics Society, American Naturalists, Society for the Study of Development and Growth, A.A.A.S., Sigma Xi, A.A.U.P.  Salvador Edward Luria was, in 1945, married to Zella Hurwitz, they have one son, Daniel, who is studying economics. His wife, Zella Hurwitz Luria, Ph. D., is a Professor of Psychology at Tufts University.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Luria, Salvador Edward, *A Slot Machine, a Broken Test Tube: an Autobiography*. Harper & Row, New York, 1984.  *Salvador E. Luria died on February 6, 1991.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0631** |
| Interview |  |
|  |  |
| ID | **0632** |
| Biographical | Robert W. Holley was born in Urbana, Illinois, on January 28th, 1922, one of four sons of Charles and Viola Holley. His parents were both educators. He attended public schools in Illinois, California and Idaho, and graduated from Urbana High School in 1938. He studied chemistry at the University of Illinois and received his B. A. degree in 1942. Graduate work was at Cornell University, where the Ph.D. degree in organic chemistry, with Professor Alfred T. Blomquist, was awarded in 1947. Graduate work was interrupted during the war. He spent two years, 1944-1946, with Professor [Vincent du Vigneaud](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1955/index.html) at Cornell University Medical College, where he participated in the first chemical synthesis of penicillin.  After completing the Ph. D. degree, Holley spent 1947-1948 as an American Chemical Society Postdoctoral Fellow with Professor Carl M. Stevens at Washington State University. He then returned to Cornell University as Assistant Professor of Organic Chemistry at the Geneva Experiment Station in 1948. He was Associate Professor there from 1950-1957. During a sabbatical year, 1955-1956, he was a Guggenheim Memorial Fellow in the Division of Biology at the California Institute of Technology. In 1958, he returned to Ithaca, New York, as a Research Chemist at the U. S. Plant, Soil and Nutrition Laboratory, a U. S. Department of Agriculture Laboratory on the Cornell University campus. He had an appointment in the University throughout this period and became Professor of Biochemistry in 1962. He rejoined the faculty of Cornell University full time in 1964 as Professor of Biochemistry and Molecular Biology, and was Chairman of the Department from 1965 to 1966. The following year, 1966-1967, was spent at the Salk Institute for Biological Studies and the Scripps Clinic and Research Foundation in La Jolla, California, as a National Science Foundation Postdoctoral Fellow. In 1968, though maintaining an affiliation with Cornell University, he joined the permanent staff of the Salk Institute, where he is a Resident Fellow and an American Cancer Society Professor of Molecular Biology. He is also an Adjunct Professor at the University of California at San Diego.  Holley’s training as a chemist did not alter his basic interest in living things. This interest has influenced his choice of research, which began with the organic chemistry of natural products. There followed a gradual drift toward more biological subjects, with work on amino acids and peptides, and eventually work on the biosynthesis of proteins. During the latter, the alanine transfer RNA was discovered. The following 10 years were spent working with this RNA, first concentrating on the isolation of the RNA, and then working on the determination of the structure of the RNA. The nucleotide sequence was completed at the end of 1964. It was for this work that the Nobel Prize was awarded. More recently, his work has been concerned with factors that control cell division in mammalian cells.  Holley is a member of the National Academy of Sciences, the American Academy of Arts and Sciences, the American Association for the Advancement of Science, The American Society of Biological Chemists and the American Chemical Society. He received the Albert Lasker Award in Basic Medical Research in 1965, the Distinguished Service Award of the U. S. Department of Agriculture in 1965, and the U. S. Steel Foundation Award in Molecular Biology of the National Academy of Sciences in 1967.  Holley was married to Ann Dworkin in 1945. They have one son, Frederick. Mrs. Holley’s professional interests are concerned with the teaching of mathematics. The three of them especially enjoy the ocean and the mountains.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1968*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1969  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Robert W. Holley died on February 11, 1993.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | **0633** |
| Biographical | Har Gobind Khorana was born of Hindu parents in Raipur, a little village in Punjab, which is now part of eastern Pakistan. The correct date of his birth is not known; that shown in documents is January 9th, 1922. He is the youngest of a family of one daughter and four sons. His father was a «patwari», a village agricultural taxation clerk in the British Indian system of government. Although poor, his father was dedicated to educating his children and they were practically the only literate family in the village inhabited by about 100 people.  Har Gobind Khorana attended D.A.V. High School in Multan (now West Punjab); Ratan Lal, one of his teachers, influenced him greatly during that period. Later, he studied at the Punjab University in Lahore where he obtained an M. Sc. degree. Mahan Singh, a great teacher and accurate experimentalist, was his supervisor.  Khorana lived in India until 1945, when the award of a Government of India Fellowship made it possible for him to go to England and he studied for a Ph. D. degree at the University of Liverpool. Roger J. S. Beer supervised his research, and, in addition, looked after him diligently. It was the introduction of Khorana to Western civilization and culture.  Khorana spent a postdoctoral year (1948-1949) at the Eidgenössische Technische Hochschule in Zurich with Professor [Vladimir Prelog](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1975/index.html). The association with Professor Prelog molded immeasurably his thought and philosophy towards science, work, and effort.  After a brief period in India in the fall of 1949, Khorana returned to England where he obtained a fellowship to work with Dr. (now Professor) G. W. Kenner and Professor (now Lord) [A. R. Todd](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1957/index.html). He stayed in Cambridge from 1950 till 1952. Again, this stay proved to be of decisive value to Khorana. Interest in both proteins and nucleic acids took root at that time.  A job offer in 1952 from Dr. Gordon M. Shrum of British Columbia (now Chancellor of Simon Fraser University, British Columbia) took him to Vancouver. The British Columbia Research Council offered at that time very little by way of facilities, but there was «all the freedom in the world», to use Dr. Shrum’s words, to do what the researcher liked to do. During the following years, with Dr. Shrum’s inspiration and encouragement and frequent help and scientific counsel from Dr. Jack Campbell (now Head of the Department of Microbiology at the University of British Columbia), a group began to work in the field of biologically interesting phosphate esters and nucleic acids. Among the many devoted and loyal colleagues of this period, there should, in particular, be mention of Dr. Gordon M. Tener (now a Professor in the Biochemistry Department of the University of British Columbia), who contributed much to the spiritual and intellectual well-being of the group.  In 1960 Khorana moved to the Institute for Enzyme Research at the University of Wisconsin. He became a naturalized citizen of the United States. As of the fall of 1970 Khorana has been Alfred P. Sloan Professor of Biology and Chemistry at the Massachusetts Institute of Technology.  Har Gobind Khorana was married in 1952 to Esther Elizabeth Sibler, who is of Swiss origin. Esther brought a consistent sense of purpose into his life at a time when, after six years’ absence from the country of his birth, Khorana felt out of place everywhere and at home nowhere. They have three children: Julia Elizabeth (born May 4th, 1953), Emily Anne (born October 18th, 1954), and Dave Roy (born July 26th, 1958).  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *H. Gobind Khorana died on 9 November 2011.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
|  |  |
| ID | **0634** |
| Biographical | Marshall Warren Nirenberg was born in New York City on April 10th, 1927, the son of Harry and Minerva Nirenberg. The family moved to Orlando, Florida in 1939. He early developed an interest in biology. In 1948 he received a B. Sc. degree, and in 1952, a M. Sc. degree in Zoology from the University of Florida at Gainesville. His dissertation for the Master’s thesis was an ecological and taxonomic study of caddis flies (Trichoptera).  During this period he became interested in biochemistry. He continued studies in this field at the University of Michigan, Ann Arbor, and in 1957 received the Ph. D. degree from the Department of Biological Chemistry. Nirenberg’s thesis, performed under the guidance of Dr. James Hogg, was a study of a permease for hexose transport in ascites tumor cells.  From 1957 to 1959 he obtained postdoctoral training with DeWitt Stetten Jr., and with William Jakoby at the National Institutes of Health as a fellow of the American Cancer society. During the next year he held a Public Health Service Fellowship and in 1960 became a research biochemist in the Section of Metabolic Enzymes, headed by Dr. Gordon Tompkins, at the National Institutes of Health.  In 1959 he began to study the steps that relate DNA, RNA and protein. These investigations led to the demonstration with H. Matthaei that messenger RNA is required for protein synthesis and that synthetic messenger RNA preparations can be used to decipher various aspects of the genetic code.  In 1962 he became head of the Section of Biochemical Genetics at the National Institutes of Health.  Nirenberg holds honorary degrees from the University of Michigan, Yale University, University of Chicago, University of Windsor (Ontario) and Harvard University. Other honours include: The Molecular Biology Award, National Academy of Sciences, 1962; Paul Lewis Award in Enzyme Chemistry, American Chemical Society, 1964; The National Medal of Science, 1965; The Research Corporation Award, 1966; the Hildebrand Award, 1966; the Gairdner Foundation Award of Merit, 1967; The Prix Charles Leopold Meyer, French Academy of Sciences, 1967; the Joseph Priestly Award, 1968; and the Franklin Medal, 1968. The Louisa Gross Horwitz Prize, Columbia University, and the Lasker Award were shared with [H. G. Khorana](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1968/index.html) in 1968. He is a member of the American Academy of Arts and Sciences and the National Academy of Sciences.  He was married in 1961 to Perola Zaltzman, a chemist from the University of Brazil, Rio de Janeiro. She is now a biochemist at the National Institutes of Health.  From [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html) *en 1968*, Editor Wilhelm Odelberg, [Nobel Foundation], Stockholm, 1969  This autobiography/biography was written at the time of the award and later published in the book series [*Les Prix Nobel/*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html)[*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*/*[*The Nobel Prizes*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/nobel-prizes.html). The information is sometimes updated with an addendum submitted by the Laureate.  *Marshall W. Nirenberg died on 15 January, 2010.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0634** |
| Interview |  |
|  |  |
| ID | **0635** |
| Biographical | Ragnar Arthur Granit was born in the parish of Helsinge, Finland, on October 30th, 1900, eldest son of the Crown forester Arthur Wilhelm Granit and his wife Albertina Helena Malmberg. The family then moved to the neighbourhood of Helsingfors where his father opened a firm dealing with sylviculture and forest produce and the son became a pupil of the Swedish Normallyceum belonging, as he did, to the Swedish population of his native country, to a sea-faring family from the island of Korpo in the Baltic waters separating Sweden and Finland. He still spends his summers on this island.  Granit matriculated at Helsingfors University in 1919. While still at school, he took part in Finland’s War of Liberation 1918 (the Svidja corps) and was decorated with the Cross of Freedom IV Cl. «with sword».  During a preliminary Summer Course at the Åbo Academy in 1919 he decided to take up experimental psychology, which as an academic subject fell within the humanities, but was well advised by his uncle, Dr. Lars Ringbom, to add a full medical degree to these studies. His teacher in experimental psychology at Helsingfors was Eino Kaila, later Professor of Philosophy. Granit became Mag. Phil. in 1923. During his medical studies he arrived at the conclusion that physiology would prove a better starting point than psychology for the visual work that he had undertaken almost from the beginning of his career and so he eagerly accepted the post of demonstrator (assistant) at the Physiological Institute, offered him in 1926 by Professor Carl Tigerstedt. He took his M.D. in December 1927 and became «Docent» in Physiology in 1929.  In 1928 he spent half a year at [Sir Charles Sherrington](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1932/index.html)‘s laboratory at Oxford and returned there as a Fellow of the Rockefeller Foundation in 1932-1933. The years 1929-1931 he spent as Fellow in Medical Physics at the Johnson Foundation of the University of Pennsylvania on the invitation of Dr. D. W. Bronk, then engaged in setting up this institute. Returning to Helsingfors Granit held the office of Professor of Physiology from 1935 and was formally appointed in 1937, his chair being at about the same time transformed into one assigned for teaching in the Swedish language. During the so-called Winter War between Finland and Russia, Granit was district physician for the three Swedish-speaking island parishes of Korpo, Houtskär and Iniö in the Baltic, simultaneously charged with the duty as physician to the forts within this region.  In 1940 he was called to Harvard University and to the [Royal Caroline Institute](http://www.ki.se/) of Stockholm, in the end deciding in favour of the latter. The appointment was based on a grant from the Foundation «Knut och Alice Wallenbergs Stiftelse» and also supported by the Rockefeller Foundation. In 1945 the Caroline Institute made his laboratory a department of the [Medical Nobel Institute](http://www.nobelprizemedicine.org/) for which new buildings were to be erected. In 1946 he received a personal research chair in Neurophysiology from the Ministry of Education. The new building was ready in 1947. He retired as Professor Emeritus in July, 1967.  Ragnar Granit was a Member of the Medical Research Council (1949-1955), President of the [Royal Swedish Academy of Sciences](http://www.kva.se/) (1963-1965), Vice President (1965-1969). Between 1956 and 1966 he was Visiting Professor at the Rockefeller Institute (since Rockefeller University), New York; in 1967 in a similar capacity at St. Catherine’s College, Oxford for the Michaelmas Term, and at the University of the Pacific, San Francisco, 1969; Fogarty Scholar, N.I.H., Bethesda, 1971-1972. Some of his major lectures are: The Thomas Young Oration of the Physical Society, London, 1945; The Silliman Lectures of Yale University, 1954; The Sherrington Memorial Lecture of the Royal Society of Medicine, London, 1967; The Sherrington Lectures, Liverpool, 1970.  Granit has honorary degrees from Oslo University, M.D., 1951; Oxford University, D. Sc., 1956; Hong Kong University, D. Sc., 1961; Loyola University, Chicago, 1969; Pisa University, 1970; Catedrático hon. from San Marco University, Lima, University of Santiago de Chile and the National University, Bogotá, all in 1958. He is a Member or Foreign Member of the Soc. Scient. Fenn., 1937; Royal Swedish Acad. Sci., 1944; Soc. Philomatique, Paris, 1947; Acad. Sci., Bologna, 1948; Amer. Philos. Soc., 1954; Royal Danish Acad. Sci., 1956; Royal Society, London, 1960; Natl. Acad. Sci., Washington, 1968; an Honorary Member of the Accad. di Medicina, Turin, 1961; Indian Acad. Sci., 1964; Amer. Acad. of Arts and Sciences, 1971; and honorary member of the following professional societies: the Swedish Societies for Neurology, for Ophthalmology and for Clinical Neurophysiology, the International Society for Clinical Electroretinography, the Biological Societies of Montevideo, Santiago de Chile and Argentina, the Finnish Society for Ophthalmology, the American Physiological Society, the American Neurological Association, the Physiological Society of England, the Finnish Society of Physicians, the Swedish Society of Physicians, the Swedish and the Finnish Societies of Physiology.  Among the many awards Ragnar Granit has received the following may be mentioned here: Hans Cronstedt’s Prize, 1926; Jubilee Medal of the Swedish Society of Physicians, 1947; Anders Retzius Gold Medal, Stockholm, 1957; F. C. Donders Medal, Utrecht, 1957; Sherrington Memorial Gold Medal, London, 1967; Purkinje Gold Medal, Prague, 1969.  From 1920 to around 1947 Ragnar Granit’s main research was in the field of vision, beginning with psychophysics in the twenties and ending up with electrophysiological work from the early thirties onwards, as briefly reported in the Nobel Lecture. He next took up muscular afferents, in particular the muscle spindles and their motor control; passing over to the spinal cord, he studied the projection of these affarents and separated tonic and phasic motoneurons, established algebraical summation of excitation and inhibition upon these cells, finally also making use of the intracellular approach for the investigation of these and several other problems of motor control. In 1965 he initiated the series of international Nobel Symposia as contributor to, and as Chairman and Editor of Nobel Symposium I, Muscular Afferents and Motor Control.  Ragnar Granit married in 1929 Baroness Marguerite (Daisy) Emma Bruun, daughter of the State Councillor, Baron Theodor Bruun and Mary Edith Henley. The son in this marriage, Michael W. Th. Granit has been Chief Architect of the Communications of Greater Stockholm since 1967. Michael Granit married Elisabet Stolpe in 1957, and they have two sons and one daughter.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Ragnar Granit died on March 12, 1991.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0635** |
| Interview |  |
|  |  |
| ID | **0636** |
| Biographical | Haldan Keffer Hartline was born in Bloomsburg, Pennsylvania, on December 22nd, 1903. His parents were teachers there in the State Normal School (now Bloomsburg State College) where he received his early education. His father, Daniel S. Hartline, was Professor of Biology, but a man whose wide interests also included Astronomy and Geology. It was through his father that Keffer became interested in Natural Sciences.  Keffer Hartline attended Lafayette College in Easton, Pennsylvania, graduating in 1923 (B. Sc.). His college teacher of biology, Beverly W. Kunkel, encouraged him to undertake research; his first scientific paper concerned visual responses of land isopods. Summers at the Marine Biological Laboratory at Woods Hole added to his biological training; there he was especially influenced by Jacques Loeb, Selig Hecht, and Merkel H. Jacobs.  In the autumn of 1923 he entered the Johns Hopkins School where he was encouraged to continue his research interest in vision in the Department of Physiology under E. K. Marshall and C. D. Snyder. Dr. Snyder let him use his [Einthoven string galvanometer](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1924/press.html) with which Hartline undertook the study of the retinal action potential using frogs, decerebrate cats and rabbits. He learned to obtain electroretinograms from intact animals, and recorded clearly recognizable retinal action potentials from human subjects. He also used intact insects for quantitative studies.  After receiving his M. D. from Johns Hopkins in 1927 a National Research Council Fellowship (Medical Sciences) enabled him to study Mathematics and Physics so as to strengthen his background for future biophysical research. He spent two years in the Physics Department of Johns Hopkins taking courses and working as a student in the laboratory of A. H. Pfund; F. D. Murnaghan was his teacher of mathematics. In 1929 he received an Eldridge Reeves Johnson Traveling Fellowship from the University of Pennsylvania, for a continuation of his studies in Physics. He spent one semester with [W. Heisenberg](https://www.nobelprize.org/nobel_prizes/physics/laureates/1932/index.html)‘s seminar group in the University of Leipzig and two semesters attending lectures by A. Somerfeld at the University of Munich.  In the spring of 1931 Hartline returned to the United States taking a position at the University of Pennsylvania, in Philadelphia, in the Eldridge Reeves Johnson Foundation for Medical Physics, which was under the directorship of Detlev W.Bronk. This was the start of a stimulating association with Bronk, which has continued to the present time.  At the Johnson Foundation Hartline began his studies on the activity of single optic nerve fibers in the eye of the horseshoe crab, *Limulus*, recording the responses of receptor units under various conditions of stimulation and adaptation. In the mid 1930’s he undertook the single fiber analysis of the optic responses of the vertebrate retina, principally in the eye of the frog. In the early 1940’s Hartline worked on problems of night vision in human subjects. In 1940-1941 he was Associate Professor of Physiology at Cornell Medical College in New York City, but returned to the Johnson Foundation where he stayed until 1949.  In 1949 Hartline accepted a position at Johns Hopkins University as Professor of Biophysics and Chairman of the Thomas C. Jenkins Department of Biophysics. There, he began with his colleagues work on intracellular recording from receptor units in the *Limulus* eye. It was at that time that he took up the study of the inhibitory interaction in the *Limulus* retina, begun briefly several years before. In 1953 he accepted his present position as Professor at the Rockefeller University (then the Rockefeller Institute). Hartline was joined there, in 1954, by Floyd Ratliff and they have continued to the present time collaboration in their joint laboratory on the study of receptor properties and inhibitory interaction in the eye of *Limulus*, and on related aspects of visual physiology.  Hartline was awarded the William H. Howell Award (Physiology) in 1927; the Howard Crosby Warren Medal (Society of Experimental Psychologists) in 1948; an Sc. D. (hon.) from Lafayette College, 1959; the Albert A. Michelson Award ( Case Institute of Technology) in 1964; a degree of LL. D. from the Johns Hopkins University in 1969; and an hon. D.Sc. from the University of Pennsylvania in 1971; the Lighthouse Award in 1969; hon. M.D. Albert-Ludwigs University, Freiburg im Breisgau, 1971.  Professor Hartline is a Member of the National Academy of Sciences; Foreign Member of the Royal Society (London); Member of the American Academy of Arts and Sciences; Member of the American Philosophical Society, American Physiological Society, Optical Society of America, Biophysical Society, etc.  In 1936 Haldan Keffer Hartline married Elizabeth Kraus, daughter of the eminent chemist C. A. Kraus. At that time she was instructor in Comparative Psychology at Bryn Mawr College. They have three sons, Daniel Keffer, Peter Haldan, and Frederick Flanders. Daniel Keffer and Peter Haldan have positions in neurophysiology in the University of California at San Diego; Frederick Flanders is still engaged in graduate studies in the biological sciences.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Keffer Hartline died on March 17, 1983.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0636** |
| Interview |  |
|  |  |
| ID | **0637** |
| Biographical | George Wald was born in New York City on November 18th, 1906, of immigrant parents, Isaac, who had come from a village near Przemysl, in what was then Austrian Poland, and Ernestine Rosenmann, from a small village near Munich, in Bavaria. After attending public primary and secondary I schools in Brooklyn, he received the degree of Bachelor of Science from Washington Square College of New York University in 1927; and then took graduate work in zoology at Columbia University, from which he received the Ph.D. in 1932. During this graduate period he was a student and research assistant of Professor Selig Hecht.  On receiving the Ph. D. he was awarded a National Research Council Fellowship in Biology (1932-1934). This was begun in the laboratory of [Otto Warburg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1931/index.html) in Berlin-Dahlem and it was there that Dr.Wald first identified vitamin A in the retina. Vitamin A had just been isolated in the laboratory of Professor [Paul Karrer](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1937/index.html) in Zurich, and Dr. Wald went to Karrer’s laboratory to complete the identification. That done, he spent a period in the laboratory of [Otto Meyerhof](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html), at the Kaiser Wilhelm Institute in Heidelberg. The second year of the fellowship was spent in the laboratories of the Department of Physiology at the University of Chicago.  Dr. Wald came to Harvard in the fall of 1934 as a tutor in Biochemical Sciences and has been there ever since; as Instructor and Tutor in Biology (1935-1939); Faculty Instructor (1939-1944); Associate Professor (1944-1948); and Professor of Biology (since 1948). He was visiting Professor of Biochemistry at the University of California for the summer term, 1956.  In 1939 Dr. Wald received the Eli Lilly Award for «Fundamental Research in Biochemistry» from the American Chemical Society. In 1952 he toured the Southwest as a National Sigma Xi lecturer. In 1953 he received the Lasker Award of the American Public Health Association «in recognition of his outstanding discoveries in biochemistry with special reference to the changes associated with vision and the function of vitamin A».In 1955 he was awarded the Proctor Medal of the Association for Research in Ophthalmology, and in 1959 the Rumford Medal by the American Academy of Arts and Sciences. In 1966 he was awarded the Ives Medal of the Optical Society of America; and in May, 1967, jointly with his wife Ruth Hubbard, the Paul Karrer Medal by the University of Zurich. In 1967 he was awarded the T. Duckett Jones Memorial Award from the Whitney Foundation.  Dr. Wald was elected to the National Academy of Sciences in 1950 and to the American Philosophical Society in 1958. He is a Fellow of the American Academy of Arts and Sciences in Boston, and of the Optical Society of America. In 1963-1964 he was a Guggenheim Fellow, spending the year at Cambridge University, England.  In 1957 Dr. Wald received the honorary degree of M. D. from the University of Berne; in 1958 an honorary D. Sc. from Yale University; in 1962 honorary D. Sc. from Wesleyan University; in 1965 honorary D. Sc. from New York University; in 1966 honorary D. Sc. from McGill Univ.; 1968 D. Sc. from Clark Univ. and from Amherst College.  Dr. Wald is a member of the American Society of Biological Chemists; the Optical Society of America; the Assoc. for Research in Ophthalmology; Sigma Xi; American Chemical Society; and the A.A.A.S.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *George Wald died on April 12, 1997.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0637** |
| Interview |  |
|  |  |
| ID | **0638** |
| Biographical | Peyton Rous was born in Baltimore in 1879. His mother’s ancestors were Huguenots who settled in Virginia after the Edict of Nantes. Just before the Civil War in the 1860’s her father, foreseeing disaster, bought land in Texas, moving his big family there after it ended. There he became a judge «riding three counties», and the family throve.  His father, a Baltimorean of English forebears, married his mother while visiting Texas, and returning home became an exporter of grain to Europe. His father died early, leaving his mother with three small children and only scanty means to support them. Yet she would not return to the security of her Texas kin because she was bent on obtaining the best possible education for her children; and what with makeshifts of one sort or another in Baltimore she did it!  During his second year in the Johns Hopkins Medical School – after getting a B.A. from its University in 1900 – Peyton Rous scraped the skin of a finger on a tuberculous bone while doing an autopsy and soon a «corpse tubercle» formed there. The disease travelled to his axillary glands, and after their removal he was told no more could be done than «to go away and try to get well». Peyton Rous went to Texas, there an uncle got him a job «for his keep» on a ranch near Quanah; and in early spring a friend living in the town told him he was sending «two covered wagons» full of hardware to the Spur Ranch, 125 miles west of the railway, and asked if Peyton would like to go along with them. On reaching «The Spur» Peyton Rous was given the job of helping on horseback in the «round ups» of cattle scattered on its huge expanse, and of course he slept on the ground like everyone. During exhilarating months there Peyton learned a superb fact not taught at college, namely that uneducated men can be as great-hearted and lovable as those who know much. This has been a continual source of cheer to him ever since.  Back at the Medical School after having lost (!) a year, he graduated in 1905 and became an interne in its Hospital. Then, finding himself unfit to be a «real doctor», he turned to medical research instead, and for this purpose became an Instructor in Pathology at the University of Michigan on a beggarly salary. His work in the laboratory turned out to be mainly that of a technician because the University had small funds only, but with noble generosity Professor Alfred Warthin, head of the Department, came to his rescue, actually offering to «teach Summer School» in his stead, and give Peyton the sum thus earned, if he would study German hard and use the money to go for the summer to a certain hospital in Dresden where morbid anatomy was taught. Dresden in 1907! Exquisite city in an exquisite land, with no hint of war in the air!  After his return Dr. Warthin told Peyton Rous that the Rockefeller Institute for Medical Research was casting a wide net of grants for beginners, and he asked him if Peyton would like him to apply for one that would free Peyton for experimental work. That grant enabled Rous to find out enough about lymphocytes to be deemed worth publishing in the *Journal of Experimental Medicine*, edited by Simon Flexner, who was also the director of the Institute; and after another few months Flexner asked Rous to take over the laboratory for cancer research which Flexner was quitting to learn more about poliomyelitis, then crippling many American children.  Since these happenings in 1909 the life of Peyton Rous as a working scientist has been halcyon. Soon after beginning it he was able to prove that some «spontaneous» chicken tumours, to all appearances classical neoplasms, are actually started off and driven by viruses which determine their forms as well. These findings led him to spend several years trying to get similar agents from mouse cancers; but, failing in this, he left off working with tumours in 1915, turning instead to the study of other problems in physiological pathology. The results of the study encouraged Rous to undertake further efforts in the same field, and he did not return to the theme of cancer until 1934 when a unique opportunity was offered to him. Dr. Richard Shope, a close friend on the Institute staff, asked Rous to work with a virus which Shope had discovered and found to be responsible for the giant warts often present on the skin of wild rabbits in the southwestern U.S.A. Were they perhaps real tumours? Rous could not resist this generous challenge and he has worked ever since not only with the «warts» themselves – which proved to be benign tumours from which cancers frequently take off – but with other problems of neoplasms.  Investigation on cancer means more to the public than that on any other disease. It may be partly for that reason that Rous has received more than a few honours and awards. Many universities have given him honorary degrees. He is a Foreign Member of the Royal Society of England, as also of its Royal Society of Medicine, and that of Denmark, and the Norwegian Academy of Science and Letters. The Weizmann Institute of Science has appointed Rous an Honorary Fellow and the Academy of Medicine in Paris a Foreign Correspondent. The Kovalenko Medal of the National Academy of Sciences, and the Distinguished Service Award of the American Cancer Society were given to him. Rous also received a Lasker Award of the American Public Health Association, as also a United Nations Prize for Cancer Research; and during 1966 a National Medal of Science has come to him from the U S.A., and the Paul Ehrlich-Ludwig Darmstädter Award from the Federal Republic of Germany.  In 1920 Peyton Rous became a Member of the Rockefeller Institute, and in 1945, when 65 years old, he became a Member Emeritus but continued to be busy in the laboratory as was the case until his death. Recently the Rockefeller Institute has become the Rockefeller University. It supported the work of Rous as amply as was his good fortune in the past.  Peyton Rous married Marion Eckford deKay; she was the daughter of a scholarly commentator on the arts. They brought to each other different likings that have delightfully widened the enjoyment of their lives together. They have three daughters: Marion, Ellen and Phoebe. Marion’s husband, [Alan Hodgkin](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/index.html) is a Professor of Biophysics at Cambridge University and received the Nobel Prize for Physiology or Medicine in 1963. Phoebe married Thomas J. Wilson who died in 1969; he was formerly Director of the Harvard University Press.  Dr Peyton Rous\* died on the 16th of February, 1970.  \* In this biography, which is based on Rous’s own autobiographical note, nothing has been said about the work on blood and liver which occupied him between 1915 and 1934. In particular Rous has not mentioned the pioneer research on blood transfusion with J.R. Turner and O.H. Robertson which led to the establishment in 1917 of the world’s first blood bank near the front line in Belgium. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0638** |
| Interview |  |
|  |  |
| ID | **0639** |
| Biographical | Charles Brenton Huggins was born on September 22nd, 1901, in Halifax, Nova Scotia, the elder son of Charles Edward Huggins, pharmacist, and his wife, Bessie Maria Spencer.  Charles B. Huggins attended the public schools in Halifax; Acadia University (B.A., 1920), Wolfville, N.S.; and Harvard University (M.D., 1924), Boston, Massachusetts. He then interned at the University of Michigan Hospital (1924-1926); he was Instructor in Surgery, University of Michigan (1926-1927). Since 1927 Huggins has been a member of the Faculty of the University of Chicago: Instructor in Surgery, 1927-1929; Assistant Professor, 1929-1933; Associate Professor, 1933-1936; Professor of Surgery, 1936-1962; Director, Ben May Laboratory for Cancer Research, from 1951; and William B. Ogden Distinguished Service Professor since 1962.  Charles B. Huggins married Margaret Wellman on July 29th, 1927. They have a son, Charles E. Huggins and a daughter, Emily Wellman Huggins Fine.  Charles Huggins holds the following honorary degrees: M. Sc., Yale University, 1947; D. Sc., Acadia University, 1946; Washington University, 1951; Leeds University, 1953; Torino, 1957; LL.D., Aberdeen University, 1966; Fellow, Royal College of Surgeons, Edinburgh, 1958; Fellow Royal College of Surgeons (hon.), 1959; Fellow, American College of Surgeons (hon.), 1963.  Among the many awards presented to him, the following may be mentioned here: Gold Medals: American Medical Association, 1936 and 1940; American Cancer Society, 1953; Rudolf Virchow Society, 1964; Charles L. Meyer Prize, National Academy of Sciences, 1943; Comfort Crookshank Prize, Middlesex Hospital, London, 1957; Cameron Prize, Edinburgh University, 1958; Valentine Prize, New York Academy of Medicine, 1962; Hunter Award, American Therapeutic Society, 1962; Laurea, University of Bologna, 1964.  Charles B. Huggins is a Member of the National Academy of Sciences and of the American Philosophical Society.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Charles B. Huggins died on January 12, 1997.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0639** |
| Interview |  |
|  |  |
| ID | **0640** |
| Biographical | François Jacob was born in June 1920 in Nancy (France). He was the only son of Simon Jacob and Thérèse Franck. After attending the Lycée Carnot in Paris, he began studying medicine at the Faculty of Paris, with the intention of becoming a surgeon. These studies were interrupted by the war. In June 1940, when in his second year of medicine, he left France and joined the Free French Forces in London. He was sent to Africa as a medical officer and saw action in Fezzan, Libya, Tripolitania and Tunisia, where he was wounded. He was posted to the Second Armoured Division, and was severely wounded in Normandy, in August 1944. He remained in the hospital for seven months, and was awarded the Croix de la Libération, the highest French military decoration of this war.  After the war, François Jacob completed his medical studies and submitted his doctoral thesis in Paris in 1947. He was unable to practise surgery on account of his injuries, and worked in various fields before turning to biology. He obtained a science degree in 1951, and then a doctorate in science in 1954 at the Sorbonne, with a thesis on «Lysogenic bacteria and the provirus concept».  In 1950, François Jacob joined the Institut Pasteur under Dr. [André Lwoff](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html). He was appointed Laboratory Director in 1956, then in 1960 Head of the Department of Cell Genetics, recently created at the Institut Pasteur. In 1964 he was appointed Professor at the Collège de France, where a chair of Cell Genetics was created for him.[1](https://www.nobelprize.org/prizes/medicine/1965/jacob/biographical/#not1)  The work of François Jacob has dealt mainly with the genetic mechanisms existing in bacteria and bacteriophages, and with the biochemical effects of mutations. He first studied the properties of lysogenic bacteria and demonstrated their «immunity», i.e. the existence of a mechanism inhibiting the activity of genes in the prophage as in infective particles of the same type. In 1954 he began a long and fruitful collaboration with Elie Wollman, in an attempt to establish the nature of the relationships between the prophage and genetic material of the bacterium. This study led to a definition of the mechanism of bacterial conjugation, and also enabled an analysis of the genetic apparatus of the bacterial cell. From this work there emerged a whole series of new concepts, such as the oriented process of genetic transfer from the male to the female, the circularity of the bacterial chromosome or the episome concept. The whole of this work was summarized in a book *Sexuality and the Genetics of Bacteria*.  In 1958 the remarkable analogy revealed by genetic analysis of lysogeny and that of the induced biosynthesis of ß-galactosidase led François Jacob, with [Jacques Monod](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html), to study the mechanisms responsible for the transfer of genetic information as well as the regulatory pathways which, in the bacterial cell, adjust the activity and synthesis of macromolecules. Following this analysis, Jacob and Monod proposed a series of new concepts, those of messenger RNA, regulator genes, operons and allosteric proteins.  In 1963, together with Sydney Brenner, François Jacob put forward the «replicon» hypothesis to account for certain aspects of cell division in bacteria. Since then, he has devoted his attention to the genetic analysis of the mechanisms of cell division. In 1970 he began to study cultured mammalian cells, particularly certain aspects of their genetic properties.[2](https://www.nobelprize.org/prizes/medicine/1965/jacob/biographical/#not2)  In 1970, François Jacob published a book *La logique du vivant, une Histoire de l’Hérédité,* in which, beginning with the 16th century, he traces the stages in the study of living beings that have led up to molecular biology.[3](https://www.nobelprize.org/prizes/medicine/1965/jacob/biographical/#not3)  François Jacob has been awarded a number of French scientific prizes, notably the Charles Léopold Mayer prize by the Académie des Sciences (1962). He is a foreign member of the Danish Royal Academy of Arts and Sciences (1962), the American Academy of Arts and Sciences (1964), the National Academy of Sciences of the United States (1969), and the American Philosophical Society (1969). He has received honorary degrees from several universities. He was invited to give a Harvey Lecture (New York, 1958) and the Dunham Lectures (Harvard, 1964).[4](https://www.nobelprize.org/prizes/medicine/1965/jacob/biographical/#not4)  In 1947 François Jacob married the pianist Lise Bloch. They have four children: Pierre (born in 1949), who has become a philosopher, Laurent and Odile (born in 1952) and Henri (born in 1954), who are still undifferentiated.[5](https://www.nobelprize.org/prizes/medicine/1965/jacob/biographical/#not5)  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  The biography was updated by the Laureate in April 2005:  1. He has been Chairman of the Board of the Institut Pasteur from 1982 to 1988.  2. In the last decade, François Jacob has shifted to the study of the early stage of development in the mouse embryo using mouse teratocarcinoma as a tool. His main goal is to analyze the regulatory circuits involved in development and cellular differenciation of the early embryo.  3. In 1981, he published *Le Jeu des Possibles*, a view on evolution and its mechanisms. In 1987, he published an autobiography *La Statue Intérieure*, and in 1997 he published La *Souris, la Mouche et l’Homme*.  4. François Jacob is a member of the Académie des Sciences, Paris (1977) and of the Académie Française, Paris (1996). He is a foreign member of the Royal Society, London (1973), the Académie Royale de Médecine de Belgique (1973), the Academy of Sciences of Hungary (1986), the Royal Academy of Sciences, Madrid (1987).  5. Lise Bloch died. Second marriage in 1999 with Geneviève Barrier.  For more biographical information, see: Jacob, François, *The Statue Within: An Autobiography*. Basic Books, New York, 1988.  *François Jacob died on 19 April 2013.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0640** |
| Interview |  |
| Q6 | Welcome to the Nobel interview, Professor François Jacob. You have written earlier that the Nobel Prize has changed your life, not only in a positive way, you also realised that it put some kind of burden on your back. |
|  | The group we had in the Pasteur Institute with Lwoff, Monod and several people was rather unknown of the French public. We had a lot of foreign students; American students, British, German and so on and so forth, but very few French students. This group was ignored of the French authorities and French university and suddenly at one certain Thursday at noon the news arrived that you were awarded the prize and it worked like a wave. I mean all the newspaper, all the TV which were around in Paris just came there, and it was just like a wave you receive in full face. And then from being completely unknown we became too much known very rapidly, and it’s a bit difficult for a time to face this situation but you finally can do it. |
| Q6 | So, what happened? |
|  | So what happened that we go on working, and it has also positive thing in the sense that you can more easily get support for your work, that you can more easily get good students and so forth. So you have a good side and a bad side on this of course. |
| Q84 | Yes. You were not only unknown, you were also kind of hidden in the attic of the Pasteur Institute. |
|  | That’s right, the attic was … Lwoff made some very important discovery before the war and he was made head of the department in the Pasteur Institute and the department which was created for him, which was bacterial physiology and he was given this attic on one of the buildings of the Pasteur Institute and when I arrived after the war I knew nothing in science. I had been wanting to do surgery and I was very heavily wounded and I had a bad arm and bad leg so I couldn’t do surgery and I tried to be an actor, I tried to do journalism, I did a lot of things and finally I tried to go into science but, as I said, I knew nothing in science and I decided that I’d give me five years, either I find something in five years or I do something else. |
| Q84 | And when was it? |
|  | This was in 1950. But the point is I learned that there were two good labs in Paris and one which was nicer than the other. The nicer one was the one which was headed by Lwoff and in which Monod was working, at the Pasteur Institute, and it was already at the Pasteur Institute, and I went and saw Lwoff and asked him whether I could work with him and he said No, I have no room, and for a year I came every month asking him whether I could work with him and finally he was so fed up with me that he said Yes and this was in the middle of 1950, yes. |
| Q84 | So you ended up on this attic? |
|  | So ended up in this attic and the attic was very interesting because it was a long corridor, at one pole there was Lwoff and his group, at the other was Monod and his group, and in the middle people were always meeting, talking, discussing, trying to put down the experiment of the other and criticising each other. It was extremely lively and extremely active and in this attic a large number of foreign people, as I said, was coming every year. So it was fantastically intellectual living place. |
| Q20 | Yes, and you had also many contacts with the American scientists? |
|  | Yes, there were many American scientists coming in, either professor for sabbatical year or post doc students. |
| Q39 | And you used also to go to Cold Spring Harbor? |
|  | Yes, I went to Cold Spring Harbor for the first time in 1953 and it was very interesting. I mean the students and the whole atmosphere was very different from what was existing in France. |
| Q39 | In what way? |
|  | In France when the professor had said something the student said Ok, well good, very good and in the States it was very funny. They were criticising strongly the professors and arguing with them. It was a very different climate but very interesting and when we went there in the States we tried to import in Europe, in France anyway, the American way of teaching and all this, yes. |
| Q11 | How do you remember Jacques Monod and André Lwoff as persons? |
|  | They were very different from each other, although Lwoff was some kind of an artist, actually he liked also to paint and he painted a lot and he had the intuition of the important problems. When he started with certain scientific problem and he went deeply in, but when you arrive at a certain success and a certain discovery then he stopped and he changed and went to another problem and he changed; I don’t know four, five times in his life and every time very successfully. He started with the vitamins and he explained what vitamins was and he came to viruses and bacteriophages showing that the genes of a virus can become part of a bacteria gene chromosome. Then he turned to other viruses, so changed he a lot.  Monod was completely the opposite. If he stared in one problem, which were his doctoral thesis then he went on all his life going deeper and deeper on this particular problem. So they were completely different but extremely good friends. |
| Q85 | And you were the third one I would say in this trio, the youngest one and what kind of scientist are you? |
|  | Oh, I wonder. I was in the middle. I worked with Lwoff finally after this, but I said that I’d be going every month to him. Finally, he told me one day, You know we have found the induction of the prophage. I said, Oh. I was very admirative, but I didn’t understand a word of what he was saying and when I came out of that I just went to library and I couldn’t find out what a prophage or induction of a prophage was. Finally, I understood later on, but I told him: I am dying to do that with you, and so he accepted me and I began to work there. So I worked with him and did my thesis with him but after that I worked with Elie Wollman, who was just a little bit older than I was and we worked on the genetics of bacteria and we were able to analyse the whole genetic system, the way bacteria can copulate. It was a system which had been found by [Josh Lederberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/lederberg-facts.html) and we analysed in detail.  … that was my role – to be in between and put the two things together …  But once we had this system in hand it was clear that it was a fantastic tool to analyse any function of the bacterial cell. So it turned out that it was important for the kind of problem that Monod was investigating, which was how the genes activity respond to environment, that our system of bacteria copulation was a very good tool to analyse that so I turned and worked with Monod at that time. And it turned out a very funny thing that Monod was working at one side on enzymes and disease and Lwoff was working on viruses and it turned out that the system were extremely similar, extremely alike and then you could make a general model of the way gene activity is regulated by using either system, that was my role – to be in between and put the two things together. |
| Q42 | Yes, in one corridor. You did also write about the way science works and you use these words that you can divide science in two parts; one is day science and one is night science. Can you elaborate a bit on that? |
|  | That’s right. When you look at books or you look at papers people write you find that science is a nice treat, that you can go from one point to another in a very classical way and very profound way but I don’t think it’s the way science is. In fact, by night, when you are in your bed and you don’t sleep you wonder what you are doing, you hesitate to do this, is what I do reasonable? And it has nothing to do with the habitual description of the glory that you have, “la jardin française”, where you can walk, it’s very different from that and that’s what I call day science, which is the finished science, that’s what you look in the books and the night science which is the actual way when you fight with everything and wonder and being sure to be wrong, in fact. |
| Q34 | This time in science where you entered it in 1950s, this was really a time of revolution in biology. How do you view the development of biology since then? |
|  | Well, there are two points which are important I think. One was that going on with the success beginning of molecular biology was to work with bacteria and viruses because it was very simple. You could analyse very simply and you could find a lot of mutants, you could make a lot of combinants, you could go to the genetic material itself, find out how it works; that was very nice and extremely successful. But when you wanted to apply these techniques to higher organisms, actually we were interested in ourselves finally, you couldn’t do that, and it became possible through genetic engineering and genetic engineering came out in the beginning of the 1970s.  It happened that you could isolate DNA, sequence DNA, pick up a gene, look at the presence of a gene, put him in a different organism or bacteria. You could do a lot of things, and then this gave access to higher organisms, that was essentially at the 1970s, and it became possible at the beginning of 1980s to tackle another absolutely fundamental problem of biology, which is embryonic development. That is how does it happen that you take a sperm cell, an egg cell, put them together, you have an egg and this gives two cells, four cells, eight cells and this gives you or me, that’s really the most fantastic problem you can imagine, that you have this four cells, eight cells; and then you have a small part which happened which has become distinct, a group of cells which is going to give the brain with which you learn to talk, to write, to come to Stockholm or to go through the street.  This was just impossible to believe 20 years ago …  This was really one of the big mysteries and it was impossible to handle seriously before this genetic engineering was possible and this we have learnt a lot and we have learnt incredible things, things which were completely incredible 20 years ago. For instance, that the same genes which make the plan of an insect, of a “drosophile”, the fly, the same gene make the plan for a human being or mouse or well … This was just impossible to believe 20 years ago. |
| Q34 | Can you see something that will come? Can you speculate on that? |
|  | No. I mean I am not Madam Soleil. In France we have a very famous predictor who’s called Madam Soleil, Mrs Sun, and she sees anything, you can say “n’importe quoi” but if you make prediction you’re sure to be wrong, that’s the only thing you can say. Except one thing that probably the brain will be the main… because the brain is the thing which know the least and probably this will be the main object of the coming year. |
| ID | **0641** |
| Biographical | André Michel Lwoff was born on 8 May 1902 in Ainay-le-Château (Allier). He joined the Institut Pasteur at the age of 19. He had graduated in science and had done one year of medicine. Lwoff completed his studies while working in the laboratory. In 1921, he had the good fortune to study under a very great microbiologist, Edouard Chatton; Lwoff remained his colleague for seventeen years. It was through him that Lwoff joined the Institut Pasteur in the laboratory of Félix Mesnil. His first investigations were on the parasitic ciliates, their developmental cycle, and morphogenesis. Later, he worked on the problems involved in the nutrition of protozoans. André Lwoff obtained his M. D. in 1927 and his Ph. D. in 1932.  In 1932-1933 a grant from the Rockefeller Foundation enabled him to spend a year in Heidelberg in the laboratory of [Otto Meyerhof](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html). He studied haematin – a growth factor for the flagellates – the specificity of protohaematin, its quantitative effect on growth, and the part it played in the respiratory catalyst system.  Then in 1936, again with the aid of a grant from the Rockefeller Foundation, Lwoff and his wife spent seven months in Cambridge in the laboratory of David Keilin; factor V, which is required by *Haemophilus influenzae*, was identified with cozymase and its physiological role for the bacterium was defined.  There were many other investigations on growth factors for flagellates and ciliates with regard to growth factors, loss of function, and physiological development until the time when Lwoff began working on the problem of lysogenic bacteria.  Dr. Lwoff was appointed Head of the Department at the Institut Pasteur in 1938, and Professor of Microbiology at the Science Faculty in Paris in 1959.  The observation of isolated bacteria led him to the conclusion that lysogenic bacteria did not secrete bacteriophages, that the production of bacteriophages led to the death of the bacterium, and above all that this production must be induced by external factors. It was this hypothesis which, together with Louis Siminovitch and Niels Kjeldgaard, led Lwoff to discover the inductive action of ultraviolet irradiation (1950).  In 1954 Prof. Lwoff began studying poliovirus. Experiments on the relations between the temperature sensitivity of viral development and neurovirulence led him to consider the problem of viral infection. In this way it became clear that non-specific factors play an important part in the development of the primary infection. He has now begun to investigate the action mechanism of specific inhibitors of viral development.  André Lwoff has been honoured by the following prizes of the Académie des Sciences: Lallemant, Noury, Longchampt, Chaussier, Petit d’Ormoy prizes and the Charles-Léopold Mayer Foundation prize. He also received the Barbier prize from the Académie de Médecine, and the Leeuwenhoek Medal of the Royal Netherlands Academy of Science and Arts (Amsterdam, 1960), as well as the Keilin Medal of the British Biochemical Society (1964).  He is a Honorary Member of the Harvey Society (1954), of the American Society of Biological Chemists (1961), of the Society for General Microbiology (1962), and a Corresponding Member of the Botanical Society of America (1956).  He is President of the International Association of Microbiological Societies, and a Member of the International Committee for the Organization of Medical Sciences. He is a Member of the Société Zoologique de France, of the Société de Pathologie exotique, of the Société de Biologie and president of the Société des Microbiologistes de langue française. Furthermore a Honorary Member of the New York Academy of Sciences (1955), Honorary Foreign Member of the American Academy of Arts and Sciences (1958), Associate of the National Academy of Sciences of the United States of America (1955), and a Foreign Member of the Royal Society, London (1958).  He holds honorary degrees from the following universities: Chicago (D. SC., 1959), Oxford (D.Sc., 1959), Glasgow (Doctor of Laws, 1963) and Louvain (M. D., 1966).  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *André Lwoff died on September 30, 1994.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0641** |
| Interview |  |
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| ID | **0642** |
| Biographical | Jacques Lucien Monod was born in Paris on February 9th, 1910. In 1917 his parents settled in the South of France, where Monod spent his early years, and he therefore thinks of himself as a Southerner rather than as a Parisian. His father was a painter, something of an unusual vocation for a Huguenot family in which doctors, ministers of the Church, civil servants, and professors predominated. His mother was American, born in Milwaukee, with a father of Scottish descent – again somewhat out of the ordinary considering French bourgeois tradition at the end of the nineteenth century. His secondary education took place at the lycée de Cannes, and he owes a great deal to some of the masters under whom he was fortunate enough to study. Monod in particular recalls Monsieur Dor de la Souchère, well known as the founder and curator of the Antibes museum. Although Monod remembers nothing of the Greek grammar studied under him, the admiration which he soon developed for this highly cultured and worthy man was of the greatest spiritual benefit for him as a youngster. It is difficult to express just how much Monod owes to his father, who combined artistic sensitivity with prodigious erudition and a passionate concern for intellectual affairs. He had a positivist faith in the joint progress of science and society. It was through his father, who used to read Darwin, that Jacques Monod developed his interest in biology very early in life.  Monod came to Paris in 1928 to begin his higher education, and registered at the Faculty for a degree in Natural Sciences, not realising (as he later found out) that this course was then some twenty years or more behind contemporary biological science. It was from others, a few years senior to himself, rather than from the professional staff, that he gained his true initiation into biology. To George Teissier he owes a preference for quantitative descriptions; [André Lwoff](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1965/index.html) initiated him into the potentials of microbiology; to Boris Ephrussi he owes the discovery of physiological genetics, and to Louis Rapkine the concept that only chemical and molecular descriptions could provide a complete interpretation of the function of living organisms.  Monod obtained his Science Degree in 1931, and his doctorate in Natural Sciences in 1941. After lecturing at the Faculty of Sciences in 1934, and spending some time at the California Institute of Technology on a Rockefeller grant in 1936, Monod joined the Institut Pasteur after the liberation as Laboratory Director in Lwoff’s Department. He was made Director of the Cell Biochemistry Department in 1954, and in 1959 was appointed Professor of the Chemistry of Metabolism at the Sorbonne. In 1967 he became Professor at the Collège de France, and in 1971 he was appointed Director of the Institut Pasteur.  The following honours and distinctions were awarded to Professor Monod: Montyon Physiology Prize of the Acadèmie des Sciences (Paris, 1955), Louis Rapkine Medal (London, 1958), Honorary Foreign Member of the American Academy of Arts and Sciences (1960), Chevalier de l’Ordre des Palmes Académiques (1961), Charles Léopold Mayer Prize of the Académie des Sciences (1962), Officier de la Légion d’Honneur (1963), Honorary Foreign Member of the Deutsche Akademie der Naturforscher «Leopoldina» (1965), D. Sc. *h. c.* University of Chicago (1965), Foreign Member of the Royal Society (1968 ), Foreign Member of the National Academy of Sciences (Washington, 1968), Foreign Member of the American Philosophical Society (1969), D. Sc. *h. c.* of the Rockefeller University (1970). His military distinctions include: Honorary Colonel of the Reserve, Chevalier de la Légion d’Honneur (military) (1945), Croix de Guerre (1945), and the Bronze Star Medal.  In 1938, Jacques Monod married Odette Bruhl, now the curator of the Guimet Museum. As an archeologist and orientalist with the most sensitive and impeccable taste, his wife brought to the marriage a culture complementary to his own. They have twin sons, Olivier and Philippe. Their father did nothing to influence them to become men of science like himself. On the contrary, he made every effort to persuade them that the realm of knowledge and ideas is not confined to the present-day connotation of the word «science». Both of them nevertheless became scientists: one a geologist, the other a physicist. These two sons gave the parents what they lacked before: two daughters, or rather daughters-in-law, and even a grand-daughter with the pretty name of Claire. The interests of Jacques Monod include almost all aspects of Arts and Sciences, his favourite recreations are music and sailing.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Jacques Monod died on May 31, 1976.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0642** |
| Interview |  |
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| ID | **0643** |
| Biographical | Konrad E. Bloch was born on 21st January 1912, in Neisse, Upper Silesia, then Germany, the son of Fritz Bloch and his wife Hedwig, née Striemer. He attended the elementary school and the Real gymnasium in the same city and in 1930 went to Munich to study chemistry at the Technische Hochschule. He became soon attracted to organic chemistry, especially the structure of natural products, an interest which he owed in large measure to the inspired teaching of [Hans Fischer](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1930/index.html). Another influential experience was to attend the Sessions of the Münchener Chemische Gesellschaft and to hear the great organic chemists of the time, [Adolph Windaus](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1928/index.html), [Heinrich Wieland](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1927/index.html) and [Rudolf Willstätter](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1915/index.html) report their researches on steroids, porphyrins and enzymes.  For racial reasons his studies in Munich ended in 1934 after he had obtained the degree of Diplom-Ingenieur in Chemistry. Leaving Germany Bloch was fortunate to find a temporary position at the Schweizerische Forschungsinstitut in Davos, Switzerland. His assignment there was to investigate the phospholipids of tubercle bacilli, his first exposure to biochemical research.  In 1936 Bloch was able to immigrate to the United States as he had long hoped. On advice by the late Max Bergmann and with the generous support of the Wallerstein Foundation, he entered the Department of Biochemistry, College of Physicians and Surgeons, Columbia University, where he became a graduate student under Hans T. Clarke. Research leading to the Ph.D. degree was completed in 1938. Rudolf Schoenheimer then asked Bloch to join his research group. The first few years spent at Columbia with Schoenheimer and his associate David Rittenberg were certainly the most influential of his «Lehrjahre». This period more than any other developed his lasting interest in intermediary metabolism and problems of biosynthesis. During that time (in 1942) Bloch in collaboration with David Rittenberg initiated the work on the biological synthesis of cholesterol which was to occupy his research interests for nearly twenty years.  In 1946 Bloch moved to the University of Chicago as Assistant Professor of Biochemistry. Appointments to Associate Professor and Professor followed in 1948 and 1950, respectively. At Chicago, in the Biochemistry Department headed by E. A. Evans Jr., the intellectual climate was stimulating and the conditions ideal for the development of young investigators. Work on cholesterol, biosynthesis was continued and progressed well with the aid of able and enthusiastic students. During the years at Chicago Bloch also investigated (with J. Snoke) the enzymatic synthesis of the tripeptide glutathione. As a Guggenheim fellow in 1953 he spent a highly rewarding year at the Organisch-Chemisches Institut, Eidgenössische Technische Hochschule in Zurich with [L. Ruzicka](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1939/index.html), [V. Prelog](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1975/index.html) and their colleagues. The biogenetic considerations on terpene-sterol relationships developed by the Swiss at that time provided rich inspiration for the experimental work in his own laboratory after his return to the United States.  In 1954 Bloch was appointed Higgins Professor of Biochemistry in the Department of Chemistry, Harvard University, and in 1968 he became Chairman of the Department. Apart from continuing research on various aspects of terpene and sterol biogenesis, he has become interested in the enzymatic formation of unsaturated fatty acids and more recently in various aspects of biochemical evolution.  Professor Bloch is a member of the American Chemical Society, National Academy of Sciences U. S., American Academy of Arts and Sciences, American Society of Biological Chemists, Harvey Society, American Philosophical Society, a honorary member of the Lombardy Academy of Sciences, and a Senior Fellow of the Australian Academy of Science. He was President of the American Society of Biological Chemists (1967), Chairman of the Section of Biochemistry, National Academy of Sciences (1966-1969), and Chairman of the National Committee for the International Union of Biochemistry (1968).  Dr. Bloch has been honored as recipient of the following medals and awards: Medal of the Société de Chimie Biologique (1958), Fritzsche Award (American Chemical Society, 1964), Centennial Science Award (University of Notre Dame, 1965), Cardano Medal (Lombardy Academy of Sciences, 1965), Distinguished Service Award (University of Chicago School of Medicine, 1964), William Lloyd Evans Award (Ohio State University, 1968). He holds honorary doctor degrees from the universities of Uruguay (1966), Brazil (1966), Nancy (1966), Columbia University (1967), Technische Hochschule, Munich (1968), and Brandeis University (1970).  In 1941 Konrad Bloch married Lore Teutsch, a native of Munich. They have two children, Peter, and Susan.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Konrad Bloch died on October 15, 2000.* |
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| ID | **0644** |
| Biographical | Feodor Lynen was born in Munich on 6 April 1911, the son of Wilhelm Lynen, Professor of Mechanical Engineering at the Munich Technische Hochschule. His mother, Frieda, was the daughter of the manufacturer Gustav Prym. Lynen completed his primary and secondary schooling in Munich, and in 1930 matriculated at the chemistry department of Munich University. Those who were to become responsible for his scientific training included Heinrich Wieland, Otto Hönigschmidt, Kasimir Fajans, and Walter Gerlach. The most enduring impression was left by [Heinrich Wieland](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1927/index.html), who had won the Nobel Prize for Chemistry in 1927 and under whom Lynen graduated in March 1937 with the work: «On the Toxic Substances in Amanita». On completion of his doctoral thesis Lynen became acquainted under his guidance with the dynamic field of biochemistry, to which he has remained faithful to this day.  Lynen has also remained faithful to Munich University, where he became a chemistry lecturer in 1942, assistant professor in 1947, and biochemistry professor in 1953. In addition, in 1954 he became head of the Max-Planck-Institut für Zellchemie, newly created for him as a result of the initiative of [Otto Warburg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1931/index.html) and [Otto Hahn](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1944/index.html), then President of the Max-Planck-Gesellschaft zur Förderung der Wissenschaften. In this way Lynen acquired outstanding opportunities for scientific research.  Lynen’s work has been devoted to the elucidation of the chemical details of metabolic processes in living cells, and of the mechanisms of metabolic regulation. The problems tackled by him, in conjunction with German and other workers, include the Pasteur effect, acetic acid degradation in yeast, the chemical structure of «activated acetic acid» of «activated isoprene», of «activated carboxylic acid», and of cytohaemin, degradation of fatty acids and formation of acetoacetic acid, degradation of tararic acid, biosynthesis of cysteine, of terpenes, of rubber, and of fatty acids.  In 1954 Lynen received the Neuberg Medal of the American Society of European Chemists and Pharmacists, in 1955 the Liebig Commemorative Medal of the Gesellschaft Deutscher Chemiker, in 1961 the Carus Medal of the Deutsche Akademie der Naturforscher «Leopoldina», and in 1963 the Otto Warburg Medal of the Gesellschaft für Physiologische Chemie.  He is a member of the Bayerische Akademie der Wissenschaften in Munich and of the Deutsche Akademie der Naturforscher «Leopoldina» in Halle, honorary member of the Harvey Society in New York, the American Society of Biological Chemists in Washington, the Asociacion Venezolana para el Avance de la Ciencia in Caracas, foreign member of the National Academy of Sciences of the United States of America in Washington, and the American Academy of Arts and Sciences in Boston. He has received an honorary doctorate from the faculty of medicine of the University of Freiburg i. Br.  On January 1st, 1972, Prof. Feodor Lynen was appointed President of the Gesellschaft Deutscher Chemiker (GDCh).  He was married on 14 May 1937 to Eva Wieland, daughter of his academic teacher. They have five children: Peter, born in 1938; Annemarie, born in 1941; Susanne, born in 1945; Heinrich and Eva-Maria, born in 1946.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Feodor Lynen died on August 6, 1979.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0644** |
| Interview |  |
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| ID | **0645** |
| Biographical | John Carew Eccles was born in Melbourne, Australia, on January 27th, 1903. He owes much to his early training by his father, William James Eccles, who was a teacher as also was his mother, née Mary Carew. He graduated from Melbourne University in Medicine with first class honours in 1925, and as Victorian Rhodes Scholar for 1925 entered Magdalen College, Oxford, as an undergraduate in order to study under [Sir Charles Sherrington](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1932/index.html).  In 1927, with first class honours in Natural Sciences, the Christopher Welch Scholarship and a Junior Research Fellowship at Exeter College, Oxford, he commenced research on reflexes with Sherrington’s colleagues. Later from 1928 to 1931 he was research assistant to Sherrington, there being eight papers published conjointly; and he also collaborated with [Ragnar Granit](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1967/index.html) on two research projects. He was awarded an Oxford D. Phil. degree in 1929 for a thesis on Excitation and Inhibition. Later Oxford appointments were to a Staines Medical Fellowship at Exeter College in 1932, a tutorial fellowship of Magdalen College, and a University Demonstratorship in 1934.  During this Oxford period research was largely on synaptic transmission both in the central nervous system and peripherally in sympathetic ganglia, smooth and cardiac muscle. Using the newly developed techniques of electrophysiology – amplifiers and cathode ray oscilloscopes. It was the period of controversy between the exponents of the rival chemical and electrical theories of synaptic transmission with Eccles in particular resisting many aspects of the chemical transmitter story that was being developed so effectively by [Dale](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1936/index.html) and his colleagues. In retrospect it can be appreciated that this controversy had the effect of defining problems and stimulating much good experimental work, but the decisive victory of the chemical theory had to await the intracellular recording both from neuromuscular junctions by Fatt and [Katz](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1970/index.html) and from nerve cells that was made possible by the technique of the microelectrode with cathode follower amplification. And now, as a final stage of this drama, electrical transmission between nerve cells is being demonstrated in many specialized synapses, not only in the invertebrate, but also in the vertebrate nervous system. These recent developments have served to increase still further the assurance with which we can accept the chemical transmitter hypothesis for an overwhelming majority of both central and peripheral synapses.  In 1937 Eccles left England for Australia to become Director of a small medical research unit in Sydney, where he was fortunate to have the distinguished collaboration of Bernard Katz and Stephen Kuffler. This period from 1937 to 1943 was devoted largely to an electrophysiological analysis of the neuromuscular junctions of cats and frogs, but in the later years his time was almost entirely occupied by applied science related to the war effort. Subsequently as Professor of Physiology at the University of Otago, New Zealand, from 1944-1951 he returned to synaptic transmission in the central nervous system; and in 1951 Brock, Coombs and Eccles succeeded for the first time in inserting microelectrodes into nerve cells of the central nervous system and in recording the electrical responses produced by excitatory and inhibitory synapses. This early work was described in the Waynflete Lectures of Magdalen College, Oxford, in 1952, which in 1953 were published as *The Neurophysiological Basis of Mind: The Principles of Neurophysiology*. The New Zealand interlude was also notable because there Eccles met the philosopher, Karl Popper, from whom he learnt the relationship of the scientist to hypotheses; how to be daring in developing hypotheses of the greatest generality, and at the same time how to test them with the utmost rigour with the consequence either of falsification in whole or in part, or at best corroboration; but never confirmation. He feels that this relationship to hypotheses has not only increased his conceptual power, but has also greatly helped emotionally! He can now rejoice even in the falsification of a cherished theory, because even this is a scientific success.  From 1952 until 1966 Eccles was Professor of Physiology of the Australian National University. In the earlier years (1953-1955) in collaboration with Coombs and Fatt, attention was concentrated on the biophysical properties of synaptic transmission, which is the research that has been cited in the Nobel Award. The conceptual basis of these investigations derived particularly from the hypotheses of the ionic mechanisms of membrane activity that had been developed by [Hodgkin](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/index.html), [Huxley](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/index.html), Katz and Keynes in England. In 1955 this stage of the investigation was described in the Herter Lectures of Johns Hopkins University, and was published in 1957 as *The Physiology of Nerve Cells*. Subsequently the ionic sieve hypothesis of inhibitory synaptic action developed from that early work has been corroborated not only in Canberra by the many associates listed in the references of the lecture, but also in several other laboratories.  There have been in recent years remarkable advances in the powerful microtechniques: electron-microscopy, microelectrode recording and micropharmacology. Eccles surveyed all these new developments in *The Physiology of Synapses* in 1964.  However, the nervous system is not simply to be understood as a system of synaptic transmissions. The organization of the pathways of communication is essential for even the simplest explanations of its performance. From 1960-1966 these organizational problems dominated the research programs of the Canberra laboratory. Soon the problems were studied at the much more challenging levels of the brain with investigations firstly of the dorsal column nuclei and thalamus, then of the hippocampus and finally of the cerebellum. The rationale of these studies is to understand the mode of operation of the structural patterns that form such a characteristic feature of the aggregations of nerve cells in the cerebellum and the hippocampus, for example.  From 1966 Eccles continued this research first at the Institute of Biomedical Research at Chicago and after 1968 at the State University of New York at Buffalo. Progress accounts appeared in two books, *The Cerebellum as a Neuronal Machine*, published conjointly with Professors M. Ito and J. Szentágothai as co-authors, and *The Inhibitory Pathways of the Central Nervous System* (1969) which are the Sherrington Lectures at the University of Liverpool.  In addition to this purely scientific study of the brain, Eccles has followed Sherrington in developing a philosophy of the human person that is consonant with the whole of brain science. Various aspects of this philosophy were developed in lectures and broadcast talks, and recently the whole of Eccles’ philosophical thought has been brought together in a book entitled *Facing Reality* published by Springer in the Heidelberg Science Library (1970).  The research work of Eccles in neurophysiology has been recognized by several honours and awards amongst which the following may be mentioned: Knight Bachelor, 1958; Fellow of the Royal Society, London, 1941 (Ferrier Lecturer, 1959; Royal Medal, 1962); Fellow Royal Australasian College of Physicians (Rennie Lecturer, 1963); Fellow Royal Society of New Zealand; Fellow Australian Academy of Science (President 1957-1961, Flinders Lecturer, 1963); Honorary Foreign Member, American Academy of Arts and Sciences, 1959; Fellow, Pontifical Academy of Sciences, 1961; Member Deutsche Akademie der Naturforscher «Leopoldina» (Cothenius Medal, 1963); Foreign Honorary Member, Accademia Nazionale dei Lincei, 1963; Honorary Fellow, Exeter College, Oxford; Honorary Member, American Philosophical Society, 1964; Hon. Sc.D. (Cantab.), 1960; Baly Medal, Royal College of Physicians, 1961; Hon. D.Sc., University of Tasmania, 1964; Hon. Fellow, Magdalen College, Oxford; Hon. Member, American Neurological Association; Hon. LL. D., University of Melbourne, 1965; Hon. Life Member, New York Academy of Sciences; Foreign Associate, National Academy of Sciences, 1966; Hon. D.Sc., University of British Columbia, Vancouver; Hon. D.Sc., Gustavus Adolphus College, 1967; Hon.Fellowship, American College of Physicians; Hon. D.Sc., Marquette University; Honorary Member, Accademia Medica Lombarda; Hon. Fellow, Indian Academy of Sciences, 1968; Hon. Member, Czechoslovak Medical Society J. E. Purkyne; Associate Member, Académie Royale de Belgique, 1969; Hon. M.D., Charles University, Prague; Hon. D.Sc., Loyola University, Chicago; Hon. M.D., Yeshiva University, New York.  In 1928 John Carew Eccles married Irene Frances Miller of Motueka, New Zealand, and there are nine children; four sons and five daughters, of whom the two eldest sons are scientists with Ph. D.’s. Rosamond collaborated with her father in much of his neurophysiological research, his son Peter is a radar meteorologist. Following divorce in 1968, Eccles married Helena Táboríková of Prague, Czechoslovakia, who is an M.D. of Charles University and a neurophysiologist. They collaborate in their research.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Sir John Eccles died on May 2, 1997.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0645** |
| Interview |  |
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| ID | **0646** |
| Biographical | Alan Lloyd Hodgkin was born in Banbury, Oxfordshire, on February 5th, 1914. His parents were George Hodgkin (who died in Baghdad in 1918) and Mary (Wilson) Hodgkin, now Mrs. Lionel Smith. Alan Lloyd Hodgkin was educated at the Downs School, Malvern (1923-1927), Greshams School, Holt (1927-1932), and Trinity College, Cambridge (1932-1936). His grandfather, Thomas Hodgkin, and uncle, Robin Hodgkin, were historians and to begin with Alan hesitated between history and science. However, he was strongly interested in natural history and that decided him to take up biology and chemistry. After he had become a scholar at Trinity, his future zoology teacher, Carl Pantin, advised him to learn as much mathematics and physics as he could. This was good, if painful, advice which has kept him busy ever since. As an undergraduate he started some rather amateur experiments on frog nerve and continued this line for several years, first as a research scholar and later as a fellow of Trinity. At that period the high table of Trinity included an astonishing array of scientific talent, and Hodgkin found it inspiring if sometimes daunting to meet people like [J. J. Thomson](https://www.nobelprize.org/nobel_prizes/physics/laureates/1906/index.html), [Rutherford](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1908/index.html), [Aston](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1922/index.html), Eddington, [Hopkins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1929/index.html), G. H. Hardy and [Adrian](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1932/index.html). In the Physiological Laboratory he learnt about cable-theory from Rushton and about amplifiers from Matthews, Grey Walter and Rawdon-Smith.  [A. V. Hill](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html), who refereed his fellowship thesis, had lent a copy to [Gasser](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1944/index.html) and this resulted in an invitation to work in the latter’s laboratory at the Rockefeller Institute in New York. During that period (1937-1938) Hodgkin spent several weeks with K. S. Cole at Woods Hole and there he learnt how to dissect squid axons. He returned to Cambridge in 1938 and in the following year started a collaboration with [A. F. Huxley](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/index.html), whom he had the good fortune to teach.  During the first few months of the war Hodgkin worked on aviation medicine with Matthews at Farnborough and from February 1940 to July 1945 in various parts of England on airborne radar. The project with which he was most concerned was the development of a scanning and display system for a 10-cm detection system in night-fighters.  After the war Hodgkin returned to Cambridge where he held a teaching post in the Physiology Laboratory; A. F. Huxley returned a few months later and they continued the collaboration which started before the war. R. D. Keynes joined them a year later and there was soon a small group interested in ionic mechanisms in living cells. Lord Adrian greatly assisted the progress, partly by lightening the teaching load and partly by arranging with the Rockefeller Foundation for a generous grant to support the work; later help was received from other bodies, particularly the Nuffield Foundation and the Royal Society. Most of the experiments on giant nerve fibres had to be done at a Marine Station, and since 1947 Hodgkin has usually spent two or three months each year at the Laboratory of the Marine Biological Association, Plymouth, where he has received much help from the director and the staff of that laboratory.  Professor Hodgkin was elected to a fellowship of the Royal Society in 1948 and in 1951 became a Foulerton Research Professor of the Royal Society. He served on the Royal Society Council from 1958-1960 and on the Medical Research Council from 1959-1963; he was foreign secretary of the Physiological Society from 1961-1967. In 1970 he was appointed John Humphrey Plummer Professor of Biophysics. He has been President of the Marine Biological Association since 1966, and President of the Royal Society since December 1970. In 1971 he was appointed Chancellor of Leicester University.  Among the honours and awards which have been given to Prof. Hodgkin the following might be mentioned: Royal Medal of the Royal Society, 1958; Copley Medal of the Royal Society, 1965; Member of the Royal Danish Academy of Sciences, 1964; Foreign Member of the American Academy of Arts and Sciences and of the American Philosophical Society; Member of the Deutsche Akademie «Leopoldina» Honorary Fellow, Indian National Science Academy; Hon. M. D. of the Universities of Berne and Louvain; Hon. D.Sc. of the universities of Sheffield, Newcastle, E. Anglia, Manchester, Leicester and London. He was made a KBE in the New Years’ Honours 1972.  While at the Rockefeller Institute in 1938 Hodgkin met [Peyton Rous](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1966/index.html), the distinguished pathologist, and he got to know his family. His daughter, Marion Rous, and Alan Lloyd Hodgkin were married in 1944, while he was on a brief war-time visit to America. They have lived in Cambridge since 1945 and have three daughters and one son. Mrs. M. R. Hodgkin is Children’s Book Editor at Macmillan Publishing Company. His eldest daughter, Sarah (Mrs. R. Hayes), is married and has worked in publishing with Gollancz Ltd. His second daughter, Deborah, is a research student in Psychology at University College London. His son, Jonathan works in Molecular Biology at Cambridge, and his youngest daughter, Rachel, is also at Cambridge reading English.  Hodgkin’s favourite recreations include travel and fishing.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Hodgkin, Alan Lloyd. *Chance & Design: Reminiscences of Science in Peace and War*. Cambridge University Press, Cambridge, 1992.  *Alan L. Hodgkin died on December 20, 1998.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0646** |
| Interview |  |
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| ID | **0647** |
| Biographical | Andrew Fielding Huxley was born in Hampstead, London, on 22nd November 1917. His father, Leonard Huxley, who was a son of the nineteenth – century scientist and writer Thomas Huxley, was for a time a classics master at Charterhouse School and later took up a literary career, writing a number of biographies and being editor of the «Cornhill» magazine. The children of his first marriage included Sir Julian Huxley the biologist and Aldous Huxley the writer. After his first wife’s death, Andrew’s father married Rosalind Bruce, and Andrew is the youngest of the two sons of this marriage. His father died in 1933.  Andrew was educated at University College School (1925-1930) and Westminster School (1930-1935, King’s Scholar); and went up to Trinity College, Cambridge in 1935 with a major entrance scholarship. He had turned over to science from classics in 1932, and went to Cambridge expecting that his career would be in the physical sciences: he has always been mechanically minded, and he was inspired at Westminster by the physics teaching of the late J. F. Rudwick. He naturally took physics, chemistry and mathematics in his Part I at Cambridge, but the rules required him to take another science and he picked physiology, largely on the recommendation of an old friend, B. Delisle Burns, now of the Physiology Department, McGill University. Huxley found physiology interesting, partly for its subject matter and partly through contact with [Adrian](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1932/index.html), Roughton, Rushton, [Hodgkin](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1963/index.html) and the late G. A. Millikan (all Fellows of Trinity) and others in the department, and he decided to specialise in it. He spent 1937-1938 doing anatomy with the intention of qualifying in medicine, and 1938-1939 doing the Part II course in physiology. In August 1939 Huxley joined Hodgkin at the Marine Biological Laboratory at Plymouth for his first introduction to research, and they succeeded in recording electrically from the inside of the squid giant axon.  For the first year of the war Huxley was a clinical student, but when medical teaching in London was stopped by air attacks, he changed to work of more immediate application, and spent the rest of the war on operational research in gunnery, first for Anti-Aircraft Command and later for the Admiralty.  In 1941 Huxley was elected to a research fellowship at Trinity College, Cambridge, and he took this up at the beginning of 1946 together with a teaching appointment in the Department of Physiology. He continued to hold college and university posts in Cambridge until 1960, when he became head of the Department of Physiology at University College London. In 1969 he was appointed to a Royal Society Research Professorship which he holds in the Department of Physiology at University College London.  From 1946 to 1951 Huxley worked mostly in collaboration with Hodgkin on nerve conduction, but also with R. Stämfli on myelinated nerve fibres. In 1952 he turned to muscle contraction, and developed an interference microscope for studying the striation pattern in isolated muscle fibres. This has continued to be his main line of work up to the present, though he has done some further computations on the generation of the action potential. Huxley has also developed a microtome for electron microscope sections, and a micromanipulator.  Huxley was an Editor of the *Journal of Physiology* from 1950-1957, he has also been an Editor of the *Journal of Molecular Biology*. He became a Fellow of the Royal Society in 1955, and served on its Council, 1960-1962. He worked at Woods Hole, Massachusetts, in 1953 as a Lalor Scholar; gave the Herter Lectures at Johns Hopkins Medical School in 1959; and the Jesup Lectures at Columbia University in 1964.  In 1947 Andrew Huxley married Jocelyn Richenda Gammell Pease, daughter of M. S. Pease, a geneticist, and the Hon. H. B. Pease (née Wedgwood). Mrs. Huxley is a Justice of the Peace, and is active in a variety of public work in Cambridgeshire. They have six children: Janet Rachel (born 20 April 1948), who read Biochemistry at Bristol University; Stewart Leonard (born 19 December 1949), who read engineering at Cambridge University; Camilla Rosalind (born 12 March 1952), who entered Cambridge University in 1971; Eleanor Bruce (born 21 February 1959); Henrietta Catherine (born 25 December 1960); and Clare Marjory Pease (born 4 November 1962).  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1963-1970*, Elsevier Publishing Company, Amsterdam, 1972  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Sir Andrew Huxley died on 30 May 2012.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview |  |
| Interview |  |
| Q83 | You have had a long scientific career, and I know that you have thought a lot about how science is being performed and also have written once an article with the title *Forgetfulness in Science.* |
|  | Yes.I’ve come across serious examples of forgetfulness repeatedly in relation to my own work. First example, I think, was in relation to the work for which [Alan Hodgkin](https://www.nobelprize.org/prizes/medicine/1963/hodgkin/facts/) and I had shares in the prize of 1963 and though that work was about the mechanism by which a nerve conducts its impulse. And just before the war, when I had just finished undergraduate work, I accompanied Alan Hodgkin to the Marine Laboratory at Plymouth to do experiments on this giant nerve fibre that squids have so we could put an electrode down inside. And we found that the action potential, the change of electric potential inside the fibre, was very much bigger than we’d expected or than was possible under the current theory.  On the current theory the inside potential should have gone from negative to approximately zero, we found it went substantially positive. And at that time, we had no explanation and we got onto the right explanation in 1945, which is that the membrane becomes momentarily a very permeable to sodium ions which are positively charged and they’re much more concentrated outside cells than inside. So when the membrane became permeable, these irons diffused in making it go positive inside. |
| Q86 | So you have something like the electricity? |
|  | Where that generated the electric change that’s been, well its existence has been known for about a hundred years and it was only after that the we came across a paper by Overton, an English scientist who worked first in Germany and then in Sweden. actually at Lund, and this was published in 1902 with the title in Germany on the *Indispensability of Sodium or Lithium Irons for the Contraction of Muscle* and how muscles work as their regards their excitability, they’re very similar to nerve. If we had known of this paper in 1939 I am sure we would have immediately realised what it was that made the inside of the fibre go positive. |
| Q84 | Why was not his paper famous? |
|  | He tried to repeat the experiment on nerve as well as on muscle and it didn’t work. He could put it in a sodium free solution and the nerve would go on working for hours. But actually in that paper he gave the correct explanation which seems not to have been accepted – I don’t know why – which is that every nerve, a group of a large number of nerve fibres, but each actual nerve is surrounded by sheath which holds the sodium salts in around the fibres. This sheath had been known from 1870 another paper in the 1890s, and Overton refers to this but nevertheless the work got forgotten. I don’t really know how, but anyway that was my first example. |
| Q13 | So how would you explain that there is such regular forgetfulness in science? Is it too much work or it’s just wrong time to get out? |
|  | Certainly in some of the other, well one or two of the other examples I have in mind, it’s due to a new discovery which becomes popular and overshadows other aspects of the particular topic and causes the old ideas to be, well, I don’t know whether one should say just forgotten or suppressed. After Hodgkin and I had finished our work on nerve, we couldn’t see what to do next in relation to nerve. Huge advances dependent on discoveries, improvement in electronics and on, well, the development of molecular genetics, Watson and Cricks work and everything that followed from it, that was all later, so we couldn’t see what to do and I moved into muscle.  … we immediately saw some things that were contrary to what was in all the text books …  And I’ve always had an interest in microscopy and I developed a new sort of microscope for looking at living muscle isolated muscle fibres and our voluntary muscle, each fibre is crossed by little bends that you can see with the microscope. And we immediately saw some things that were contrary to what was in all the text books and my collaborator Dr Niedergerke from Germany remembered that he had come across some papers of the mid-19th century, notably by Kraus about the striations … |
| Q86 | So they were like 100 years old? |
|  | Yes, nearly a 100 years old, 1870, and we were doing this in the early 1950s and I followed this up and beautiful work showing the things that Niedergerke and I had discovered and been surprised by, which lead on to the current theory of muscle contraction, which is that there are two lots of filaments that slide past each other. And another great coincident at that time is that this same theory was reached by a namesake of mine, Hugh Huxley, no detectable relative, by a quite different approach by electron microscopy. But as regards the old work being forgotten, I think the main reason why it was forgotten is the rise of classical biochemistry which got going round about 1900.  Influential papers say contractility must be a molecular process, you can’t see molecules with a light microscope, which is perfectly true, but then drawing the conclusion that you won’t learn anything from what you can see with the light microscope which as it happens is not true because there’s this larger scale of things representing well the lengths of these filaments which are clearly visible in the microscope. They were first seen by van Leeuwenhoek in the 17th century and this was what we had been measuring and dutiful measurements had been made back in the 19th century, Kraus notably Engelmann but this got forgotten because primarily I think because of the switch of interest to the molecular level. |
| Q13 | So this sounds like there was space on it for one idea at the time, you don’t have two ideas in parallel? |
|  | Yes, the same thing happened in relation to genetics. I’ve not been personally involved in this but of course there was Darwin’s theory published in 1859 and by the end of the 19th century that was universally accepted that evolution was mostly due to natural selection, survival of the fittest. But then Mendel’s papers on the mechanism of heredity were rediscovered in 1900 and the science of genetics was started by that and the early geneticists insisted that evolution was driven by the particular mutations that happened to happen and this was the generally accepted idea and for 30 years after that rediscovery, Darwinian natural selection was, well not entirely disregarded, but the majority of people in the field did not think of it as the important thing. |
| Q12 | But this sounds also that the young people that are fostered into doing research and into science they are also fostered to be quite opportunistic. |
|  | Yes, well that’s natural and inevitable. Because it’s difficult to make the history of science interesting to the young, it’s very difficult to avoid making it seem that people who had well what are believed that any one time to be wrong ideas, it’s difficult not to make it appear that those people were stupid. I mean, well, ideas like flogiston and so on tend to be laughed at. But at the time they were very reasonable. |
| Q18 | I would like to ask you about your family, your father, your grandfather, two of your half-brothers are very famous persons, can you tell us something about them? |
|  | Yes, well, my grandfather was T H Huxley, Thomas Henry Huxley, commonly known as’ Darwin’s bulldog’ and notable for defending Darwin in the controversies, that were very strong for a short time after the publication of *On the Origin of Species*, they didn’t go on very long in *The Origin of Species*, the only reference I think to possible human origin is in the final sentence where I think Darwin says: Light will be thrown on the origin of man and his history or something of that kind.  But it was obvious to everybody that the implication was that we are descended from apes and Darwin had avoided this topic because he knew it would be controversial, but he published a full length, very important book called *The Descent of Man* only just over 10 years later, I think, it was published in 1870, and the storm was over by then. And in 1880 my grandfather gave a lecture which was published in printed form entitled *The Coming of Age of the Origin of Species*, it was 21 years after the publication and he says it’s now difficult to realize the strength of feeling that there was in the first few years, these things now seem like prehistoric discussions and I think it’s not often realised how short lived the serious objections were. |
| ID | **0648** |
| Biographical | Francis Harry Compton Crick was born on June 8th, 1916, at Northampton, England, being the elder child of Harry Crick and Annie Elizabeth Wilkins. He has one brother, A. F. Crick, who is a doctor in New Zealand.  Crick was educated at Northampton Grammar School and Mill Hill School, London. He studied physics at University College, London, obtained a B.Sc. in 1937, and started research for a Ph.D. under Prof E. N. da C. Andrade, but this was interrupted by the outbreak of war in 1939. During the war he worked as a scientist for the British Admiralty, mainly in connection with magnetic and acoustic mines. He left the Admiralty in 1947 to study biology.  Supported by a studentship from the Medical Research Council and with some financial help from his family, Crick went to Cambridge and worked at the Strangeways Research Laboratory. In 1949 he joined the Medical Research Council Unit headed by [M. F. Perutz](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1962/index.html) of which he has been a member ever since. This Unit was for many years housed in the Cavendish Laboratory Cambridge, but in 1962 moved into a large new building – the Medical Research Council Laboratory of Molecular Biology – on the New Hospital site. He became a research student for the second time in 1950, being accepted as a member of Caius College, Cambridge, and obtained a Ph.D. in 1954 on a thesis entitled «X-ray diffraction: polypeptides and proteins».  During the academic year 1953-1954 Crick was on leave of absence at the Protein Structure Project of the Brooklyn Polytechnic in Brooklyn, New York. He has also lectured at Harvard, as a Visiting Professor, on two occasions, and has visited other laboratories in the States for short periods.  In 1947 Crick knew no biology and practically no organic chemistry or crystallography, so that much of the next few years was spent in learning the elements of these subjects. During this period, together with W. Cochran and V. Vand he worked out the general theory of X-ray diffraction by a helix, and at the same time as [L. Pauling](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1954/index.html) and R. B. Corey, suggested that the alpha-keratin pattern was due to alpha-helices coiled round each other.  A critical influence in Crick’s career was his friendship, beginning in 1951, with [J. D. Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html), then a young man of 23, leading in 1953 to the proposal of the double-helical structure for DNA and the replication scheme. Crick and Watson subsequently suggested a general theory for the structure of small viruses.  Crick in collaboration with A. Rich has proposed structures for polyglycine II and collagen and (with A. Rich, D. R. Davies, and J. D.Watson) a structure for polyadenylic acid.  In recent years Crick, in collaboration with S. Brenner, has concentrated more on biochemistry and genetics leading to ideas about protein synthesis (the «adaptor hypothesis»), and the genetic code, and in particular to work on acridine-type mutants.  Crick was made an F.R.S. in 1959. He was awarded the Prix Charles Leopold Meyer of the French Academy of Sciences in 1961, and the Award of Merit of the Gairdner Foundation in 1962. Together with J. D. Watson he was a Warren Triennial Prize Lecturer in 1959 and received a Research Corporation Award in 1962. With J. D. Watson and [M. H. F. Wilkins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) he was presented with a Lasker Foundation Award in 1960. In 1962 he was elected a Foreign Honorary Member of the American Academy of Arts and Sciences, and a Fellow of University College, London. He was a Fellow of Churchill College, Cambridge, in 1960-1961, and is now a non-resident Fellow of the Salk Institute for Biological Studies, San Diego, California.  In 1940 Crick married Ruth Doreen Dodd. Their son, Michael F. C. Crick is a scientist. They were divorced in 1947. In 1949 Crick married Odile Speed. They have two daughters, Gabrielle A. Crick and Jacqueline M. T. Crick. The family lives in a house appropriately called «The Golden Helix», in which Crick likes to find his recreation in conversation with his friends.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Crick, F.H.C., *What Mad Pursuit: A Personal View of Science.* Basic Books, New York, 1988.  *Francis Crick died on July 28, 2004.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0648** |
| Interview |  |
|  |  |
| ID | **0649** |
| Biographical | James Dewey Watson was born in Chicago, Ill., on April 6th, 1928, as the only son of James D. Watson, a businessman, and Jean Mitchell. His father’s ancestors were originally of English descent and had lived in the midwest for several generations. His mother’s father was a Scottish-born tailor married to a daughter of Irish immigrants who arrived in the United States about 1840. Young Watson’s entire boyhood was spent in Chicago where he attended for eight years Horace Mann Grammar School and for two years South Shore High School. He then received a tuition scholarship to the University of Chicago, and in the summer of 1943 entered their experimental four-year college.  In 1947, he received a B.Sc. degree in Zoology. During these years his boyhood interest in bird-watching had matured into a serious desire to learn genetics. This became possible when he received a Fellowship for graduate study in Zoology at Indiana University in Bloomington, where he received his Ph.D. degree in Zoology in 1950. At Indiana, he was deeply influenced both by the geneticists [H. J. Muller](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1946/index.html) and T. M. Sonneborn, and by [S. E. Luria](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1969/index.html), the Italian-born microbiologist then on the staff of Indiana’s Bacteriology Department. Watson’s Ph.D. thesis, done under Luria’s able guidance, was a study of the effect of hard X-rays on bacteriophage multiplication.  From September 1950 to September 1951 he spent his first postdoctoral year in Copenhagen as a Merck Fellow of the National Research Council. Part of the year was spent with the biochemist Herman Kalckar, the remainder with the microbiologist Ole Maaløe. Again he worked with bacterial viruses, attempting to study the fate of DNA of infecting virus particles. During the spring of 1951, he went with Kalckar to the Zoological Station at Naples. There at a Symposium, late in May, he met [Maurice Wilkins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) and saw for the first time the X-ray diffraction pattern of crystalline DNA. This greatly stimulated him to change the direction of his research toward the structural chemistry of nucleic acids and proteins. Fortunately this proved possible when Luria, in early August 1951, arranged with [John Kendrew](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1962/index.html) for him to work at the Cavendish Laboratory, where he started work in early October 1951.  He soon met [Crick](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) and discovered their common interest in solving the DNA structure. They thought it should be possible to correctly guess its structure, given both the experimental evidence at King’s College plus careful examination of the possible stereochemical configurations of polynucleotide chains. Their first serious effort, in the late fall of 1951, was unsatisfactory. Their second effort based upon more experimental evidence and better appreciation of the nucleic acid literature, resulted, early in March 1953, in the proposal of the complementary double-helical configuration.  At the same time, he was experimentally investigating the structure of TMV, using X-ray diffraction techniques. His object was to see if its chemical sub-units, earlier revealed by the elegant experiments of Schramm, were helically arranged. This objective was achieved in late June 1952, when use of the Cavendish’s newly constructed rotating anode X-ray tubes allowed an unambiguous demonstration of the helical construction of the virus.  From 1953 to 1955, Watson was at the California Institute of Technology as Senior Research Fellow in Biology. There he collaborated with Alexander Rich in X-ray diffraction studies of RNA. In 1955-1956 he was back in the Cavendish, again working with Crick. During this visit they published several papers on the general principles of virus construction.  Since the fall of 1956, he has been a member of the Harvard Biology Department, first as Assistant Professor, then in 1958 as an Associate Professor, and as Professor since 1961. During this interval, his major research interest has been the role of RNA in protein synthesis. Among his collaborators during this period were the Swiss biochemist Alfred Tissières and the French biochemist François Gros. Much experimental evidence supporting the messenger RNA concept was accumulated. His present principal collaborator is the theoretical physicist [Walter Gilbert](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1980/index.html) who, as Watson expressed it, «has recently learned the excitement of experimental molecular biology».  The honours that have to come to Watson include: the John Collins Warren Prize of the Massachusetts General Hospital, with Crick in 1959; the Eli Lilly Award in Biochemistry in the same year; the Lasker Award, with Crick and Wilkins in 1960; the Research Corporation Prize, with Crick in 1962; membership of the American Academy of Arts and Sciences and the National Academy of Sciences, and Foreign membership of the Danish Academy of Arts and Sciences. He is also a consultant to the President’s Scientific Advisory Committee.  Watson is unmarried. His recreations are bird-watching and walking.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Watson, J.D., *The Double Helix.* Atheneum, New York, 1968. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0649** |
| Interview |  |
|  |  |
| ID | **0650** |
| Biographical | Maurice Hugh Frederick Wilkins was born at Pongaroa, New Zealand, on December 15th, 1916. His parents came from Ireland; his father Edgar Henry Wilkins was a doctor in the School Medical Service and was very interested in research but had little opportunity for it.  At the age of 6, Wilkins was brought to England and educated at King Edward’s School, Birmingham. He studied physics at St. John’s College, Cambridge, taking his degree in 1938. He then went to Birmingham University, where he became research assistant to Dr. J. T. Randall in the Physics Department. They studied the luminescence of solids. He obtained a Ph.D. in 1940, his thesis being mainly on a study of thermal stability of trapped electrons in phosphors, and on the theory of phosphorescence, in terms of electron traps with continuous distribution of trap depths. He then applied these ideas to various war-time problems such as improvement of cathoderay tube screens for radar. Next he worked under Professor M. L. E. Oliphant on mass spectrograph separation of uranium isotopes for use in bombs and, shortly after, moved with others from Birmingham to the Manhattan Project in Berkeley, California, where these studies continued.  In 1945, when the war was over, he was lecturer in physics at St. Andrews’ University, Scotland, where Professor J. T. Randall was organizing biophysical studies. He had spent seven years in physics research and now began in biophysics. The biophysics project moved in 1946 to King’s College, London, where he was a member of the staff of the newly formed Medical Research Council Biophysics Research Unit. He was first concerned with genetic effects of ultrasonics; after one or two years, he changed his research to development of reflecting microscopes for ultraviolet microspectrophotometric study of nucleic acids in cells. He also studied the orientation of purines and pyrimidines in tobacco mosaic virus and in nucleic acids, by measuring the ultraviolet dichroism of oriented specimens, and he studied, with the visible-light polarizing microscope, the arrangement of virus particles in crystals of TMV and measured dry mass in cells with interference microscopes. He then began X-ray diffraction studies of DNA and sperm heads. The discovery of the well-defined patterns led to the deriving of the molecular structure of DNA. Further X-ray studies established the correctness of the [Watson](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html)–[Crick](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1962/index.html) proposal for DNA structure. Relevant publications are «The molecular configuration of deoxyribonucleic acid. I. X-ray diffraction study of a crystalline form of the lithium salt», by R. Langridge, H. R. Wilson, C. W. Hooper, M. H. F. Wilkins, and L. D. Hamilton in *J. Mol. Biol.*, 2 (1960) 19, and «Determination of the helical configuration of ribonucleic acid molecules by X-ray diffraction study of crystalline amino-acid-transfer ribonucleic acid», by M. Spencer, W. Fuller, M. H. F. Wilkins, and G. L. Brown in *Nature*, 194 (1962) 1014.  Wilkins became Assistant Director of the Medical Research Council Unit in 1950 and Deputy Director in 1955. A sub-department of Biophysics was formed in King’s College, and he was made Honorary Lecturer in it. In 1961 a full Department of Biophysics was established.  He was elected F.R.S. in 1959, given the Albert Lasker Award (jointly with Watson and Crick) by the American Public Health Association in 1960, and made Companion of the British Empire in 1962.  He married Patricia Ann Chidgey in 1959; they have a daughter Sarah and a son George. He finds his recreations in his collection of sculptures and in gardening.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Wilkins, Maurice, *The Third Man of the Double Helix: The Autobiography of Maurice Wilkins.* Oxford University Press, Oxford, 2003.  *Maurice Wilkins died on October 5, 2004.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0650** |
| Interview |  |
|  |  |
| ID | **0651** |
| Biographical | Georg von Békésy was born in Budapest, Hungary, on June 3, 1899, the son of Alexander von Békésy, a diplomat, and his wife, Paula. He received his early education in Munich, Constantinople, Budapest, and in a private school in Zurich. Having passed the Swiss «Maturitätsprüfung» he studied chemistry at the University of Berne. After a short military service he received his Ph.D. in Physics in 1923 from the University of Budapest. Later on he entered the services of the Hungarian Post Office in Budapest where he stayed until 1946. He worked one year at the Central Laboratory of Siemens and Halske A.G. in Berlin, at that time one of the centers in the development of telecommunication. During vacations he spent his free time in different workshops learning how to use a file for many hours without hurting the hands.  His work in the research laboratory of the Hungarian Post Offce was concerned mainly with problems of long-distance telephone transmission. The friendly and efficient atmosphere of this laboratory made it possible for him to spend considerable time in the study of the ear as a main component of the transmission system. Soon he became a nuisance to the autopsy rooms of the hospitals and the mechanical workshops of the Post Office. There they did not like to find their drill press full of human-bone dust in the morning. But the wonderful laboratory spirit helped to overcome all difficulties, except those produced by the destructions of World War II.  During the years 1939-1946 he was also Professor of Experimental Physics at the University of Budapest. He left Hungary in 1946 for Sweden, where he was a guest of the [Karolinska Institute](http://www.ki.se/) and did research at the Technical Institute in Stockholm. It was during this period that he developed a new type of audiometer which is operated by the patient and has applications outside the field of hearing. For instance, it has permitted the determination of the change in sensitivity of the eye of pigeons during dark adaptation.  In 1947 he went to the United States and has worked since then at Harvard University in the Psycho-Acoustic Laboratory. Lately he has been interested in developing a mechanical model of the inner ear with nerve supply, the nerve supply being represented by the skin of the arm. This model shows such close similarity to phenomena in hearing that it has become a useful tool in the investigation of some specific problems that have been pursued for many years.  His honours include the Denker Prize in Otology (1931), the Guyot Prize for Speech and Otology of Groningen University (1939) and the Shambaugh Prize in Otology (1950). He was the recipient of the Leibnitz Medal of the Berlin Academy of Sciences (1937), the Academy Award of the Budapest Academy of Science (1946), the Howard Crosby Warren Medal of the Society of Experimental Psychologists (1955), and the Gold Medals of the American Otological Society (1957) and the Acoustical Society of America (1961). Honorary doctorates (M.D.) were conferred on him by the Universities of Munster (1955) and Berne (1959).  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Georg von Békésy died on June 13, 1972.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0651** |
| Interview |  |
|  |  |
| ID | 0652 |
| Biographical | Sir Frank Macfarlane Burnet was born at Traralgon, Victoria, Australia, on September 3rd, 1899. He is the son of the Manager of the branch of the Colonial Bank in that town. He was educated at the Victoria State Schools and at Geelong College, completing his medical course at the University of Melbourne, where he graduated M.B., B.S., in 1922, and M.D., in 1923.  In 1923, Burnet went to the Walter and Eliza Hall Institute of the University of Melbourne to do research work on the agglutinin reactions in typhoid fever. He was from 1923-1924 Resident Pathologist at the Melbourne Hospital.  In 1926 he was awarded a Beit Fellowship for Medical Research and worked for a year at the Lister Institute, London.  In 1932 he spent a year at the National Institute for Medical Research, Hampstead, London. Otherwise, apart from many visits to various countries to give lectures or for other purposes, he has worked continuously at the Hall Institute in Melbourne.  In 1944 he became Director of this Institute and Professor of Experimental Medicine in the University of Melbourne.  It is impossible to give, in a brief space, an adequate idea of the range and fundamental importance of Burnet’s work. His work on the agglutinins of typhoid fever mentioned above was followed by the work on viruses for which he is nowadays justly famous. In 1935 he isolated a strain of influenza A virus in Australia, and subsequently did much work on serological variations of the influenza virus and on Australian strains of the swine influenza. He also published papers on variations in the virulence of influenza virus and on the mutation rates in it, which he calculated.  In 1946, in collaboration with W. I. B. Beveridge, Burnet devised a technique for cultivating viruses on the chorioallantoic membrane of chicken embryos and a method for determining the relative concentration of the material inoculated into these membranes by counting and statistically analysing the number of lesions that then appear on the membranes.  In 1947 he discovered, in collaboration with Stone, the receptor-destroying enzyme present in *Vibrio cholerae*, a discovery which led to the synthesis of neuraminic acid and to the demonstration, by Gottschalk and [Cornforth](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1975/index.html), that purified influenza virus will quantitatively split the acetylgalactosamine neuraminic acid compound. Later it was shown that this enzyme derived from *Vibrio cholerae* can prevent infection by the influenza to a significant degree.  Burnet did much other important work on certain aspects of the prevention of virus infections and on important biological aspects of virus growth inside the cells in which they can live. He found that the filamentous forms of some viruses (e.g. those of myxoviruses such as those which cause influenza, mumps, fowl plague, and Newcastle disease) can be ruptured by suspending them in water, and suggested that their infectivity is limited to their tips, so that these filamentous forms can, as later work showed, be regarded as having an infective «warhead» composed of nucleic acid and a long tail composed of non-infective viral haemagglutinin.  Other aspects of Burnet’s work are his work on the surface properties of these filamentous forms, which are, he found, similar to those of cell surfaces, and his work with the haemagglutinin found in extracts of tissue infected with vaccinia, which can, he found, be precipitated by a saturated solution of ammonium sulphate and by cobra venom. He has also added much to our knowledge of the haemagglutination of red blood cells by various animal viruses, and has made contributions of fundamental importance to our knowledge of the genetic complexity of virus particles, and to the genetic interactions between related viruses which simultaneously infect the same cell and their relations to the transfer of neuropathogenicity. In addition, he has increased our knowledge of the inhibition of viruses by various substances, and of the complex details of immunological methods of studying viruses and of the immunology of viral infections.  Burnet has embodied his experience and experimental results, not only in numerous scientific papers, but in several books which show that he is a master, not only of a clear and attractive literary style, but also of lucid exposition of complex ideas and scientific facts.  Burnet received many honours and distinctions, among which the Fellowship of the Royal Society of London (1942), where he was awarded the Royal Medal in 1947 and the Copley Medal in 1959, and where he delivered the Croonian Lecture in 1950. He holds an honorary doctorate of the University of Cambridge, and was made a Fellow of the Royal College of Surgeons in 1953. He was knighted in 1951, and in 1958 he received the Order of Merit.  Burnet married Edith Linda Druce in 1928. They have one son, Ian, and two daughters, Elizabeth (Mrs. Paul M. Dexter) and Deborah (Mrs. John Giddy).  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Burnet, Frank Macfarlane. *Changing Patterns: An Atypical Autobiography*. Heinemann, Melbourne, 1968.  *Sir Frank Macfarlane Burnet died on August 31, 1985.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0652** |
| Interview |  |
|  |  |
| ID | **0653** |
| Biographical | Peter Brian Medawar was born on February 28, 1915, in Rio de Janeiro. He is the son of a business man who is a naturalized British subject, born in the Lebanon.  Medawar was educated at Marlborough College, England, where he went in 1928. Leaving this College in 1932, he went to Magdalen College, Oxford, to study zoology under Professor J. Z. Young. After taking his bachelor’s degree at Oxford, Medawar worked for a time at Sir [Howard Florey](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1945/index.html)‘s School of Pathology at Oxford and there became interested in research in fields of biology that are related to medicine.  In 1935 he was appointed Christopher Welch Scholar and Senior Demonstrator at Magdalen College, Oxford, and in 1938 he became, by examination, a Fellow of Magdalen College. In 1942 he was Rolleston Prizeman and in 1944 he became Senior Research Fellow of St John’s College, Oxford, and University Demonstrator in zoology and comparative anatomy. In 1946 he was elected a Fellow of Magdalen College, Oxford, and in 1947 he was appointed Mason Professor of Zoology at the University of Birmingham. In 1951 he moved to London as Jodrell Professor of Zoology at University College, London. Here he remained until 1962, when he was appointed Director of the National Institute for Medical Research, London.  Medawar’s earlier research, done at Oxford, was on tissue culture, the regeneration of peripheral nerves and the mathematical analysis of the changes of shape of organisms that occur during this development. During the early stages of the Second World War he was asked by the Medical Research Council to investigate why it is that skin taken from one human being will not form a permanent graft on the skin of another person, and this work enabled him to establish theorems of transplantation immunity which formed the basis of his further work on this subject. When he moved to Birmingham in 1947 he continued to work on it, in collaboration with R. Billingham, and together they studied there problems of pigmentation and skin grafting in cattle, and the use of skin grafting to distinguish between monozygotic and dizygotic twins in cattle. In this work they took into consideration the work of R. D. Owen and concluded that the phenomenon that they called «actively acquired tolerance» of homografts could be artificially reproduced. For this earlier work on transplantation and growth, Medawar was elected a Fellow of the Royal Society, London. When he moved to London in 1951, Medawar continued to work with R. Billingham and L. Brent, on this phenomenon of tolerance, and his detailed analysis of it occupied him for several years. He also carried out other researches into transplantation immunity.  The Royal Society of London, where he was the Croonian Lecturer in 1958, awarded him the Royal Medal in 1959. In the same year, he was Reith Lecturer for the British Broadcasting Corporation. He has been elected a Foreign Member of the New York Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society.  In 1937 Medawar married Jean Shinglewood Taylor, daughter of a Cambridge physician. They have two sons, Charles and Alexander, and two daughters, Caroline and Louise.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Medawar, Peter Brian. *Memoirs of a Thinking Radish: An Autobiography*. Oxford University Press, Oxford, 1986.  *Peter Medawar died on October 2, 1987.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0653** |
| Interview |  |
|  |  |
| ID | **0654** |
| Biographical | Severo Ochoa was born at Luarca, Spain, on September 24th, 1905. He is the son of Severo Ochoa, a lawyer and business man, and Carmen de Albornoz.  Ochoa was educated at Málaga College, where he took his B.A. degree in 1921.[\*](https://www.nobelprize.org/prizes/medicine/1959/ochoa/biographical/#footnote) His interest in biology was greatly stimulated by the publications of the great Spanish neurologist, [Ramón y Cajal](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1906/index.html), and he went to the Medical School of the University of Madrid, where he obtained his M.D. degree (with honours) in 1929. While he was at the University he was Assistant to Professor Juan Negrin and he paid, during the summer of 1927, a visit to the University of Glasgow to work under Professor D. Noel Paton.  After graduating in 1929 Ochoa went, with the aid of the Spanish Council of Scientific Research, to work under [Otto Meyerhof](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html) at the Kaiser Wilhelm Institut für Medizinische Forschung at Heidelberg. During this period he worked on the biochemistry and physiology of muscle, and his outlook and training were decisively influenced by Meyerhof.  In 1931, Ochoa was appointed Lecturer in Physiology at the University of Madrid, a post he held until 1935. In 1932 he went to the National Institute for Medical Research, London, where he worked with Dr. H. W. Dudley on his first problem in enzymology.  Returning to Madrid in 1934, he was appointed Lecturer in Physiology and Biochemistry there and later became Head of the Physiology Division of the Institute for Medical Research, Madrid. In 1936 he was appointed Guest Research Assistant in Meyerhof’s Laboratory at Heidelberg, where he worked on some of the enzymatic steps of glycolysis and fermentation. In 1937 he held a Ray Lankester Investigatorship at the Plymouth Marine Biological Laboratory and from 1938 until 1941 he worked on the biological function of vitamin B1 with Professor R. A. Peters at Oxford University, where he was appointed Demonstrator and Nuffield Research Assistant.  While he was at Oxford he became interested in the enzymatic mechanisms of oxidative metabolism and in 1941 he went to America and worked, until 1942, at the Washington University School of Medicine, St. Louis, where he was appointed Instructor and Research Associate in Pharmacology and worked with [Carl and Gerty Cori](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1947/index.html) on problems of enzymology. In 1942 he was appointed Research Associate in Medicine at the New York University School of Medicine and there subsequently became Assistant Professor of Biochemistry (1945), Professor of Pharmacology (1946), Professor of Biochemistry (1954), and Chairman of the Department of Biochemistry. In 1956 he became an American citizen.  Ochoa’s research has dealt mainly with enzymatic processes in biological oxidation and synthesis and the transfer of energy. It has contributed much to the knowledge of the basic steps in the metabolism of carbohydrates and fatty acids, the utilization of carbon dioxide, and the biosynthesis of nucleic acids. It has included the biological functions of vitamin B1, oxidative phosphorylation, the reductive carboxylation of ketoglutaric and pyruvic acids, the photochemical reduction of pyridine nucleotides in photosynthesis, condensing enzyme – which is the key enzyme of the Krebs citric acid cycle, polynucleotide phosphorylase and the genetic code.  Ochoa holds honorary degrees of the Universities of St. Louis (Washington University), Glasgow, Oxford, Salamanca, Brazil, and the Wesleyan University. He is Honorary Professor of the University of San Marcos, Lima, Peru. He was awarded the Neuberg Medal in Biochemistry in 1951, the Medal of the Société de Chimie Biologique in 1959, and the Medal of New York University in the same year. He is a member of several learned societies in the U.S.A., Germany, Japan, Argentina, Uruguay, and Chile, and President of the International Union of Biochemistry.  In 1931 Ochoa married Carmen Garcia Cobian.  \*According to other sources, Severo Ochoa graduated from high school at the Instituto de Bachillerato de Málaga in 1921.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Severo Ochoa died on November 1, 1993.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0654** |
| Interview |  |
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| Biographical | Arthur Kornberg was born in Brooklyn, New York in 1918 and educated in its public schools. He received his undergraduate degree in science from the City College of New York in 1937 and the M.D. degree from the University of Rochester in 1941. After a year’s internship in internal medicine, he served as a commissioned officer in the U.S. Public Health Service. He was first assigned to the Navy as a ship’s doctor, and then as a research scientist at the National Institutes of Health (NIH) in Bethesda, Maryland, from 1942 to 1953. He obtained training in enzymology with Professor Severo Ochoa at New York University School of Medicine in 1946 and with Professor Carl Cori at Washington University School of Medicine in 1947. Upon returning to Bethesda, he organized and directed the Enzyme Section. He resigned in 1953 with the rank of Medical Director, to assume the chairmanship of the Department of Microbiology of Washington University School of Medicine in St. Louis, Missouri. In 1959, he organized the Department of Biochemistry of the Stanford University School of Medicine, serving as its chairman until 1969 and thereafter as professor. He accepted the title of Professor *Emeritus* in 1988 and has been on active status to the present. The members of the Stanford Biochemistry Department – Robert Baldwin, [Paul Berg](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1980/index.html), David Hogness, Dale Kaiser, Arthur Kornberg and Robert Lehman – stayed together as a cohesive unit for forty years until retirement.  From his early studies of the mechanisms of the enzymatic synthesis of coenzymes and inorganic pyrophosphate, he extended his interest to the biosynthesis of the nucleic acids, particularly DNA. After elucidating key steps in the pathways of pyrimidine and purine nucleotide synthesis, including the discovery of PRPP as an intermediate, he found the enzyme that assembles the building blocks into DNA, named DNA polymerase. This ubiquitous class of enzymes make genetically precise DNA and are essential in the replication, repair and rearrangements of DNA. Many other enzymes of DNA metabolism were discovered responsible for the start and elongation of DNA chains and chromosomes. These enzymes were the basis of discovery of recombinant DNA which helped ignite the biotechnology revolution.  Since 1991, he switched his research focus from DNA replication to inorganic polyphosphate (poly P), a polymer of phosphates that likely participated in prebiotic evolution and is now found in every bacterial, plant and animal cell. Neglected and long regarded a molecular fossil, he has found a variety of significant functions for poly P that include responses to stresses and stringencies and factors responsible for motility and virulence in some of the major pathogens.  Although the pursuit of research has been his primary concern, other interests include the formal teaching of graduate, medical and postdoctoral students, and the authorship of major monographs: *DNA Synthesis* in 1974, *DNA Replication* in 1980, *Supplement to DNA Replication* in 1982, and *DNA Replication, Second Edition*, in 1992. A scientific autobiography, *For the Love of Enzymes: The Odyssey of a Biochemist*, Harvard University Press, appeared in 1989. *The Golden Helix: Inside Biotech Ventures*, University Science Books, was released in July of 1995, and provides an insider’s view of biotechnology.  In his academic career, he has served as departmental chairman, on the committees of the Medical School and university, as president of the American Society of Biological Chemistry (1965), and on the advisory boards and councils of numerous university, governmental and industrial research institutes. He is a founder of the DNAX Research Institute of Molecular and Cellular Biology (a Division of Schering-Plough, Inc.), and a member of its Policy and Scientific Advisory Boards. He serves on the Scientific Advisory Boards of Regeneron Pharmaceuticals, Inc., Maxygen, and the XOMA Corp., and is also a member of the Board of Directors of XOMA Corp.  Among his honors are memberships in the National Academy of Sciences, the Royal Society, American Philosophical Society, a number of honorary degrees, the Nobel Prize in Physiology or Medicine (1959), the National Medal of Science (1979), the Cosmos Club Award (1995) and other medals and awards.  He was married in 1943 to Sylvy Ruth Levy, who died in 1986. He has three sons and eight grandchildren. Roger is a Professor of Structural Biology at Stanford; Thomas is a Professor of Biochemistry and Biophysics at the University of California in San Francisco; Kenneth is an architect and founder of Kornberg Associates in Menlo Park and Delmar, California, specializing in laboratory design. In 1988 he married Charlene Walsh Levering, who died in September of 1995. In 1998 he married Carolyn Frey Dixon. Dr. Kornberg resides in Portola Valley, California. He enjoys tennis, travel, music, and time with his family. |
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| Telephone  interview | **0655** |
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| Q88 | Arthur Kornberg, welcome back to Stockholm again, another family get-together in Stockholm. You were here with your son [Roger](https://www.nobelprize.org/prizes/chemistry/2006/kornberg/facts/) when you received the Nobel Prize in Physiology or Medicine in 1959 and now you’re back to see him receive the Nobel Prize in Chemistry this year, the sixth father/son team to do this. It must be very pleasant to be back? |
|  | Yes, it’s a great, great pleasure to be resurrected after all these years through Roger’s awesome achievements. He’s done things that I could have dreamed of but never accomplished and without going into great detail, he’s moved from biochemistry, taking genetics along with it and onto structural studies of crystallography and x-ray defraction which he learned entirely on his own and put this piece together. That is, I would say, perfectly awesome. Very proud. |
| Q89 | In some ways your beginnings were similar in that you both came from a chemistry background and when I spoke with Roger yesterday he was saying that chemistry was really the fundamental thing you needed to know in order to understand biology and he said that in very elegant terms. I presume, since you majored in chemistry yourself, that you’d agree with him totally? |
|  | That’s not quite correct. Roger has had, I might say, almost a royal training in chemistry because I arranged, during his high school and college years, to spend summers working with distinguished chemists and biochemists and geneticists. I never had that background. When I entered college, I didn’t know what I would do. When I left college, I had a chemistry major but a very mild one and almost by defect, went into medicine. Medicine was not chemical and trained as an internist after medical school and really came into chemistry by a wide detour. Shall I go on and tell you the…?  When I was given leave to complete my clinical training after 1941, outside of war. I then in July of that year was mustered into the coastguard as a doctor and I was then part of a navy and so I was on ships for about six months, as the doctor on the ship. Then through some devious way in which some research that I’d done as a medical student gained me an invitation to come to the National Institute of Health. I was assigned to rat nutrition, which I did for three years. Then got bored with feeding rats and counting the sick and dead ones, became convinced that I needed to understand what vitamins did, which I was feeding them and keeping some alive including folic acid as an important component and gained a special dispensation from the NIH, still in uniform, to work in an entomology laboratory of [Severo Ochoa](https://www.nobelprize.org/prizes/medicine/1959/ochoa/facts/), who later I shared the prize with in 1959. He was very kind and patient and I learned the rudiments and then progressed to doing something more meaningful. Then he persuaded me, and I didn’t need that much persuasion, to borrow another half year from the NIH, still in uniform, to work with two Nobelists later, [Carl](https://www.nobelprize.org/prizes/medicine/1947/cori-cf/facts/) and [Gerty Cori](https://www.nobelprize.org/prizes/medicine/1947/cori-gt/facts/) in St Louis. That was again a major episode that utterly separated me from ever returning to medicine, let alone things that are more physiological. Returning to the NIH, I then took up a privilege that had been given to me to start a laboratory of entomology and from there on, I’ll say briefly, I fell in love with enzymes. |
| Q49 | Your path really took you from an applied approach to research back to a very basic approach. I’ve read that you described your approach to physiology as being to isolate the actors with which you can then investigate the dramas they perform. That’s a direct quote from you. |
|  | Aren’t you nice to remember that?Yes, and I still find that in essence what one needs to do, faced with a biologic event, but I’ve come around in recent years to appreciate that that’s only part of the story. That one has ultimately to put it into the context of a functioning entity, a cell, because many of the players have been eliminated in that reduction to simplicity of an enzyme reaction or even an enzyme pathway. And also, I’ve been persuaded that even with bacteria, which I’ve worked with almost all my life, that they have a defined ultra structure, they’re not simply a bag of enzymes, but unfortunately it’s too late in life to make up for all that lost ground but it’s part of our future in biology and science. |
| Q90 | Sure, but despite your being persuaded that there’s more than the reductionist approach, which of course you knew, there is nevertheless I think now quite a rush towards in vivo work. And does that, do you think confuse issues, the fact that people want to get into the animal as quickly as they can? |
|  | It’s worse than that. In trying to see a broad picture, the power of genomics and proteomics and metabolomics and economics. All of that has contrived to separate people from what I’d say the wet nature of life. We may pick this up later, the subject that I’m working on intensely now, or try to. I appreciate how little has been done at that level of breaking the cell open perturbing it minimally, but still being able to introduce and extract things from that broken cell, that has a world of mystery in it. |
| Q90 | In thinking about the appeal of science to people coming into the subject, do you think that the move towards genomics and metabolomics and the rest of it, has in some way distanced people from the ability to become excited by science? |
|  | Oh, I can’t comment on that. People doing the current work and sitting at the front of their computers, which is now commonplace in my lab and department, and not over an ice bucket with chilled reagents and pipetting from one to another. They’re so different and I’m not prepared to say that this generation has gone off the deep end, but it will have to come back. I don’t think any system as refined as genomics can be, and I’ve used it because it’s so informative about other aspects of living systems that relate to what you’re doing. Still the urgency, let’s say in Roger’s work, which I won’t for a moment denigrate in any way. But when I’ve talked to him about the subject that I’m interested in and I told you I’d get to it, polyphosphate, it’s there, /- – -/ in abundance but they’re not in the reduced, refined, almost atomically resolved system for which he’s getting this highly deserved credit. So that’s your mode and who might be doing that kind of work. I had breakfast with Dave Bushnell, a very devoted and highly capable research associate of Roger’s and checked with him, David, is anyone even thinking about that, oh no, it’s another world. |
| Q34 | Tell us a little bit about the work that you’re currently doing then? |
|  | I didn’t think you’d get around to asking me so soon. I don’t want to extend this, as you said earlier, having in many people’s minds the image of a molecular fossil. But in fact let me reflect on when I first heard the word. It was in the laboratory of Carl and Gerty Cori in 1947. It was that second interval or half year bonus that I had to study entomology. A Belgian came through, Wiame, and he brought the news that a particle had been known from the turn of the century, called Viatine, which had the property of metachromatic staining. It was prominent in many organisms, abundance and less so. No one knew what it did. They had discovered in that Belgian laboratory that it was inorganic polyphosphate. At that time, the nature of those bonds which are high energy phosphor and hydroid bonds, we didn’t know about mitochondria. We knew about ATP but in 1947, we didn’t know about mitochondria and immediately set to wonder, could this inorganic polyphosphate be somehow involved in the generation of ATP. As it turned out, that was not a part of the picture. ATP and ATP synthase and ultimately the proton motive force that drives the synthesis of ATP from ADP was elucidated and the ATP synthase, the enzyme because better known and polyphosphate was forgotten.  In fact, when I was in St Louis, about that time, it coincided with an asbestos scare. People were being diagnosed and dying from asbestosis, which was being used to coat all kinds of ducts and insulating infants clothing from fire. It was a determined that people were dying of asbestosis, a pulmonary disease in the shedding of the asbestos from industrial and even domestic use. Monsanto set about to replace asbestos with some mineral fibre and that was polyphosphate and you could make polyphosphate, much like it was made on Earth billions of years ago, by heating phosphate rock and you get long chains of polyphosphate. The cost was pennies a pound and so they developed very good technology for making fibrous constructions out of this polyphosphate. Until the marketing people said it won’t sell, it won’t go because it’s a fibre. The fact that it’s biodegradable in your body and nature and the fact now that it’s used in making meats resistant to bacteria, packed meats commonly had polyphosphate. They glisten as a result of it and many dental flosses, toothpastes have polyphosphate. It’s utterly innocuous but it has origins and has kinds of either utter indifference or even fear that’s made its marketing and acceptance so delayed. |
| Q23 | So, polyphosphates are with us all the time, despite the fact that scientifically they’ve been somewhat ignored? |
|  | More than that, I conjecture, no-one knows how life started but I would think polyphosphate would have been an ideal candidate for the first vesicle that surrounded something and called a cell because it’s a phosphorylating agent, it helps in the creation of peptides and fatty acids, it’s a reservoir of energy, it makes ATP, it phosphorylates sugars and it’s responsive to the environment. It grows and recedes of course by adding enzymes and permeases and what not, but enough of that. But incidentally, people who write about the origin of life and speculate about it, rarely mention polyphosphate, isn’t that astonishing?  Yes, exactly, but long before there was an RNA world or a carbon word, poly P was there. And the fact is, and this is what persuaded me, polyphosphate is in every cell in nature. Every bacterium, fungus, plant, every animal, every tissue, every sub-cellular element in a cell, in the nervous system, it’s chains of thousands and it’s in the nuclei, the mitochondria, attached to the ribosomes, a variety of vesicles, it’s everywhere. |
| Q91 | You see it now as a very good candidate for a drug target in microbiology? |
|  | I came about, I should say, blossomed. We then made our bug as *E. coli*. We’ve done so much with it and DNA replication and we could show that when we deprive this bacterium of these enzyme, we established the enzyme that makes it called PPK, polyphosphate kinase, converts ATP, takes the phosphate ATP, puts it on a growing chain and it just whizzes off and we really don’t know the intimate details of how that process goes from one to many. We were able to purify the enzyme, characterise it and make mutants of it. We found very early on that they didn’t survive. They might grow through the typical expediential phase, but they couldn’t survive and then they couldn’t swim. They couldn’t talk to each other and make biofilms and eventually we moved more towards Pseudomonas Aeruginosa, a fascinating organism, and found that it was not pathogenic and that’s a bad bug because it kills children with cystic fibrosis, with pneumonia. It’s the bane of surgeons because it causes wounds that cannot be healed and it makes such firm biofilms. |
| Q91 | Biofilms are another area that hasn’t been very investigated. |
|  | Biofilms is what bugs behave in almost 98% of the time. They’re not simple little rods or spheres, they collect under a variety of circumstances and aggregate as a film, which they have totally different properties and very resistant to antibodies. Anyway, you need poly P, we’ll call it poly P then, shall we, to make biofilms and pseudomonas, that is deprived of the kinase that makes polyphosphate is no longer pathogenic. We’re not sure that’s true, salmonella, shigella, vibrio cholerae, helical bacteria that forms peptic ulcers /- – -/ for cancer. Each of these when we isolate the enzyme, mutate it, these bugs no longer are pathogens. Which brings me to my current involvement, which is really current, I’ve been in touch with people several days last week, tuberculosis. It so happens that mycobacterium tuberculosis, the agent that causes tuberculosis, has firstly the same enzyme as the one in *E. coli*, that enzyme has been conserved in terms of its amino acid chain almost intact.  That enzyme could be a target and we arranged some years ago through friends and contacts, to have a company call ICOS in Washington, near Seattle, to screen libraries for their capacity of hundreds of thousands of compounds to inhibit that enzyme with a very high affinity. Found many, many, more important they had 62 compounds that they could play with and this may not, digress for a moment, two things happened in that history of … that’s socially interesting, their Chief Scientific Advisor of ICOS, very good friend of mine, Stanley Falkow at Stanford advised that the FDA, The Federal Drug Administration, likely wouldn’t approve a drug that wasn’t killing bugs, it’s seen that polyphosphate was a bacteria static drug. I’m not sure, FDA has now for some time been happy to give approval to compounds that weaken the organism and could be used in conjunction with another drug. The second thing is that ICOS had a contract with Lilly to produce Cialis. Cialis is the Viagra drug and two weeks ago, Lilly bought out ICOS for two billion dollars and just dissolved the company. Anyway, so polyphosphate didn’t do well on either score… |
| Q91 | Except you have your candidate molecules. |
|  | But the tubercle bacillus, and this comes now very recently, there are two groups in India, Datta, Santanu Datta, who’s at the AstraZeneca in Bangalore and Kundu, now I can’t remember, it’s M, rather a long name, in Bose Institute in Calcutta and they’ve been showing now something extraordinary. Tuberculosis is difficult to treat because it has such a long growth period, not minutes and hours but days and weeks and then it needs a given level of ATP to keep growing and polyphosphate is essential for that. So PPK, which we understand very well is a wonderful target and the face of a global problem of drug resistant tuberculosis, kills millions in underdeveloped countries or India and incompromise people, immunologically compromise. So that’s what I mentioned was the current, the excitement at the level of marketing. Marketing, by that I mean giving advice and there’s a global alliance that the Gates Foundation has and another group, again Gates sponsored for diarrhoeal diseases that kill children. Anyway, we’ve gotten away from science, but not really. |
| Q2 | No, no, not at all. The ICOS story in particular raises the spectre of biotech and the enzymes you discovered are at the very heart of the biotechnology industry and you yourself have been very intimately involved in it. Would it be fair to ask you what influence you think biotech has had on the practice of life science? |
|  | I’ve written about that and whatever I’ve written is probably changing or has changed a lot. As you mentioned, I was involved in starting a biotech company or two and was with them and to date I’m on the board of directors of Xoma, which is a biotech company. I’d say that biotechnology, in fact, Thomas Friedman who writes op-ed articles for the New York Times, three times a week I always read Tom Friedman. I don’t know him and I don’t write letters to the editor but in this case, I thought there was an occasion when he talks about global problems, which he does. The occasion was to mention that biotech was important now and would be even more so in dictating the practice of medicine and all kinds of real life problems and he wrote me a note saying thank you for your letter and I haven’t heard that he’s mentioned anything like that since. Biotech by definition, it’s etymology, it’s a hybrid of biology and technology and they really don’t belong together. Biology, we want to find out how nature is put together and how it operates, we don’t want to be annoyed with what use to which that information can be put, exaggerated. Technology is, can we get a market or marketable product to use this information for the public welfare and to make a profit? They’re really socially distinct but yet they do blend in some very meaningful ways. Biology is basic to what technology can do to define the molecules, the enzymes, the targets, the receptors. Technology has done wonders for biology by providing and accelerating the genomics and the proteomics and the reagents we have and the instruments we have. There wouldn’t be a market for a very specialised instrument if it weren’t that the biotech industry drove it, so I say it could be a very happy marriage, but with care. |
| Q13 | Do you think the climate of funding academic research is changing towards favouring? |
|  | It’s always in danger. I know this again intimately from recent days in which a very talented, accomplished post-doctoral fellow from Spain, Maria Rosario Gomez-Garcia. I’ve been trying very hard to get her a place to do research in Europe which she contributed enormously from her background and her ability, very tough, very tough. It isn’t simply maintaining the status of basic science is preventing an erosion of it that is frightening. I once wrote an essay for *Science* I think called ‘NIH Alma Mater’ because I wanted to give proper due to what the NIH did for me, to create me as a scientist and I’ve mentioned that I came from a coastguard and did rat research and until a couple of years ago, there was a drive and I tried to be helpful in that, to double the NIH budget. Now in doing so you realise there are twenty-seven disease institutes within the NIH, there’s one called GMS, General Medical Sciences, which has about one tenth of that budget or less. The other institutes are quite good too because they do have a reasonable regard for the basic chemistry and physiology that underlies cancer and heart disease and stroke. Now with this squeeze, the budget’s been reduced in effect because of the expansion of cost of technology and worst of all, people are running scared. My NIH grant was terminated a year ago. It was a very mild, small grant and people increasingly, one of my son’s, Roger’s younger brother, who does excellent work on the development of *Drosophila*, had three modest grants. They were terminated and he’s now been able to wangle, wangle might be a good word, two back to a moderate level but not to support his research programme which was vigorous. So, with the threat of losing support, people make more applications, and the applications are increasingly safe rather than adventurous. |
| Q6 | …and think about the almost 50 years since you were awarded the Nobel Prize and I’d like to ask you what you think the influence of the Nobel Prize is on the subject in which it’s awarded, so in particular in medicine and physiology, how do you think the Nobel Prize influences the progresses of research? |
|  | I would hope and I’m going to be daring, that it has no influence on the investigator. That’s of course extreme. The Nobel Prize in Chemistry, I have a special liking for that because in a number of cases, someone’s been awarded the Nobel Prize in Chemistry and the chemist don’t even know because it’s been a tradition that the committee regards biochemistry as a form of chemistry. In Roger’s case, he was trained as a chemist and I don’t think there’s any confusion about that but my colleague, a very close colleague and former post-doc of mine, Paul Berg got a prize in chemistry for recombinant DNA. Chemists in the major departments, Stanford, Harvard, Yale, anywhere, never heard of it.  I wouldn’t say large but a reasonable percentage. So that’s going very well. The medicine prize, with which I’m much more familiar, has on occasion gone to someone who’s done something notable or saleable or in the news without a sufficient background in the fundamentals of that discovery or any future beyond that award and I’m not going to name them, there are very few, very, very few. |
| Q4 | That’s for another day. I think you were going to use the word notoriety there and I wanted to ask you whether you have any advice for your son about how to balance the notoriety that the prize would bring? |
|  | I don’t have anything to offer him in the way of advice. From the time he was a youngster, he knew what he wanted to do and all I could do was watch it and admire it. I saw him a few minutes ago and he seemed worn and tired and concerned about the wear and tear that’s been going on for two months. |
| ID | **0656** |
| Biographical | George Wells Beadle was born at Wahoo, Nebraska, U.S.A., October 22, 1903, the son of Chauncey Elmer Beadle, a farmer, and his wife Hattie Albro. George was educated at the Wahoo High School and might himself have become a farmer if one of his teachers at school had not directed his mind towards science and persuaded him to go to the College of Agriculture at Lincoln, Nebraska. In 1926 he took his B.Sc. degree at the University of Nebraska and subsequently worked for a year with Professor F.D. Keim, who was studying hybrid wheat. In 1927 he took his M.Sc. degree, and Professor Keim secured for him a post as Teaching Assistant at Cornell University, where he worked, until 1931, with Professors R.A. Emerson and L.W. Sharp on Mendelian asynopsis in *Zea mays*. For this work he obtained, in 1931, his Ph.D. degree. In 1931 he was awarded a National Research Council Fellowship at the California Institute of Technology at Pasadena, where he remained from 1931 until 1936. During this period he continued his work on Indian corn and began, in collaboration with Professors Th. Dobzhansky, S. Emerson, and A.H. Sturtevant, work on crossing-over in the fruit fly, *Drosophila melanogaster*.  In 1935 Beadle visited Paris for six months to work with Professor Boris Ephrussi at the *Institut de Biologie physico-chimique*. Together they began the study of the development of eye pigment in *Drosophila* which later led to the work on the biochemistry of the genetics of the fungus *Neurospora* for which Beadle and [Edward Lawrie Tatum](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html) were together awarded the 1958 Nobel Prize for Physiology or Medicine.  In 1936 Beadle left the California Institute of Technology to become Assistant Professor of Genetics at Harvard University. A year later he was appointed Professor of Biology (Genetics) at Stanford University and there he remained for nine years, working for most of this period in collaboration with Tatum. In 1946 he returned to the California Institute of Technology as Professor of Biology and Chairman of the Division of Biology. Here he remained until January 1961 when he was elected Chancellor of the University of Chicago and, in the autumn of the same year, President of this University.  During his career, Beadle has received many honours. These include the Hon. D.Sc. of the following Universities: Yale (1947), Nebraska (1949), Northwestern University (1952), Rutgers University (1954), Kenyon College (1955), Wesleyan University (1956), Birmingham University and Oxford University, England (1959), Pomona College (1961), and Lake Forest College (1962). In 1962 he was also given the honorary degree of LL.D. by the University of California, Los Angeles. He also received the Lasker Award of the American Public Health Association (1950), the Dyer Award (1951), the Emil Christian Hansen Prize of Denmark (1953), the Albert Einstein Commemorative Award in Science (1958), the Nobel Prize in Physiology or Medicine 1958 with E.L. Tatum and [J. Lederberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html), the National Award of the American Cancer Society (1959), and the Kimber Genetics Award of the National Academy of Sciences (1960).  He is a member of several learned societies, among which the National Academy of Sciences (Chairman of Committee on Genetic Effects of Atomic Radiation), the Genetics Society of America (President in 1946), the American Association for the Advancement of Science (President in 1955), the American Cancer Society (Chairman of Scientific Advisory Council), the Royal Society of London, and the Danish Royal Academy of Science.  Beadle has married twice. By his first wife he had a son, David, who now lives at The Hague, the Netherlands. His second wife, Muriel McClure, a well-known writer, was born in California. Beadle’s chief hobbies are rockclimbing, skiing, and gardening.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *George Beadle died on June 9, 1989.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0656** |
| Interview |  |
|  |  |
| ID | **0657** |
| Biographical | Edward Lawrie Tatum was born on December 14th, 1909, at Boulder, Colorado, U.S.A. He was the eldest son of Arthur Lawrie Tatum, Professor of Pharmacology at the University of Wisconsin Medical School, and Mabel Webb Tatum. After the death of his mother, his father married the former Celia Harriman.  Tatum was educated at the University of Chicago and Wisconsin, taking his A.B. degree in Chemistry in 1931, his M.S. degree in Microbiology in 1932 and his Ph.D. degree in Biochemistry in 1934. For the Ph.D. degree his thesis was on work on the nutrition and metabolism of bacteria which he had done under the direction of Edwin Broun Fred and William Harold Peterson. This work no doubt laid the foundations of his later work with [George Wells Beadle](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html), which was to earn for their book, in 1958, the Nobel Prize in Physiology or Medicine.  After taking his doctor’s degree, Tatum studied for a year at the University of Wisconsin and then was awarded a General Education Fellowship at the University of Utrecht, Holland. He then joined the Department of Biological Sciences at Stanford University, California, where he was Research Associate from 1937 until 1941, and Assistant Professor from 1941 until 1945. From 1945 until 1948 he was successively Assistant Professor of Botany and Professor of Microbiology at Yale University. In 1948 he returned to Stanford University as Professor of Biology and later became Professor of Biochemistry there. It was during this period of his life and work at Stanford University that he collaborated with George Wells Beadle, who was Professor of Biology (Genetics) at that University until 1946.  Tatum’s research has been concerned primarily with the biochemistry, nutrition and genetics of microorganisms and of the fruit fly, *Drosophila melanogaster*. During his fruitful collaboration with George Wells Beadle he took charge of the chemical aspects of their joint work on the genetics of eye-colour in *Drosophila* and, when he and Beadle decided to give up their work on *Drosophila* and to work instead with the fungus *Neurospora crassa*, it was Tatum who discovered that biotin was necessary for the successful cultivation of this fungus on simple inorganic media and thus provided these two workers with the genetic material that they needed for the work which gained them, together with [Joshua Lederberg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html), the Nobel Prize.  In 1953, he received the Remsen Award of the American Chemical Society. He is a member of the Advisory Committee of the National Foundation and has served on research advisory panels of the American Committee of the National Research Council on Growth. He also served for 10 years on the Editorial Board of the *Journal of Biological Chemistry*. He is now a member of the Editorial Board of *Science* and of *Biochimica et Biophysica Acta*.  Tatum is married to Viola Kantor. He has two daughters, Margaret and Barbara, born to him and his first wife, June Alton.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Edward Tatum died on November 5, 1975.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0657** |
| Interview |  |
|  |  |
| ID | **0658** |
| Biographical | Joshua Lederberg was born in Montclair, N.J. on May 23, 1925. He was brought up in the Washington Heights District of Upper Manhattan, New York City, where he received his education in Public School 46, Junior High School 164 and Stuyvesant High School. From 1941 to 1944 he studied at Columbia College, where he obtained his B.A. with honours in Zoology (premedical course), and from 1944 to 1946 at the College of Physicians and Surgeons of Columbia University Medical School. Here he carried out part-time research with Professor F.J. Ryan in the Department of Zoology. Subsequently he went to the Department of Microbiology and Botany at Yale University, New Haven, Conn., as Research Fellow of the Jane Coffin Childs Fund for Medical Research and, during 1946-1947, as a graduate student with Professor [E.L. Tatum](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html). He was awarded his Ph.D. degree in 1948.  In 1947, he was appointed Assistant Professor of Genetics at the University of Wisconsin, where he was promoted to Associate Professor in 1950 and Professor in 1954. He organized the Department of Medical Genetics in 1957, of which he was Chairman during 1957-1958.  Stanford University Medical School entrusted to him the organization of its Department of Genetics and appointed him Professor and Executive Head in 1959. Since 1962, he has been Director of the Kennedy Laboratories for Molecular Medicine.  Lederberg was Visiting Professor of Bacteriology at the University of California, Berkeley, in 1950; and Fulbright Visiting Professor of Bacteriology at Melbourne University, Australia, in 1957. In the latter year, he was also elected to the National Academy of Sciences (USA).  While at Yale, Lederberg married Esther M. Zimmer in 1946. They have no children. Mrs. Lederberg had obtained her M.A. at Stanford with Professor [G.W. Beadle](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html) during 1944-1946, and her Ph.D. degree at the University of Wisconsin in 1950. She is working full time as research associate.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  Copyright © The Nobel Foundation 1958 Addendum, December 1997 Joshua Lederberg was born in Montclair NJ, near New York, the son of Rabbi Zwi H. and Esther Lederberg, recently emigrated from Israel, on May 23 1925. He was educated in New York. After a period of study at Columbia P&S medical school, where he began his life-long research in molecular biology, he received his Ph.D. in microbiology at Yale. Then he served as professor of genetics at the University of Wisconsin, then at Stanford School of Medicine, before coming to the Rockefeller in 1978. His life long research, for which he received the [Nobel Prize in 1958](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1958/index.html) (at the age of 33), has been in genetic structure and function in microorganisms. He has been actively involved in artificial intelligence research (in computer science) and in the NASA experimental programs seeking life on Mars. He has also been a consultant on health-related matters for government and the international community, e.g. having had long service on WHO’s Advisory Health Research Council. He received the US National Medal of Science in 1989, where his consultative role was specifically cited. He has been a member of the National Academy of Sciences since 1957, and a charter member of its Institute of Medicine, has served as Chairman of the President’s Cancer Panel, and of the Congress’ Technology Assessment Advisory Council, as well as on numerous other consultative panels.  From 1978 to 1990, he served as president of the Rockefeller University. He continues his research activities there in the field of interactions of gene functionality and mutagenesis in bacteria. His current station there is Sackler Foundation scholar and professor-emeritus of molecular genetics and informatics.  His wife Marguerite Stein Lederberg was born in Paris, was educated as a physician in the U.S. and now serves as Clinical Professor of Psychiatry at Memorial Sloan Kettering Cancer Center in New York. They have two children, David Kirsch and Anne Lederberg.  Copyright © The Nobel Foundation 1997 Addendum, June 2005 Please consult [http://profiles.NLM.nih.gov/BB](http://profiles.nlm.nih.gov/BB/) for extensive archival and biographical detail. The focus of my research has shifted to “What is the fastest rate possible for the growth of a bacterial cell, (and why?)”.  J*oshua Lederberg died on February 2, 2008.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0658** |
| Interview |  |
|  |  |
| ID | **0659** |
| Biographical | Daniel Bovet was born at Neuchâtel, Switzerland, on March 23, 1907. He was the son of Pierre Bovet, Professor of Pedagogy in the University of Geneva and his wife Amy Babut.  After completing his secondary education at Geneva, Bovet graduated at the University of Geneva in 1927. He then spent some years as Assistant in Physiology to Professor F. Batelli. He then worked under Professor Guyenot, preparing a thesis on zoology and comparative anatomy for which he was awarded the degree of D.Sc. in 1929.  From 1929 until 1947 he worked at the Pasteur Institute in Paris then under the direction of Professor E. Roux. Here he worked first as assistant and later as Chief of the Laboratory of Therapeutic Chemistry. This Department was directed by Professor Ernest Fourneau and daily contact with him determined the course of Bovet’s future researches.  In 1947 he accepted the invitation of Professor Domenico Marotta, Director of the Istituto Superiore di Sanità in Rome, to go to Italy and to organize a Laboratory of Therapeutic Chemistry. He then became Chief of the Laboratory of Therapeutic Chemistry of the Istituto Superiore di Sanità, Rome.  Bovet has published more than 300 papers on biology, general pharmacology, chemotherapy, the sulphonamide drugs, the pharmacology of the sympathetic nervous system, the therapy of allergic conditions, the synthesis of antihistamines, on curare and curare-like drugs and the use of curare as an adjuvant to anaesthesia, on various modifications of hormonal equilibrium, and on various aspects of the pharmacology of the central nervous system (drugs used for the treatment of Parkinsonism, strychnine and tranquillizers). Important aspects of these researches are embodied in a book by Bovet and his wife, published in 1948 and entitled *Structure chimique et activité pharmacodynamique des médicaments du système nerveux végétatif* (The chemical structure and pharmacodynamic activity of drugs of the vegetative nervous system), and in the book by Bovet, his wife, and G. B. Marini-Bettòlo, published in 1959 and entitled *Curare and Curare-like Agents*. In 1957 he was awarded the Nobel Prize for Physiology or Medicine for his discovery relating to synthetic compounds for the blocking of the effects of certain substances occurring in the body, especially in its blood vessels and skeletal muscles.  Bovet has received honorary degrees of the Universities of Palermo, Rio de Janeiro, Geneva, Montpellier, Paris, Nancy, Prague and Strasbourg.  In 1946, he was elected a Chevalier of the Legion of Honour of France, and in 1959 a Grand Official of the Order of Merit of the Italian Republic.  Apart from the Nobel Prize in 1957, Bovet has received the following awards: Plantamour Prize of the Faculty of Science of the University of Geneva (1934), Martin Damourette Prize of the Academy of Sciences of the Institute of France (1936), General Muteau Prize of the Italian Academy of Science (1941), Cameron Prize of the University of Edinburgh, Scotland (1949), Bürgi Prize of the Faculty of Medicine, Berne, Switzerland (1949), «E. Paterno» Prize, jointly with his wife, F. Bovet-Nitti (1949), the Scientific Illustration Prize of the Italian National Research Council, jointly with his wife (1951), and the Addingham Gold Medal, University of Leeds (1952). He is a member of several learned societies in Italy, France, Great Britain, the USA, Brazil, Argentine, and India.  Bovet married Filomena Nitti, sister of the bacteriologist F. Nitti, who has closely and continuously collaborated with him in his work.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Daniel Bovet died on April 8, 1992.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0659** |
| Interview |  |
|  |  |
| ID | **0660** |
| Biographical | André Frédéric Cournand was born in Paris on 24th September, 1895, the second of the four children of Jules Cournand, a stomatologist, and his wife Marguérite Weber.  He received his early education to secondary school level at the Lycée Condorcet, and obtained his bachelor’s degree at the Faculté des Lettres of the Sorbonne in 1913, taking the Diploma of Physics, Chemistry, and Biology of the Faculté des Sciences, the following year.  The medical studies, begun in 1914, were interrupted by his volunteering for service in the French Army. From 1915 to 1918 he was successively a private in an infantry regiment, a corpsman, and a battalion surgeon, and he was awarded the Croix de Guerre with three bronze stars.  On leaving the Army at the end of the First World War, he resumed his medical studies and became Interne des Hôpitaux de Paris in 1925. During the next few years he gained much clinical experience: in internal medicine under de Massary and Professor Achard; in chest diseases under Rist; in pediatrics under Professor Debré, and in neurology under Professor Guillain. He published a thesis submitted on Acute Disseminated Sclerosis, and was awarded the M.D. degree of the Faculté de Médecine de Paris in May, 1930.  Anxious to study and work in the United States of America, Cournand secured a residency in the Tuberculosis (later Chest) Service of the Columbia University Division at Bellevue Hospital, New York, which was directed by Professors James Alexander Miller and J. Burns Amberson. Offered the opportunity to become Chief Resident of this service and to conduct, under the guidance of [D. W. Richards](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html), research on the physiology and physiopathology of respiration, he decided to settle in the United States, and became an American citizen in 1941. His work in collaboration with Richards, which earned them Nobel Prizes, has extended over a quarter of a century.  Cournand’s work in the field of full-time medical investigation has been performed exclusively in the Chest Service of Bellevue Hospital, where he is a Visiting Physician. In the hospital’s Cardio-Pulmonary Laboratory, many clinical investigators from the United States and other countries were trained in and worked on the development of physiologic methods of exploration of the cardiopulmonary system. Cournand’s academic appointments at Columbia University College of Physicians and Surgeons have ranged from Instructor in Medicine (1934) to Professor of Medicine (1951).  Professor Cournand has served on the Editorial Boards of many medical and physiological publications: *Circulation, Physiological Reviews, The American Journal of Physiology,* and also *Journal de Physiologie* and *Revue Française d’Etúdes Cliniques et Biologiques*. During the Second World War he held the post of responsible investigator of the Office of Scientific and Research Developments and was a consultant of the Chemical Warfare Service. He was the Chairman of the Cardiovascular Study Section of the National Heart Institute of the Public Health Service (1956-1959).  André Cournand is a member of the American Physiological Society, the Association of American Physicians, the American Clinical and Climatological Association, and the American Association of Thoracic Surgery. and also, in 1958, of the National Academy of Sciences of the United State of America. His foreign associations include Associé Etranger de l’Académie Nationale de Médecine, Paris (1960); honorary membership of the Swedish Society for Internal Medicine, the Swedish Cardiac Society, the British Cardiac Society, and the Societé Médicale des Hôpitaux de Paris. He is also Foreign Corresponding Member of the Académie Royale de Médecine de Belgique and a Membre Associé Etranger de l’Académie des Sciences de l’Institut de France.  In 1950, Professor Cournand was appointed Lecturer of the Harvey Society (of which he was elected President 1960-1961), and of the Royal College of Physicians and Surgeons of Canada (1952), and was selected by the Association des Médecins de Langue Française in 1951 to present a report on the physiopathology of chronic cardiac failure. He gave the Einthoven Memorial Lecture at the University of Leiden (Holland) in 1958, and the Dr. Albert Wanderer Gedenkvorlesung at the University of Berne (Switzerland) in 1962. Many seats of medical research have recognized his work, and he has received the Anders Retzius Silver Medal of the Swedish Society for Internal Medicine (1946), the Lasker Award of the United States Public Health Association (1949), the John Philipps Memorial Award of the American College of Physicians (1952), the Gold Medal of the Académie Royale de Médecine de Belgique and of the Académie Nationale de Médecine, Paris (1956). He was elected Doctor (*honoris causa*) of the Universities of Strasbourg (1957), Lyon (1958), Brussels (1959), Pisa (1961), and D.Sc. of the University of Birmingham (1961). He is Advisor to the Délégué Général de la Recherche Scientifique et Technique of the French Government since 1958, and is Officier de la Légion d’Honneur and Commandeur des Palmes Académiques.  As a young man Cournand was a sports enthusiast, playing both soccer and tennis, and he also took up high-mountain climbing. He was formerly a member of the G.H.M. of the Club Alpin Français, and is a member of the American Alpine Club.  Cournand was married to the former Sibylle Blumer, who died in 1959; she was the widow of Birel Rosset, and he had adopted her son Pierre Birel Rosset-Cournand who was killed in action in France in 1944 after a brilliant military career. Their three daughters are Muriel (Mme. J. F.Jaeger) who lives in Paris; Marie-Eve (Mrs. Norman Stewart Walker) living in New York; and Marie-Claire.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *André F. Cournand died on February 19, 1988.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0660** |
| Interview |  |
|  |  |
| ID | **0661** |
| Biographical | Werner Theodor Otto Forssmann was born in Berlin on August 29, 1904, the son of Julius Forssmann and Emmy Hindenberg. He was educated at the Askanische Gymnasium (secondary grammar school) in Berlin. Leaving school in 1922, he went to the University of Berlin to study medicine, passing his State Examination in 1929. For his clinical training he went to the University Medical Clinic, working under Professor Georg Klemperer, and he studied anatomy under Professor Rudolph Fick. For clinical instruction in surgery he went, in 1929, to the August Victoria Home at Eberswalde near Berlin.  It was here that he was the first to develop a technique for the catheterization of the heart. This he did by inserting a cannula into his own antecubital vein, through which he passed a catheter for 65 cm and then walked to the X-ray department, where a photograph was taken of the catheter lying in his right auricle.  Subsequently he worked at the Charité, Berlin, and the City Hospital at Mainz, and then went to the Rudolf Virchow Hospital in Berlin for specialist training in urology under Dr. Karl Heusch. He was appointed Chief of the Surgical Clinic of the City Hospital at Dresden-Friedrichstadt and at the Robert Koch Hospital, Berlin. At the beginning of the Second World War, Forssmann served as a Sanitary Officer, reaching the rank of Surgeon-Major; but he became a prisoner of war until his release in 1945, when he went into practice with his wife, in the Schwarzwald.  From 1950 onwards he practised as a urological specialist at Bad Kreuznach, and since 1958 he has been Chief of the Surgical Division of the Evangelical Hospital at Düsseldorf, where he now lives.  In 1956 he was awarded, together with [André Cournand](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html) and [Dickinson W. Richards](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html), the Nobel Prize for Physiology or Medicine and he was, in the same year, appointed Honorary Professor of Surgery and Urology at the Johannes Gutenberg University, Mainz.  In 1954 he was awarded the Leibniz Medal of the German Academy of Sciences; in the same year he was Guest of Honour at the National University of Cordoba, Argentina, where he was appointed Honorary Professor in 1961.  Since 1962 he is a Member of the Executive Board of the German Surgical Society. He is also a Member of the American College of Chest Physicians, and Honorary Member of the Swedish Society of Cardiology, the German Society of Urology, and the German Child Welfare Association.  In 1933 Forssmann married Dr. Elsbet Engel, who is also a specialist in urology. They have six children: Klaus (b. 1934), Knut (b. 1936), Jörg (b. 1938), Wolf (b. 1939), Bernd (b. 1940), and Renate (b. 1943).  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Werner Forssmann died on June 1, 1979* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0661** |
| Interview |  |
|  |  |
| ID | **0662** |
| Biographical | Dickinson Woodruff Richards Jr. was born on October 30, 1895, in Orange, New Jersey, U.S.A. He is the son of Dickinson W. Richards, a New York lawyer and Sally Lambert, whose father and three of her brothers practised medicine in New York. He was educated at the Hotchkiss School in Connecticut, and, in 1913, went to Yale University to study English and Greek. In June, 1917, he was given his A.B. degree, but had, three months earlier, joined the United States Army. After a period as instructor in artillery during 1917-1918, Richards served, during 1918-1919 as an artillery officer in France.  After the war, Richards entered Columbia University College of Physicians and Surgeons and received his M.A. degree in physiology in 1922, and his M.D. degree in 1923. He then spent the years 1923-1927 on the Staff of the Presbyterian Hospital, New York, and then went to work for a year at the National Institute for Medical Research, London, under [Sir Henry Dale](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1936/index.html), on the control of the circulation in the liver.  Returning to the Presbyterian Hospital and the College of Physicians and Surgeons, Richards began his researches on pulmonary and circulatory physiology under the direction of Professor L. J. Henderson of Harvard.  In 1931 he began to collaborate with [André Cournand](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html) at the Bellevue Hospital, New York, and this work resulted, in 1940, in the development of a technique for catheterization of the heart and in studies (carried out between 1941 and 1956) of traumatic shock, the diagnosis of congenital heart diseases, the physiology of heart failure, measurement of the actions of cardiac drugs, and various forms of dysfunction in chronic cardiac and pulmonary diseases and their treatment. For this work he was awarded, together with [André Cournand and Werner Forssmann](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1956/index.html), the Nobel Prize for Physiology or Medicine for 1956.  From 1935 onwards he has been medical adviser to Merck & Co., Inc., New Jersey.  In 1945 Richards was appointed Professor of Medicine at Columbia University and Visiting Physician and Director of the First (Columbia) Division of the Bellevue Hospital, New York, and in 1947 he became Lambert Professor of Medicine.  In 1961 he retired from this Chair and became Emeritus Lambert Professor.  Professor Richards is a former Editor of *The American Review of Tuberculosis*, and was also on the Editorial Board of *Medicine* and of *Circulation*.  Richards married in 1931 Constance Burrell Riley, they have four daughters: Ida Elizabeth (Mrs. Robert W. Chamberlin, Jr.), Gertrude Woodruff (Mrs. Isaac Daw Russell), Ann Huntington Richards, and Constance Lord Richards.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Dickinson W. Richards died on February 23, 1973.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0662** |
| Interview |  |
|  |  |
| ID | **0663** |
| Biographical | Axel Hugo Theodor Theorell was born at Linköping, Sweden, on July 6, 1903. He was the son of Thure Theorell, surgeon-major to the First Life Grenadiers practising medicine in Linköping, and his wife Armida Bill.  Theorell was educated for nine years at a State Secondary School in Linköping and passed his matriculation examination there on May 23, 1921. In September, 1921, he began to study medicine at the [Karolinska Institute](http://www.ki.se/) and in 1924 he graduated as a Bachelor of Medicine. He then spent three months studying bacteriology at the Pasteur Institute in Paris under Professor Calmette.  In 1930 he obtained his M.D. degree with a thesis on the lipids of the blood plasma, and was appointed lecturer in physiological chemistry at the Karolinska Institute.  Since 1924, however, Theorell had been on the Staff of the Medico-Chemical Institution, first as an associate assistant and during the years 1928-1929 as a temporary Associate Professor. Here, under Professor Einar Hammarsten, he carried out his first work on the influence of the lipids on the sedimentation of the blood corpuscles. In 1931 he studied in [Svedberg](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1926/index.html)‘s institute at Uppsala University, the molecular weight of myoglobin with the aid of the ultracentrifuge.  In 1932 he was appointed Associate Professor in Medical and Physiological Chemistry at Uppsala University, and here he continued and extended his work on myoglobin. From 1933 until 1935 Theorell held a Rockefeller Fellowship and worked with [Otto Warburg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1931/index.html) at Berlin-Dahlem, and here he became interested in oxidation enzymes, a subject to which he has given his attention ever since. At Berlin-Dahlem he produced, for the first time, the oxidation enzyme called «the yellow ferment» and he succeeded in splitting it reversibly into a coenzyme part, which was found to be flavinmononucleotide, and a colourless protein part.  Returning to Sweden in 1935, Theorell worked at the Karolinska Institute and in 1936 he was appointed Head of the newly established Biochemical Department of the Nobel Medical Institute, which was opened in 1937. For ten years this Institute was housed in the Karolinska Institute, but in 1947 it was able to occupy its own building.  Since 1935, Theorell has, with Swedish and other collaborators, carried out researches on various oxidation enzymes, and he has contributed especially to our knowledge of cytochrome *c*, peroxidases, catalases, flavoproteins, and «pyridine»-proteins, particularly the alcohol dehydrogenases. For his work on the nature and effects of oxidation enzymes he was awarded the Nobel Prize for Physiology or Medicine for 1955.  Theorell is a member of learned societies in Sweden, Denmark, Norway, Finland, the U.S.A., France, Italy, Poland, Belgium and India. He was Chairman of the Swedish Medical Society in 1947-1948 and 1957-1958, and served as Secretary of that Society during 1940-1946, he was a member of the Swedish Society for Medical Research during 1942-1950, the State Research Council for the Natural Sciences during 1950-1954, and the State Medical Research Council as from 1958.  He was also Chairman of the Association of Swedish Chemists from 1947-1949. Since 1954 he has been Chief Editor of the journal *Nordisk Medicin*. He has been a member of many Government Committees and is Chairman of the Swedish National Committee for Biochemistry, of the Board of the Wenner-Gren Society and of the Wenner-Gren Center Foundation.  His interest in music is shown by the facts that he is also a Member of the Swedish Royal Academy of Music and Chairman of the Stockholm Symphony Society.  Theorell holds honorary doctorates of the Universities of Paris, Pennsylvania, Louvain, Brussels and Rio de Janeiro, and is a Foreign Member of the Royal Society of London, and the National Academy of Sciences of Washington.  In 1931 he married Elin Margit Elisabeth Alenius. They had one daughter, Eva Kristina, who died in 1935, end three sons: Klas Thure Gabriel (b. 1935), Henning Hugo (b. 1939), and Per Gunnar Töres (b. 1942). Theorell now lives in Stockholm.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Hugo Theorell died on August 15, 1982.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0663** |
| Interview |  |
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| ID | **0664** |
| Biographical | John Franklin Enders was born on February 10th, 1897, at West Hartford, Connecticut, U.S.A. He is the son of John Ostrom Enders, a banker in Hartford, and Harriet Goulden Enders (*née* Whitmore).  Enders was educated at the Noah Webster School at Hartford and St. Paul’s School in Concord, New Hampshire. Finishing school in 1915, he went to Yale University, but in 1917 left his studies there to join the U.S. Naval Reserve (Air Force). Early in 1918 he qualified as a pilot and received the grade of Ensign. After the First World War he returned to Yale and was given, in 1919, the degree of B.A. (*honoris causa*) and the normal degree in 1920.  He then went into business in real estate in Hartford, but, becoming dissatisfied with this, he entered Harvard University. For four years he studied English literature and Germanic and Celtic languages with the idea of becoming a teacher of English, but he was not satisfied with this career either. He had been for a long time interested in biology and this interest was reawakened by his friendships with medical students at Harvard, with the result that he decided to enter as a candidate for the Ph.D. degree in bacteriology and immunology. In coming to this decision he was influenced by the late Professor Hans Zinsser, who was then Head of the Department of Bacteriology and Immunology at Harvard and by Dr. H. K. Ward, who later became Professor of Bacteriology at the University of Sidney, Australia.  In 1930, Enders received the degree of Ph.D. at Harvard for a thesis which presented evidence that bacterial anaphylaxis and hypersensitivity of the tuberculin type are distinct phenomena.  From 1930 until 1946, Enders remained at Harvard as a member of the teaching staff. During this period he studied, first, the elucidation of certain factors related to bacterial virulence and the resistance of the host organism. He then clarified, in collaboration with Ward, Shaffer, Wu, and others the inhibitory effect of the type specific capsular polysaccharides of *Pneumococcus* upon the phagocytic process. This work discovered a new form of Type I polysaccharide and produced evidence that complement played a catalytic-like part in the opsonization of bacteria by specific antibody.  In 1938, Enders began the study of some of the mammalian viruses, and undertook, in 1941, in collaboration with Cohen, Kane, Levens, Stokes and others, a study of the virus of mumps. This work provided serological tests for the diagnosis of this disease and a skin test for susceptibility to it, and demonstrated the immunizing effect of inactivated mumps virus and the possibility of attenuating the virulence of this virus by passing it through chick embryos. It was shown that mumps often occurs in a form that is not apparent, but nevertheless confers a resistance which is as effective as that conferred by the visible disease.  In 1946, Enders was asked to establish a laboratory for research in infectious diseases at the Children’s Medical Center at Boston. In this laboratory much outstanding work on the viral diseases of man has been done under his direction and it was here that the work was done on the cultivation of the poliomyelitis viruses for which Enders was awarded, together with [T. H. Weller](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html) and [F. C. Robbins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html), the Nobel Prize for Physiology or Medicine in 1954.  Since this time Enders has returned, in collaboration with Peebles, to his earlier work on measles. He is now Higgins University Professor at Harvard University and Chief of the Research Division of Infectious Diseases of the Children’s Hospital, Boston, Massachusetts, U.S.A.  Enders is a member of a great number of American learned societies, the Society for General Microbiology and the Royal Society for the Promotion of Health in Great Britain, the Deutsche Akademie der Naturforscher (Leopoldina), and is Foreign Corresponding Member of the British Medical Association and the Académie Royale de Médicine de Belgique.  He married Sarah Frances Bennett, of Brookline, Massachusetts, in 1927. She died in 1943, and in 1951 Enders married Carolyn B. Keane of Newton Center, Massachusetts. He has one son John Ostrom Enders II, one daughter, Sarah Enders, and a stepson, William Edmund Keane.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *John F. Enders died on September 8, 1985.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0664** |
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| ID | **0665** |
| Biographical | Thomas Huckle Weller was born at Ann Arbor, Michigan, on June 15th, 1915. He was educated at the public schools there, and later at the University of Michigan, where his father, Carl Vernon Weller had an appointment in the Pathology Department of the Medical School. Entering this University in 1932, T. H. Weller graduated in 1936, taking the A.B. degree. Early in life he had shown an interest in natural history, and this no doubt influenced him during his University life in the direction of medical zoology. He was also influenced in this direction by Professors G. R. LaRue, and A. E. Woodhead and, after his graduation, he worked for two summers at the University of Michigan Biological Station under Professors L. J. Thomas and W. W. Cort on the parasites of fish. In 1937 he was awarded the M.S. degree for this work.  In 1936, however, he had entered the Harvard Medical School in Boston and there he was given, by Drs. E. E. Tyzzer and Donald L. Augustine, facilities for research in the Department of Comparative Pathology and Tropical Medicine. His experiences under the direction of these two distinguished parasitologists, whose outstanding discoveries in protozoology and helminthology are well-known, must have been very valuable.  The course of much of Weller’s later work was, nevertheless, influenced by the fact that he was accepted, in 1939, as a tutorial student by Dr. [J. F. Enders](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html), who introduced him to the field of virus research and to the study of tissue-culture techniques as a means of studying the causes of infectious disease. In 1940 he took his M.D. degree and began his clinical training at the Children’s Hospital in Boston. His work here was, however, interrupted by military service in the Second World War, for he joined, in 1942, the Army Medical Corps and was stationed at the Antilles Medical Laboratory in Puerto Rico for 32 months. There he was Head of the Departments of Bacteriology, Virology and Parasitology and attained the rank of Major. He then returned to the Children’s Hospital, Boston, for a further year of clinical training and, in 1947, he joined Dr. Enders in the organization of the new, Research Division of Infectious Diseases at the Children’s Medical Centre.  In 1949 he was appointed Assistant Director of this Division and subsequently was appointed Instructor, Assistant Professor, and then Associate Professor in the Department of Comparative Pathology and Tropical Medicine of Harvard Medical School. The department was renamed and transferred to the Harvard School of Public Health. In July 1954, he was appointed Richard Pearson Strong Professor of Tropical Public Health and head of the Department at the Harvard School of Public Health.  In his researches, Weller was interested, partly in the helminth parasites of man, and partly in virology. In helminthology he contributed to the literature on the nematode *Trichirella spiralis* and also to that on the schistosome trematodes which cause schistosomiasis of man, his contributions including methods of cultivating the schistosomes *in vitro* and modifications of methods for the recovery and counting of the eggs of these parasites.  In virology his studies of varicella and herpes zoster resulted in his isolation for the first time of the viruses responsible for these diseases, and also in the development of diagnostic tests and in the demonstration that the same virus apparently causes both these diseases. In 1955 he also isolated the virus which causes cytomegalic inclusion disease in infants and, after working for five years on these diseases, he was able to show that the human foetus, while it is in the uterus, is particularly susceptible to attack by these viruses and that, if the foetus survives attack by them, the infant is often born with severe damage to its brain which causes mental retardation and cerebral palsy. Weller’s subsequent work has included studies of the Coxsackie viruses as causes of epidemic pleurodynia and on the behaviour of *Toxoplasma gondii* in tissue culture. He is also studying the propagation *in vitro* of the viruses that cause varicella and herpes zoster.  In addition to the appointments already mentioned, Weller served, from 1953 till 1959, as Director of the Commission on Parasitic Diseases of the American Armed Forces Epidemiological Board.  In 1945 he married Kathleen Fahey and they have two sons, Peter Fahey and Robert Andrew, and two daughters, Janet Louise and Nancy Kathleen.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  Copyright © The Nobel Foundation 1954 Addendum, August 2005 My addendum features my work in academic tropical medicine at Harvard. When I arrived at Harvard Medical School in 1936, the Department of Tropical Medicine had disappeared; for financial reasons it had been fused with the Department of Comparative Pathology which was located in Building E-2 of the Harvard Medical School (HMS). The head of Tropical Medicine, Dr. Richard Strong, had retired; only a senior associate, Dr. Watson Sellards, remained active. The main task of the fused department was to teach a required course in medical parasitology for second year HMS students. As a student with a classmate, Wallace Sorenson, I investigated the prevalence and associated symptoms of pinworm infections in Boston school children; the results were published in the New England Journal of Medicine. One summer was spent studying malaria in Florida at Rockefeller training centers. My interest and training in tropical medicine was the basis for my army assignment in 1942 to a laboratory in Puerto Rico that was responsible for malaria control at our numerous bases throughout the Caribbean.  After the war in 1946 major organizational changes occurred in the medical-health area at Harvard. Former General Steve Simmons was appointed by President Conant as dean of the newly independent Harvard School of Public Health (HSPH). The hybrid department of comparative pathology and tropical medicine was renamed the department of Tropical Public Health (TPH) and was transferred to the HSPH. In 1953, Nathan Pusey became president of Harvard. Dean Simmons died in July 1954 and was replaced by Dr. John Snyder. In July 1954 I was Pusey’s first professorial appointee being named head of TPH. I was pleased that my appointment occurred before the Nobel award.  When in 1954 I was appointed head of the Department of Tropical Public Health at the Harvard School of Public Health (HSPH), a position held until 1981, academic responsibilities occupied a major proportion of my time. With the support of training grants from the National Institutes of Health I was able to expand the academic faculty by adding Dr. Eli Chernin, a protozoologist, Dr. Steve Pan, a parasitologist, Dr. Ed Michelson, a medical malacologist, and Dr. Andrew Spielman, a medical entomologist. These individuals served throughout my tenure, providing a harmonious multidisciplinary teaching group. In the School of Public Health we usually attracted over 80 students to our basic course required for a MPH degree. Smaller numbers attended courses in malariology, malacology, medical entomology, and the clinicopathology of tropical diseases. In each subject the ecological and epidemiological aspects were emphasized. Seventeen doctoral degrees were awarded and usually each faculty member had one or two post-doctoral research fellows. Each year we offered a course in medical parasitology required for all second year medical students that involved three afternoons a week for a month. When Dr. John Snyder was appointed Dean of the Public Health School in 1954 the Department received excellent support, a situation persisting until his retirement in 1971.  In 1954, the new Department occupied three floors in the E-2 wing of the Medical School. An immediate objective was to plan and to raise money to rehouse the Department in new buildings, a goal achieved in 1969 when we occupied three floors in two new HSPH buildings.  My research efforts continued to utilize tissue culture techniques to study viral and parasitic diseases. Studies on the varicella-zoster viruses were continued and definitive papers on the cultural and immunologic characteristics of viruses from the two diseases were published in 1958.  In 1957 we recorded the first recovery of cytomegaloviruses (CMV) from living children with cytomegalic inclusion disease and demonstrated that such children continued to excrete viruses in their urine for many months. The viruria provided a useful diagnostic approach and indicated why the infection could spread rapidly in groups of preschool children. Evidence was obtained that the cytomegaloviruses constituted a closely related but antigenically heterogeneous group of agents. Like other herpes viruses the cytomegalviruses remained latent in infected individuals, becoming active when the host was immunosuppressed as an organ transplant recipient or by an HIV viral infection. Information indicating that the CMV was the major cause of damaging viral congenital infections was obtained by many virologists.  With the rapid utilization of tissue cultures, knowledge of the damaging congenital rubella syndrome led many investigators to attempt to isolate the etiological virus. We investigated four different outbreaks of German measles in schools with negative results. Then in 1960, my ten year old son, Robert, developed a febrile illness that had some characteristics of German measles but was much more severe than the usual case. I was worried and inoculated roller cultures of human amnion cells with his urine. I observed the cultures microscopically for a longer period than customary and on the 26th day after innoculation observed peculiar rounding of scattered cells with refractile bodies in the nucleus and cytoplasm. The cytopathic changes progressed and the causative agent could be readily subcultured. The question was “had we finally isolated the rubella virus”? I enlisted the collaboration of Dr, Franklin Neva, then a faculty associate. Fortuitously at that time, we learned of a rubella outbreak at the Phillips Exeter Academy. Franklin was able to collect urine specimens from two Exeter cases and from a Harvard student with rubella. Each specimen produced cell changes similar to those seen in my son’s cultures.  We then found that we were not alone in the field. Beginning in 1961 a group at the Walter Reed Institute of Research in Washington had isolated viruses from cases of rubella using cultures of monkey kidney cells. No cytopathic changes were seen but application of a viral interference method, originally developed by David Tyrrell in England, demonstrated that the rubella virus was present. With the help of Drs. Albert Sabin and Joe Smadel we exchanged viruses with the Washington group and found the isolates identical. Dr. Smadel arranged that papers from each group be published “back to back” in the October 1962 issue of the Proceedings of the Society of Experiment, Dr. Charles Alford on the viral aspects of the congenital rubella syndrome.  In 1963 in recognition of my isolation of the CMV and rubella viruses I was greatly pleased by the award by Harvard of the George Ledlie prize, an award given every two years to the Harvard faculty member considered to have made the major contribution to human welfare.  Research on the etiology of rubella was my final major study in the area of virology. Since our initial paper in 1949 on the cultivation *in vitro* of the polio viruses the utilization of tissue culture procedures by many virologists had resulted in the isolation of hundreds of new viruses and in the development of vaccines for the major viral diseases of children. When we received the Nobel Prize in 1954 Professor Sven Gard stated that tissue cultures will do for virology what [Koch](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1905/index.html) accomplished when he revolutionized bacteriology by the development of culture media. Events have proven the truth of his prediction.  The disease schistosomiasis was a major research focus of TPH. One goal was the development of techniques for the control of the snail vectors. A search for specific pathogens of snails failed but it was determined that the introduction of certain nonvector snails would displace the vector snails. Working with doctoral candidates or post-doctoral fellows the growth *in vitro* of schistosomules of *S. mansoni* was accomplished. A specific circulating antigen elaborated by the worms was demonstrated in the blood and urine of infected animals. This finding has stimulated other workers to develop sero-diagnostic tests, thus providing an alternative to classic diagnostic tests based on the demonstration of eggs of the worms. One objective, the cultivation of the cells of schistosomes, although pursued many years with hundreds of different media, was not achieved.  Although time consuming, service on national and international health agencies was a scientifically valuable experience. Such included membership of committees of the World Health Organization, the Pan American Health Organization, and the International Health Organization of the Rockefeller Foundation. Consultative assignments included meetings in St. Lucia, Trinidad, Egypt, Thailand, South Africa, Saudi Arabia, and Kuwait. With the valuable support of Dr. Peter Williams of the Wellcome Trust, a research and training center for young physicians and scientists interested in tropical medicine was established in a rural area of Salvador, Bahia, Brazil where Chagas disease and schistosomiasis were highly endemic. Initiated in 1972 this project was active through 1983.  In 2004 I published an autobiographical volume: Weller, Thomas H., *Growing pathogens in tissue cultures. Fifty years in academic tropical, medicine, pediatrics, and virology*, pp. 1-292. Science History Publishers, Canton, Mass. Dr. Eli Chernin in 1985 published a historical manual on TPH: Chernin, Eli, *Tropical Medicine at Harvard. The Weller Years, 1954-1981. A personal memoir*, pp. 1-95. Harvard School of Public Health.  *Thomas H. Weller died 23 August, 2008.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0665** |
| Interview |  |
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| ID | **0666** |
| Biographical | Frederick Chapman Robbins was born in Auburn, Alabama, on August 25, 1916. He is the son of William J. Robbins, a plant physiologist, who became Director of the New York Botanical Gardens, and Christine, *née* Chapman.  He was educated at the University of Missouri, where he took the A.B. degree in 1936 and the B.S. in 1938. In 1940 he graduated from Harvard Medical School and was appointed as resident physician in bacteriology at The Children’s Hospital Medical Center in Boston, Massachusetts. He continued his training there until 1942 when he left to serve in the United States Army.  During military service he was assigned to the Fifteenth Medical General Laboratory as Chief of the Virus and Rickettsial Disease Section, and in this capacity served in the United States, North Africa, and Italy. Most of his work during this period consisted of investigations on infectious hepatitis, typhus fever and Q fever, and supervision of a diagnostic virus laboratory. He has also studied the immunology of mumps. In 1945 he received the Bronze Star for Distinguished Service and at the time of discharge from the Army in 1946 held the rank of Major.  Returning to civilian life, Robbins resumed his training at The Children’s Hospital Medical Center and completed this in January 1948. From 1948 to 1950 he held a Senior Fellowship in Virus Diseases of the National Research Council and worked with Dr. [John F. Enders](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1954/index.html) in the Research Division of Infectious Diseases, The Children’s Hospital Medical Center. During this time he was a member of the Faculty of the Harvard Medical School. While he was working with Enders, Robbins chiefly studied the cultivation of poliomyelitis virus in tissue culture and the application of this technique. He also investigated the viruses of mumps, herpes simplex and vaccinia.  While in Boston, he was appointed Associate in Pediatrics on the Faculty of the Harvard Medical School, Associate in the Research Division of Infectious Diseases, and Associate Physician and Associate Director of the Isolation Service at The Children’s Hospital Medical Center, and also Research Fellow in Pediatrics at The Boston Lying-in Hospital and Assistant to the Children’s Medical Service, Massachusetts General Hospital.[1](https://www.nobelprize.org/prizes/medicine/1954/robbins/biographical/#not1)  In May, 1952, he moved to Cleveland, Ohio, where he had been appointed Professor of Pediatrics at Western Reserve University School of Medicine and Director of the Department of Pediatrics and Contagious Diseases, Cleveland Metropolitan General Hospital, the position which he at present occupies.[2](https://www.nobelprize.org/prizes/medicine/1954/robbins/biographical/#not2)  Robbins has served as Chairman of the Committee on Medical Education of Western Reserve University School of Medicine since 1958.  He is an associate member of the Commission on Viral Diseases of the Armed Forces Epidemiological Board, United States Department of Defense, of the Board of Scientific Counselors of the Division of Biologics Standards, Public Health Service, United States Department of Health, Education and Welfare, of the Physician’s Council, the Scientific Research Advisory Board of the National Association for Retarded Children; he is also Chairman of District V of the Committee on Medical Education of the American Academy of Pediatrics, and of the Awards Committee of this Academy, and served on the Public Health Council of the Ohio State Department of Health. He is also a consultant to the Infectious Diseases and Tropical Medicine Training Grant Award Committee of the National Institute of Allergy and Infectious Diseases, and to the Oregon Primate Research Center.  In 1955, John Carroll University of Cleveland conferred upon him the honorary degree of Doctor of Science, and in 1958, the University of Missouri, his alma mater, did the same.  In 1961 he was elected President of the Society for Pediatric Research, and in 1962 a member of the American Academy of Arts and Sciences.  Robbins married in 1948 Alice Havemeyer Northrop and they have two daughters, Alice Christine and Louise Enders.  1. During this time he continued to work with Dr. Enders.  2. Frederick C. Robbins is now University Professor and Dean Emeritus at the Case Western Reserve University.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  Copyright © The Nobel Foundation 1954 Addendum, August 2001  |  | | --- | | Honors & Awards | | Award for Distinguished Achievement (Modern Medicine), 1963 | | Honorary Degree, Doctor of Laws, University of New Mexico, 1968 | | Medical Mutual Honor Award, 1969 | | Ohio Governor’s Award, 1971 | | Honorary Fellow, All-India Institute of Medical Sciences, 1977 | | Honorary Fellow, National Academy of Medical Sciences (India), 1977 | | Honorary Degree, Doctor of Science, University of North Carolina, 1979 | | Honorary Degree, Doctor of Science, Tufts University, 1983 | | Honorary Degree, Doctor of Science, Medical College of Ohio, 1983 | | Honorary Degree, Doctor of Science, Albert Einstein College of Medicine, 1984 | | Honorary Degree, Doctor of Science, Medical College of Wisconsin, 1984 | | Honorary Degree, Doctor of Medical Science, The Medical College of Pennsylvania, 1984 | | Honorary Degree, Doctor of Laws, University of Alabama, Birmingham, 1985 | | Abraham Flexner Award of AAMC for Distinguished Service to Medical Education, 1987 | | Judge Baker Children’s Center Camille Cosby World of Children Award, 1988 | | NASA Public Service Award, 1989 | | Ohio Science and Technology Hall of Fame, 1992 | | Case Western Reserve University Medical Alumni Assocication Board of Trustees Award, 1993 | | Honorary Degree, Doctor of Science, honoris causa, Case Western Reserve University, May 24, 1992 | | Frank and Dorothy Humel Hovorka Prize, Case Western Reserve University, May 22, 1994 | | Honorary Degree, Doctor of Science, Kirksville College of Osteopathic Medicine, Kirksville, Missouri, June 7, 1998 | | Benjamin Franklin Medal, American Philosophical Society, Philadelphia, PA, April 22, 1999 |   *Frederick C. Robbins died on August 4, 2003.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0666** |
| Interview |  |
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| ID | **0667** |
| Biographical | Sir Hans Adolf Krebs was born at Hildesheim, Germany, on August 25th, 1900. He is the son of Georg Krebs, M.D., an ear, nose, and throat surgeon of that city, and his wife Alma, *née* Davidson.  Krebs was educated at the Gymnasium Andreanum at Hildesheim and between the years 1918 and 1923 he studied medicine at the Universities of Göttingen, Freiburg-im-Breisgau, and Berlin. After one year at the Third Medical Clinic of the University of Berlin he took, in 1925, his M.D. degree at the University of Hamburg and then spent one year studying chemistry at Berlin. In 1926 he was appointed Assistant to Professor [Otto Warburg](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1931/index.html) at the Kaiser Wilhelm Institute for Biology at Berlin-Dahlem, where he remained until 1930.  In 1930, he returned to hospital work, first at the Municipal Hospital at Altona under Professor L. Lichtwitz and later at the Medical Clinic of the University of Freiburg-im-Breisgau under Professor S. J. Thannhauser.  In June 1933, the National Socialist Government terminated his appointment and he went, at the invitation of [Sir Frederick Gowland Hopkins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1929/index.html), to the School of Biochemistry, Cambridge, where he held a Rockefeller Studentship until 1934, when he was appointed Demonstrator of Biochemistry in the University of Cambridge.  In 1935, he was appointed Lecturer in Pharmacology at the University of Sheffield, and in 1938 Lecturer-in-Charge of the Department of Biochemistry then newly founded there.  In 1945 this appointment was raised to that of Professor, and of Director of a Medical Research Council’s research unit established in his Department. In 1954 he was appointed Whitley Professor of Biochemistry in the University of Oxford and the Medical Research Council’s Unit for Research in Cell Metabolism was transferred to Oxford.  Professor Krebs’ researches have been mainly concerned with various aspects of intermediary metabolism. Among the subjects he has studied are the synthesis of urea in the mammalian liver, the synthesis of uric acid and purine bases in birds, the intermediary stages of the oxidation of foodstuffs, the mechanism of the active transport of electrolytes and the relations between cell respiration and the generation of adenosine polyphosphates.  Among his many publications is the remarkable survey of energy transformations in living matter, published in 1957, in collaboration with H. L. Kornberg, which discusses the complex chemical processes which provide living organisms with high-energy phosphate by way of what is known as the Krebs or citric acid cycle.  Krebs was elected a Fellow of the Royal Society of London in 1947. In 1954 the Royal Medal of the Royal Society, and in 1958 the Gold Medal of the Netherlands Society for Physics, Medical Science and Surgery were conferred upon him. He was knighted in 1958. He holds honorary degrees of the Universities of Chicago, Freiburg-im-Breisgau, Paris, Glasgow, London, Sheffield, Leicester, Berlin (Humboldt University), and Jerusalem.  He married Margaret Cicely Fieldhouse, of Wickersley, Yorkshire, in 1938. They have two sons, Paul and John, and one daughter, Helen.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Hans Krebs died on November 22, 1981.* |
| Podcast |  |
| Telephone  interview | **0667** |
| Interview |  |
|  |  |
| ID | **0668** |
| Biographical | Fritz Albert Lipmann was born on June 12th, 1899, at Koenigsberg, Germany. He was the son of Leopold Lipmann and his wife Gertrud Lachmanski.  Lipmann was educated, during the years 1917-1922, at the Universities of Koenigsberg, Berlin, and Munich, where he studied medicine. He took his M.D. degree in 1924 at Berlin. He was, during his pre-clinical year of medical study, strongly impressed by what he has called «a dramatic chemistry course» given by Professor Klinger at Koenigsberg. Later, he took a primer course in biochemistry given in Berlin by Professor Rona and in 1923 he definitely took up biochemistry, and held for a time a Fellowship in the Department of Pharmacology, at the University of Amsterdam, under Professor Ernst Laqueur. Feeling then the need for further study of chemistry, Lipmann returned to Koenigsberg to study chemistry under Professor Hans Meerwein, who had then succeeded Professor Klinger. In 1926 he went as an assistant in [Otto Meyerhof](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1922/index.html)‘s laboratory at the Kaiser Wilhelm Institute, Berlin, to prepare a thesis for the degree of Ph.D., Berlin, which he took in 1927. He then went with Meyerhof to Heidelberg, where he did further research on the biochemical reactions occurring in muscle.  In 1930 Lipmann went back to the Kaiser Wilhelm Institute in Berlin to work as a research assistant in the laboratory of Albert Fischer, who was interested in applying biochemical methods to tissue culture. Fischer was then getting ready to occupy a new Institute in Copenhagen and he asked Lipmann to accompany him there, which he did in 1932. The years 1931 and 1932, however, he spent as a Rockefeller Fellow in the laboratory of P. A. Levene at the Rockefeller Institute in New York, where he identified serine phosphate as the constituent of phosphoproteins which contains the phosphate.  When he went to Copenhagen in 1932, as Research Associate in the Biological Institute of the Carlsberg Foundation there, Lipmann became interested in the metabolism of fibroblasts and this prompted him to investigate the Pasteur effect, which led to important papers on the mechanism of this reaction and on the part played by glycolysis in the metabolism of the cells of embryos.  In 1939 Lipmann became Research Associate in the Department of Biochemistry, Cornell Medical School, New York, and in 1941 joined the research staff of the Massachusetts General Hospital in Boston, first as a Research Associate in the Department of Surgery, then heading his own group in the Biochemical Research Laboratory of the Hospital. In 1949 he became Professor of Biological Chemistry at Harvard Medical School, Boston. In 1957, he was appointed a Member and Professor of the Rockefeller Institute, New York, a post which he still holds.  During the late forties and early fifties, the wealth of problems opened up by the discovery of coenzyme A attracted much attention. He left this post to explore the chemical nature of some seemingly unusual phosphate derivatives arising in the process of group activation through phosphoryl transfer from ATP. Thus, through observations on a phosphorolysis of citrulline, his attention was drawn to the probability of carbamyl phosphate (CMP) representing the metabolically active carbamyl donor. The suspicion proved justified, and proof of metabolic formation and its function, in collaboration with Mary Ellen Jones and Leonard Spector, was greatly simplified by the latter’s discovery of an unexpectedly simple method of chemical CMP synthesis through condensation of cyanate and phosphate at room temperature and in excellent yield.  Another unusual phosphate derivative had been indicated through the function of ATP in sulphate activation. Work with Hilz and Robbins in this area brought out the existence of a new class of chemical compounds, the mixed anhydrides between phosphate and sulphate; adenosine-5′-phosphosulphate (APS) and 3′-phosphoadenosine-5′-phosphosulphate (PAPS) were identified as «active» sulphates. The latter compound, PAPS, was found in animals and plants to be the common sulphate donor in the sulphurylation of mono- or poly-saccharides and other sulphate derivatives.  Recently, most of his attention has returned to development of the biological mechanism of peptide and protein synthesis. At present, this is what has become his major interest.  Lipmann is a member of several learned societies in the U.S.A., the Faraday Society, and the Danish Royal Academy of Sciences and is a Foreign Member of the Royal Society of England. He holds honorary degrees of the Universities of Marseilles, Chicago and Chile, and is Doctor of Humane Letters of Brandeis University. In 1931, he married Elfreda M. Hall, and they have one son, Steven.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Fritz Lipmann died on July 24, 1986.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0668** |
| Interview |  |
|  |  |
| ID | **0669** |
| Biographical | Selman Abraham Waksman was born in Priluka, near Kiev, Russia, on July 22nd, 1888, as the son of Jacob Waksman and Fradia London. He received his early education primarily from private tutors, and completed his school training in Odessa in an evening school and with private tutors. He obtained his matriculation diploma in 1910 from the Fifth Gymnasium in Odessa as an extern, and left for the United States immediately afterwards.  In the autumn of 1911 he entered Rutgers College, having won a State Scholarship the previous spring. He received his B.Sc. degree in Agriculture from Rutgers in 1915. He was then appointed research assistant in soil bacteriology under Dr. J. G. Lipman at the New Jersey Agricultural Experiment Station, and was allowed to continue graduate work at Rutgers, obtaining his M.Sc. degree in 1916. In the same year, he became a naturalized United States citizen and was appointed a Research Fellow at the University of California where he received his Ph.D. in Biochemistry in 1918.  He was invited by Dr. Lipman to return to Rutgers, where he received an appointment as microbiologist at the Experiment Station and as Lecturer in Soil Microbiology at the University. He was appointed Associate Professor in 1925 and Professor in 1930. When the Department of Microbiology was organized in 1940, he became Professor of Microbiology and Head of the Department. In 1949, he was appointed Director of the Institute of Microbiology. He retired in 1958. However, he has a laboratory and office at the Institute to continue a limited amount of research and considerable writing and lecturing.  Apart from his activities at Rutgers, he was invited to organize a division of Marine Bacteriology at the Woods Hole Oceanographic Institution in 1931; he was also appointed marine bacteriologist at the same institution, where he served until 1942. He was then elected as a Trustee, and later a Life Trustee. On various occasions, he held industrial positions for limited periods of time and served as consultant to industrial laboratories, government and other scientific institutions.  Professor Waksman’s fields of work include, in chronological order, the microbiological population of the soil, sulphur oxidation by bacteria, microorganisms and soil fertility; decomposition of plant and animal residues, nature and formation of humus; occurrence of bacteria in the sea and their role in marine processes; production and nature of antibiotic substances; taxonomy, physiology, and biochemistry of the actinomycetes. He has published more than 400 scientific papers and has written, alone or with others, 18 books.  He has isolated, together with his students and associates, a number of new antibiotics, including actinomycin (1940), clavacin, streptothricin (1942), streptomycin (1943), grisein (1946), neomycin (1948), fradicin, candicidin, candidin, and others. Two of these, streptomycin and neomycin, have found extensive application in the treatment of numerous infectious diseases of men, animals and plants. They have been covered by patents, that on streptomycin having been recently listed as one of the ten «patents that shaped the world».  Professor Waksman holds honorary doctor’s degrees in medicine, science, agriculture, law or letters from the Universities of Liège, Athens, Pavia, Madrid, Strasbourg, Jerusalem, Göttingen, Perugia, Keio (Japan) and several American universities and colleges. He is a member, honorary member or fellow of a number of scientific societies in the USA, France, Sweden, Mexico, India, Germany, Brazil, Spain, and Israel. He is a Former President of the American Society for Microbiology.  His work in the field of microbiology has been recognized by numerous scientific and other societies in the USA, Denmark, The Netherlands, Canada, Sweden, Japan, Israel, Italy, Spain, and Turkey. In 1950 he was made Commander of the French Légion d’Honneur, and in 1952 he was voted as one of «the most outstanding 100 people in the world today» (Little, Brown & Co.).  In 1949, the Trustees of Rutgers University voted to establish an Institute of Microbiology and made Professor Waksman its first Director. The larger portion of the funds derived from the royalties obtained from streptomycin and neomycin have been assigned for the building and support of this Institute, which is being used for research and advanced teaching on a doctorate and post-doctorate level in microbiology. Out of the small portion of the royalties assigned to him personally, Dr. and Mrs. Waksman established the «Foundation for Microbiology», for the support of research and publications in the field of microbiology at various institutions of the world. Professor Waksman continues as President of this Foundation. He and his wife have also established a scholarship for an immigrant student, or the son or daughter of an immigrant, at Rutgers University, and Mrs. Waksman has established a music scholarship at Douglass College, Rutgers University.  Professor Waksman’s wife is Deborah B. Mitnik. They have one son, Byron H. Waksman, M.D., who was a Research Associate at Massachusetts General Hospital, Boston, and Assistant Professor at Harvard University Medical School, and more recently Professor of Microbiology at Yale University Medical School, and two grandchildren, Nan and Peter.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  For more updated biographical information, see: Waksman, Selman Abraham, *My Life With Microbes*. Simon and Schuster, New York, 1954.  *Selman A. Waksman died on August 16, 1973.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0669** |
| Interview |  |
|  |  |
| ID | **0670** |
| Biographical | Max Theiler was born on January 30, 1899, in Pretoria, South Africa, one of the four children of Sir Arnold and Emma (*née* Jegge) Theiler. His father was a well-known veterinary scientist. He attended local schools except for one year in Basle, Switzerland (his father was of Swiss origin), then went on to Rhodes University College, Grahamstown and the University of Capetown Medical School (1916-1918). He then went to England to study at St. Thomas’ Hospital and at the London School of Tropical Medicine, receiving his medical degree in 1922. In the same year he became a Licentiate of the Royal College of Physicians and a Member of the Royal College of Surgeons.  In 1922 he joined the Department of Tropical Medicine at the Harvard Medical School, Boston, Massachusetts, first as an assistant, then being appointed instructor. In 1930 he joined the staff of the International Health Division of the Rockefeller Foundation, becoming, in 1951, Director of Laboratories of the Rockefeller Foundation’s Division of Medicine and Public Health, New York.  His early work, at Harvard, dealt with amoebic dysentery and rat bite fever. He also worked on the problem of yellow fever, a subject in which he had become interested whilst still in London. This was to become his major interest. By 1927 he and his colleagues had proved that the cause of yellow fever was not a bacterium but a filterable virus. He also demonstrated that the disease could be readily transmitted to mice. Previously, laboratory work on this topic had been done using monkeys as experimental animals; the use of mice enabled the cost of such research to be greatly reduced. In 1930, when he joined the Rockefeller Foundation, that body was engaged in a broad attack on the problem of yellow fever. Here, Theiler and his colleagues worked on vaccines against the disease and eventually developed a safe, standardized vaccine, 17D, one advantage of which was its ready adaptability to mass production.  His other work for the Institute has been connected with the causes and immunology of certain disorders which include Weil’s disease. He has also been engaged in research on dengue fever and Japanese encephalitis. The problem of poliomyelitis has been of great interest to him and he discovered an apparently identical disorder in laboratory mice which is now sometimes called Theiler’s disease (encephalomyelitis).  Dr. Theiler has been a contributor to two books, *Viral and Rickettsial Infections of Man* (1948) and *Yellow Fever* (1951). He has also written numerous papers in *The American Journal of Tropical Medicine* and *Annals of Tropical Medicine and Parasitology.*  Honours awarded to him include the Chalmer’s Medal of the Royal Society of Tropical Medicine and Hygiene (London, 1939), the Flattery Medal (Harvard, 1945), and the Lasker Award of the Lasker Foundation (1949).  He married Lillian Graham in 1928. They have one daughter.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Max Theiler died on August 11, 1972.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0670** |
| Interview |  |
|  |  |
| ID | **0671** |
| Biographical | Edward Calvin Kendall was born on March 8, 1886, at South Norwalk, Connecticut, U.S.A. He was educated at Columbia University, where he obtained the degrees of Bachelor of Science in 1908 and Master of Science, specializing in Chemistry, in 1909. From 1909 until 1910 he was Goldschmidt Fellow of this University, and in 1910 he obtained his Ph.D. in Chemistry.  From 1910 until 1911 he was research chemist for Parke, Davis and Co., at Detroit, Michigan, U.S.A. Here he did research on the thyroid gland, and from 1911 until 1914 he continued this work at St. Luke’s Hospital, New York.  In 1914 he was appointed Head of the Biochemistry Section in the Graduate School of the Mayo Foundation, Rochester which is affiliated with the University of Minnesota, and in 1915 he was appointed Director of the Division of Biochemistry there and subsequently Professor of Physiological Chemistry. On April 1, 1951, Kendall reached the age of retirement from the Mayo Foundation and he accepted the position of Visiting Professor in the Department of Biochemistry at Princeton University, a position, which at the time of writing, he still holds.  Kendall’s name will always be associated with his isolation of thyroxine, the active principle of the thyroid gland, but he is also known for his crystallization of glutathione, the chemical nature of which he established, and also for his work on the oxidation systems in animals. Perhaps his greatest achievement, however, was his work on the hormones of the cortex of the adrenal glands. Chemical investigation of the adrenal cortex was carried out simultaneously but independently by Kendall and [T. Reichstein](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1950/index.html) with their associates. The former at the Mayo Foundation, Rochester, Minnesota; the latter at Zurich, Switzerland.  After many years the hormones of the adrenal cortex were isolated, identified, and prepared by synthetic methods in small amounts. Subsequently, they were made commercially on a scale sufficiently large to permit a study of their physiological effects. Previous to this, Dr. [Philip Hench](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1950/index.html), also at the Mayo Foundation, had observed that patients who had rheumatoid arthritis were sometimes relieved if they developed jaundice. In women, rheumatoid arthritis was sometimes relieved during pregnancy. When one of the hormones of the adrenal cortex was given to patients by Dr. Hench, the anti-inflammatory effect of the compound, cortisone, was discovered. It was then found that many other diseases of an inflammatory nature were relieved by cortisone. Although it was found later that cortisone, like insulin, acts only so long as it is given to the patient, and that it does not cure the disease, the discovery of the activity of cortisone was a great step forward. It has led to our modern knowledge of the hormones of the adrenal cortex and their uses in medicine. For their work, Kendall, Hench, and Reichstein jointly were given the Nobel Prize for Physiology and Medicine for 1950. Since his retirement to Princeton University, Kendall has continued his studies of the chemistry of the adrenal cortex.  Kendall received many awards and other honours, some of these (Lasker Award of the American Public Health Service, Passano Award of the Passano Foundation in San Francisco, and Page One Award of the Newspaper Guild of New York) jointly with Dr. Hench. On December 1915, he married Rebecca Kennedy; they have two children.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Edward C. Kendall died on May 4, 1972.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0671** |
| Interview |  |
|  |  |
| ID | **0672** |
| Biographical | Tadeus Reichstein was born on July 20th, 1897, at Wloclawek, Poland. He was the son of Isidor Reichstein and Gastava Brockmann. After passing his early childhood at Kiev, where his father was an engineer, Reichstein was educated, first at a boarding-school at Jena and later, when his family moved to Zurich (where he was naturalized), he first went to a private tutor and later to the Oberrealschule (technical school of junior college grade) and the Eidgenössische Technische Hochschule (E.T.H.) (State Technical College).  In 1916 Reichstein passed his school-leaving examination and began to study chemistry at the E.T.H. at Zurich, taking his diploma there in 1920. He then spent a year in industry and then began to work for his doctorate under Professor [H. Staudinger](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1953/index.html). In 1922 he graduated and then began research under Professor Staudinger on the composition of the flavouring substances in roasted coffee.  After leaving Professor Staudinger, he continued to work for nine years on this subject, being financed for this purpose by an industrial firm, who provided him with an assistant. The aroma of coffee is, he found, composed of extremely complex substances, among which are derivatives of furan and pyrrole, and substances containing sulphur. Reichstein published during this period a series of papers on these substances and on new methods of demonstrating and making them, and also on the aromatic substances in chicory.  In 1929 he qualified as a lecturer at the E.T.H. Here he lectured on organic and physiological chemistry and in 1931, when his work on aromatic substances in coffee and chicory ended, he became assistant to Professor [L. Ruzicka](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1939/index.html) and was then able to devote himself exclusively to scientific research.  In 1934 he was appointed Titular Professor, in 1937 Associate Professor, and in 1938 Professor in Pharmaceutical Chemistry, and Director of the Pharmaceutical Institute in the University of Basel. In 1946 he took over, in addition, the Chair of Organic Chemistry and he held both these appointments until 1950, when a new Director of the Pharmaceutical Institute was appointed.  Between the years 1948-1952 he supervised the building and equipment of a new Institute of Organic Chemistry, which was ready for occupation in 1952, Reichstein becoming its Director in 1960. He now lives in Basel.  In 1933 Reichstein succeeded, independently of [Sir Norman Haworth](https://www.nobelprize.org/nobel_prizes/chemistry/laureates/1937/index.html) and his collaborators in Birmingham, in synthesizing vitamin C (ascorbic acid). Otherwise he has worked on the glycosides of plants, and during the years 1953-1954 he worked in collaboration with S. A. S. Simpson and J. F. Tait (London), with A. Wettstein and R. Neher (Ciba Ltd., Basel), and M. Tausk (N.V. Organon, Oss, The Netherlands), and isolated and explained the constitution of aldosterone, a hormone of the adrenal cortex, which until then had not been isolated. Reichstein also collaborated with [E. C. Kendall](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1950/index.html) and [P. S. Hench](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1950/index.html) in their work on the hormones of the adrenal cortex which culminated in the isolation of cortisone and the discovery of its therapeutic value in the treatment of rheumatoid arthritis. For this work, Reichstein, Kendall, and Hench were jointly awarded the Nobel Prize for Physiology or Medicine in 1950.  In 1947 he received the Honorary Doctorate of the Sorbonne, Paris, and in 1952 he was elected a Foreign Member of the Royal Society, London.  Reichstein married Henriette Louise Quarles van Ufford, of Dutch nobility, in 1927. They have one daughter.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Tadeus Reichstein died on August 1, 1996.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0672** |
| Interview |  |
|  |  |
| ID | **0673** |
| Biographical | Philip Showalter Hench was born in Pittsburgh, Pennsylvania on February 28, 1896, the son of Jacob Bixler Hench and Clara Showalter. After attending local schools he entered Lafayette College, Easton, Penn., where he graduated Bachelor of Arts in 1916. He enlisted in the Medical Corps of the United States Army in 1917 but was transferred to the reserve corps to finish his medical training. In 1920 he received his doctorate in medicine from the University of Pittsburgh. After a year as an interne at Saint Francis Hospital, Pittsburgh, he became a Fellow of the Mayo Foundation, the graduate school of the University of Minnesota’s Department of Medicine. His association with the Mayo Clinic began in 1923 when he became first an assistant, then, three years later, Head of its Department of Rheumatic Diseases. Between 1928 and 1929, Dr. Hench studied abroad, at Freiburg University and at the von Müller Clinic, Munich. He was appointed an instructor in the Mayo Foundation in 1928, Assistant Professor 1932, Associate Professor 1935 and, in 1947, Professor of Medicine, a position which he still holds.  In 1942 Dr. Hench entered military service as a lieutenant-colonel in the Medical Corps, becoming Chief of the Medical Service and Director of the Army’s Rheumatism Centre at the Army and Navy General Hospital. Leaving the army with the rank of colonel, in 1946, he became expert consultant to the Army Surgeon General, which position is still held by him.  At the Mayo Clinic he specialized in arthritic disease. In the course of his work he observed the favourable effects of jaundice on arthritic patients, causing a remission of pain. Other bodily changes, for example pregnancy, produced the same effect. These and other observations led him gradually to the conclusion that the pain-alleviating substance was a steroid.  In the period 1930-1938, Dr. [E. C. Kendall](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1950/index.html) had isolated several steroids from the adrenal gland cortex. After several years of collaboration with Dr. Kendall, it was decided to try the effect of one of these substances, Compound E (later named cortisone), on arthritic patients. Delay in implementing this decision was caused by Dr. Hench’s military service in World War II and by the costly and complicated isolation of the substance. In 1948-1949, cortisone was successfully tested on arthritic patients. Hench also treated patients with ACTH, a hormone produced by the pituitary gland which stimulates the adrenal gland.  Dr. Hench is the author of several papers in the field of rheumatology, contributed mainly to *Hygeia* and the *Annals of Rheumatic Diseases.* His many awards include the Heberden Medal (London), the 1949 Lasker Award, presented by the American Public Health Association, the Passano Foundation Award and the Criss Award (1951). He has received honorary doctorates in science from Lafayette College, Washington and Jefferson College, Western Reserve University, the National University of Ireland and the University of Pittsburgh. He holds the degree of master of science from the University of Minnesota.  A Fellow of the American Medical Association and of the American College of Physicians, he is one of the leaders in American rheumatology. He is a founder member of the American Rheumatism Association (President 1940-1941), and holds office in many rheumatism organizations. He holds honorary membership of the Royal Society of Medicine (London) and of rheumatism societies in Argentina, Brazil, Canada, Denmark and Spain.  In 1927, Dr. Hench married Mary Genevieve Kahler, daughter of John Henry Kahler. They have two sons and two daughters. He is interested in music, photography and tennis, and is an authority on medical history.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Philip S. Hench died on March 30, 1965.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0673** |
| Interview |  |
|  |  |
| ID | **0674** |
| Biographical | Walter Rudolf Hess was born in Frauenfeld, East Switzerland, on March 17, 1881. His father was a teacher of physics who allowed him, at a very early age, great freedom in dealing with apparatus, and taught him a proper carefulness. He also obtained a self-reliant gift of observation during excursions through forests and meadows, and on lakes and rivers, in the environment of the town of his birth. Here, he also visited the Gymnasium, completing the course in 1900. As a medical student, he visited Lausanne, Berne, Berlin, Kiel, and Zurich. In the University of the latter town he took his degree of Doctor of Medicine in 1906.  Although his aim always was to be a physiologist, external reasons first necessitated him to be an assistant in surgery, later in ophthalmology, and finally a practising opthalmologist. This detour, however, was by no means a disadvantage, as he learned, particularly in ophthalmology, to investigate and operate with precision. Also the contact with pathological physiology has proved in many respects a positive advantage.  In 1912 he took the great decision – although already the father of a family – of leaving a prosperous practice and going back to the position of assistant, this time in physiology itself. He obtained his training from Professor Gaule, a pupil of Ludwig, and from Professor Verworn in Bonn. In 1917 he was nominated – not without great opposition – Director of the Physiological Institute at Zurich, with corresponding teaching responsibilities. After the First World War, he visited many English institutes and got to know the English doyens of physiology such as Langley, [Sherrington](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1932/index.html), Starling, [Hopkins](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1929/index.html), [Dale](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1936/index.html), and others.  The scientific interests of Professor Hess were primarily directed towards haemodynamics and, in connection with this, the regulation of respiration. While the experimental work on the subject of the central coordination of vegetative organs has in general been extended, a comprehensive picture has emerged of the representation of the vegetative nervous system in the diencephalon, which has been accorded distinction by the Nobel Prize.  During the experimental investigations of the diencephalon, setting aside the evidence of the regulatory representations, which control the activity of the internal organs in a coordinated fashion, somatomotor effects were observed relatively often. Following this, the symptoms were analysed in more detail, and in the process a relationship was demonstrated between supporting functions, automatic correcting movements, and the differentiated maintenance of tone in the skeletal musculature, as also were connections with actions due to the vestibular apparatus. Other investigations dealt with the control of parts of the forebrain (area orbitalis), in which Hess together with K. Akert has achieved some insight into the cortical representation of sight, and oral and pharyngeal regions.  When the professorship and the directorship of the Physiological Institute had to be given up in accordance with the regulations, Hess had the right to transfer all the material which had been acquired over the previous years to the rooms placed at his disposal in the Physiological Institute. The possibility also existed here of allocating a workplace; to co-workers, and of using the «cerebro-biological collection», which he had built up, for research purposes. So the work went on, albeit restricted in terms of space, and above all of staff.  It had already occurred earlier to Hess that in the experiments on diencephalic stimulation modes of behaviour were occasionally evident in the experimental animal, which suggested a manifestation of psychic powers. Thus was the theme of *The Biological Aspect of Psychology* (1962) established; this was taken up, after the fundamental findings on stimulation or extirpation at defined sites in the diencephalon had previously been described in an atlas (1956).  Out of this work on the integration of the experimental material in question concerning psychologically motivated expressions of the functional organization of the brain, among other things a contribution has been brought about towards bridging the gap which, until then, had yawned between physiology and psychiatry. At the same time in the monograph where his findings were summarized, the physiological foundations of the clinically important study of psychosomatic phenomena were dealt with, and the understanding of the mode of action of the so-called psychotropic drugs was advanced. Also, certain guiding principles for a closer contact between the investigation of behaviour and the type-specific organization of the central nervous system were included.  In the course of the last few years, the goal of satisfying the prerequisites for continuing and broadening research on the brain was finally pursued.  As the result of combined efforts, a special professorship for research on the brain with an independent institute at the University of Zurich has been established, of which his former co-worker, Professor K. Akert, has been elected director.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Walter Hess died on August 12, 1973.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0674** |
| Interview |  |
|  |  |
| ID | **0675** |
| Biographical | (António Caetano de Abreu Freire) Egas Moniz was born in Avanca, Portugal, on November 29, 1874, the son of Fernando de Pina Rezende Abreu and Maria do Rosário de Almeida e Sousa. He received his early education from his uncle Abbé Caetano de Pina Rezende Abreu Sa Freire, before joining the Faculty of Medicine at Coimbra University. He received further education at Bordeaux and Paris and became Professor at Coimbra in 1902. In 1911 he transferred to the new Chair in Neurology at Lisbon where he remained until his death. He also worked for a time as a physician in the Hospital of Santa Maria, Lisbon.  Moniz entered politics in 1903 and served as a Deputy in the Portuguese Parliament until 1917 when he became Portuguese Ambassador to Spain. Later in 1917 he was appointed Minister for Foreign Affairs and he was President of the Portuguese Delegation at the Paris Peace Conference in 1918.  Moniz discovered cerebral angiography and prefrontal leucotomy and the extent of his work is perhaps best indicated by listing his more important publications:  *Alterações anátomo-patológicas na difteria* (Anatomo-pathologic changes in diphtheria), Coimbra, 1900.  *A vida sexual (fisiologia e patologia)* (Physiological and pathological aspects of sex life), 19 editions, Coimbra, 1901.  *A neurologia na guerra* (Neurology in war), Lisbon, 1917.  *Um ano de política* (A year of politics), Lisbon, 1920.  *Júlio Diniz e a sua obra* (Julio Denis and his works), 6 editions, Lisbon, 1924.  *O Padre Faria na história do hipnotismo* (Abbé Faria in the history of hypnotism), Lisbon, 1925.  *Diagnostic des tumeurs cérébrales et épreuve de l’encéphalographie artérielle* (Diagnostics of cerebral tumours and application of arterial encephalography), Paris, 1931.  *L’angiographie cérébrale, ses applications et résultats en anatomic, physiologie te clinique* (Cerebral angiography, its applications and results in anatomy, physiology, and clinic), Paris, 1934.  *Tentatives opératoires dans le traitement de certaines psychoses* (Tentative methods in the treatment of certain psychoses), Paris, 1936.  *La leucotomie préfrontale. Traitement chirurgical de certaines psychoses* (Prefrontal leucotomy. Surgical treatment of certain psychoses), Turin, 1937.  *Clinica dell’angiografia cerebrale* (Clinical cerebral angiography), Turin, 1938.  *Die cerebrale Arteriographie und Phlebographie* (Cerebral arteriography and phlebography), Berlin, 1940.  *Ao lado da medicina* (On the side of medicine), Lisbon, 1940.  *Trombosis y otras obstrucciones de las carótidas* (Thrombosis and other obstructions of the carotids), Barcelona, 1941.  *História das cartas de jogar* (History of playing-cards), Lisbon, 1942.  *Como cheguei a realizar a leucotomia pré-frontal* (How I came to perform leucotomy), Lisbon, 1948.  *Die präfrontale Leukotomie* (Prefrontal leucotomy), Archiv für Psychiatrie und Nervenkrankheiten, 1949.  Moniz received the Gran-Cruz da Instrução e Benemerência (Portugal) and the Gran-Cruz de Izabella Catolica (Spain): he was appointed Grand Officier de la Couronne d’Italie, and Commandeur de la Légion d’Honneur (France). He was Doctor, *honoris causa,* of the Universities of Bordeaux and Lyon; Membre de Mérite, and President at various times, of the Academy of Sciences, Lisbon; Member of the Academy of Medicine, Paris; of the Academy of Medicine, Madrid; of the Society of British Neurological Surgeons; Honorary Member of the Royal Society of Medicine, London; of the Académie Nationale de Médecine de Rio de Janeiro; of the American Society of Neurology; and of several South American institutions among many others.  Prof. Moniz married Elvira de Macedo Dias in 1902; he died in 1955.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Egas Moniz died on December 13, 1955.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0675** |
| Interview |  |
|  |  |
| ID | **0676** |
| Biographical | Paul Hermann Müller was born at Olten, Solothurn, Switzerland, on January 12th, 1899, and his early childhood was spent at Lenzburg, Aargau, the birthplace of his father who was an employee of the Swiss Federal Railway. The family moved to Basle where Paul attended primary school and, later, Free Evangelical elementary and secondary schools. He commenced work in 1916 as a laboratory assistant at Dreyfus and Company and the following year he joined Lonza A.G. as an assistant chemist in the Scientific-Industrial Laboratory of their electrical plant, gaining a wealth of practical knowledge which later stood him in good stead in his career as an industrial chemist. He matriculated in 1918 and returned to school to obtain his diploma (1919) which entitled him to attend Basle University: he studied there under Professors Fichter and Rupe for his Doctorate which he received in 1925. He began his career with J. R. Geigy A.G., Basle, in May, 1925, to become Deputy Director of Scientific Research on Substances for Plant Protection in 1946.  Müller’s first researches concerned the chemical and electrochemical oxidation of *m*-xylidine, and his early work at J. R. Geigy concerned vegetable dyes and natural tanning agents. He devoted some of his spare time to research on tanning agents and he invented synthetic agents which tanned hides pure white – they were, however, not fast to light. Later, in 1930, he developed the light-fast synthetic tanning agents Irgatan FL and Irgatan FLT. He worked on disinfectants for a short while, on moth-proofing agents for textiles, on pesticides in general, and he developed Graminone, a mercury-free seed disinfectant, before, in 1935, he started his researches on new synthetic contact insecticides.  Four years of intensive work led to the synthesis of dichlorodiphenyltrichloroethane (DDT) and the basic Swiss patent was granted in 1940. This compound was originally made in 1873 by an Austrian student, but had never received any particular attention. Field trials now showed it to be effective not only against the common housefly, but also against a wide variety of pests, including the louse, Colorado beetle, and mosquito; and two products based on DDT, Gesarol and Neocide, were marketed in 1942. These formulations were brought to the notice of British and American medical entomologists at a time, during World War II, when supplies of pyrethrum were rapidly falling short of demand. Production was soon established on both sides of the Atlantic and they proved to be of enormous value in combatting typhus and malaria – malaria was, in fact, completely eradicated from many island areas. These compounds have also had great value in agricultural entomology and they have provided a great stimulus in the search for other insecticides.  Müller has had several papers on his work published in *Helvetica Chimica Acta.* He married Friedel Rüegsegger in 1927. They have two sons, Heinrich (b. 1929) and Niklaus (b. 1933), and one daughter, Margaretha (b. 1934), all married.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Paul Müller died on October 12, 1965.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0676** |
| Interview |  |
|  |  |
| ID | **0677** |
| Biographical | Carl Ferdinand Cori was born in Prague on December 5th, 1896. His father, Dr. Carl I. Cori, was Director of the Marine Biological Station in Trieste, and it was here that young Carl spent his childhood. He received an early introduction to science from his father and this was stimulated on summer visits to the Tyrol, to the home of his grandfather, Ferdinand Lippich, Professor of Theoretical Physics at Prague. He studied at the gymnasium in Trieste and graduated in 1914 when he entered the German University of Prague to study medicine. During World War I, he served as a lieutenant in the Sanitary Corps of the Austrian Army on the Italian front; he returned to University, where he studied with his future wife, Gerty, to graduate Doctor of Medicine in 1920. He spent a year at the University of Vienna and a year as assistant in pharmacology at the University of Graz until, in 1922, he accepted a position as biochemist at the State Institute for the Study of Malignant Diseases in Buffalo, New York. In 1931, he was appointed Professor of Pharmacology at the Washington University Medical School in St. Louis, where he later became Professor of Biochemistry.  Gerty Theresa Cori, née Radnitz, was born in Prague on August 15th, 1896. She received her primary education at home before entering a *Lyceum* for girls in 1906; she graduated in 1912 and studied for the University entrance examination, which she took and passed at the Tetschen Realgymnasium in 1914. She entered the Medical School of the German University of Prague and received the Doctorate in Medicine in 1920. She then spent two years at the Carolinen Children’s Hospital before emigrating to America with her husband, Carl, whom she married in 1920. They worked together in Buffalo and when he moved to St. Louis, she joined him as Research Associate. Gerty Cori was made Professor of Biochemistry in 1947.  The Cori’s have collaborated in most of their research work, commencing in their student days and stemming from their mutual interest in the preclinical sciences. Their first joint paper resulted from an immunological study of the complement of human serum.  In America, they first studied the fate of sugar in the animal body and the effects of insulin and epinephrine. The presence of glycolysis of tumours *in vivo* was demonstrated. Their work on carbohydrate metabolism passed from studies of whole animal to isolated tissues and, later, tissue extracts and isolated enzymes, some in crystalline form, were studied. In 1936, they isolated glucose-1-phosphate, «Cori ester», and traced its presence to the activity of the phosphorylase, which catalyzes the breakdown and synthesis of polysaccharides: this discovery made possible the enzymatic synthesis of glycogen and starch *in vitro.* Subsequently, phosphorylase and other enzymes were crystallized.  The Cori’s have been consistently interested in the mechanism of action of hormones and they have carried out several studies on the pituitary. They observed that the marked decrease in glycogen and lowering of blood sugar in hypophysectomized rats occurred with a concomitant increase in the rate of glucose oxidation. Subsequently, by a study of the action of hormones on hexokinase, they observed that some pituitary extracts inhibit this enzyme *in vivo* and *in vitro* and that insulin counteracts this inhibition.  In addition to their own highly original personal work, the Cori’s have always been a source of inspiration to their colleagues at the active centres of biochemical research which they have directed. They have contributed many articles to *The Journal of Biological Chemistry* and other scientific periodicals.  Carl Cori is a member, and Gerty Cori a late member, of the American Society of Biological Chemists, the National Academy of Sciences, the American Chemical Society and the American Philosophical Society. They were presented jointly with the Midwest Award (American Chemical Society) in 1946 and the Squibb Award in Endocrinology in 1947. In addition, Gerty Cori received the Garvan Medal (1948), the St. Louis Award (1948), the Sugar Research Prize (1950), the Borden Award (1951) and honorary Doctor of Science degrees from Boston University (1948), Smith College (1949), Yale (1951), Columbia (1954), and Rochester (1955). Carl Cori, a Member of the Royal Society ( London) and the American Association for the Advancement of Science, also received the Willard Gibbs Medal (1948), the Sugar Research Foundation Award (1947, 1950) and honorary Doctor of Science degrees from Western Reserve University (1946), Yale (1946), Boston (1948), and Cambridge (1949). He was President of Fourth International Congress of Biochemistry (Vienna, 1958).  Carl and Gerty Cori married in 1920 and had one son. They became naturalized Americans in 1928. They have always been fond of outdoor hobbies.  Dr Gerty Cori died on October 26th, 1957, and in 1960 Carl Cori married Anne Fitz-Gerald Jones.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Carl Cori died on October 20, 1984.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0677** |
| Interview |  |
|  |  |
| ID | **0678** |
| Biographical | Gerty Theresa Cori, née Radnitz, was born in Prague on August 15th, 1896. She received her primary education at home before entering a *Lyceum* for girls in 1906; she graduated in 1912 and studied for the University entrance examination, which she took and passed at the Tetschen Realgymnasium in 1914. She entered the Medical School of the German University of Prague and received the Doctorate in Medicine in 1920. She then spent two years at the Carolinen Children’s Hospital before emigrating to America with her husband, Carl, whom she married in 1920. They worked together in Buffalo and when he moved to St. Louis, she joined him as Research Associate. Gerty Cori was made Professor of Biochemistry in 1947.  Carl Ferdinand Cori was born in Prague on December 5th, 1896. His father, Dr. Carl I. Cori, was Director of the Marine Biological Station in Trieste, and it was here that young Carl spent his childhood. He received an early introduction to science from his father and this was stimulated on summer visits to the Tyrol, to the home of his grandfather, Ferdinand Lippich, Professor of Theoretical Physics at Prague. He studied at the gymnasium in Trieste and graduated in 1914 when he entered the German University of Prague to study medicine. During World War I, he served as a lieutenant in the Sanitary Corps of the Austrian Army on the Italian front; he returned to University, where he studied with his future wife, Gerty, to graduate Doctor of Medicine in 1920. He spent a year at the University of Vienna and a year as assistant in pharmacology at the University of Graz until, in 1922, he accepted a position as biochemist at the State Institute for the Study of Malignant Diseases in Buffalo, New York. In 1931, he was appointed Professor of Pharmacology at the Washington University Medical School in St. Louis, where he later became Professor of Biochemistry.  The Cori’s have collaborated in most of their research work, commencing in their student days and stemming from their mutual interest in the preclinical sciences. Their first joint paper resulted from an immunological study of the complement of human serum.  In America, they first studied the fate of sugar in the animal body and the effects of insulin and epinephrine. The presence of glycolysis of tumours *in vivo* was demonstrated. Their work on carbohydrate metabolism passed from studies of whole animal to isolated tissues and, later, tissue extracts and isolated enzymes, some in crystalline form, were studied. In 1936, they isolated glucose-1-phosphate, «Cori ester», and traced its presence to the activity of the phosphorylase, which catalyzes the breakdown and synthesis of polysaccharides: this discovery made possible the enzymatic synthesis of glycogen and starch *in vitro.* Subsequently, phosphorylase and other enzymes were crystallized.  The Cori’s have been consistently interested in the mechanism of action of hormones and they have carried out several studies on the pituitary. They observed that the marked decrease in glycogen and lowering of blood sugar in hypophysectomized rats occurred with a concomitant increase in the rate of glucose oxidation. Subsequently, by a study of the action of hormones on hexokinase, they observed that some pituitary extracts inhibit this enzyme *in vivo* and *in vitro* and that insulin counteracts this inhibition.  In addition to their own highly original personal work, the Cori’s have always been a source of inspiration to their colleagues at the active centres of biochemical research which they have directed. They have contributed many articles to *The Journal of Biological Chemistry* and other scientific periodicals.  Carl Cori is a member, and Gerty Cori a late member, of the American Society of Biological Chemists, the National Academy of Sciences, the American Chemical Society and the American Philosophical Society. They were presented jointly with the Midwest Award (American Chemical Society) in 1946 and the Squibb Award in Endocrinology in 1947. In addition, Gerty Cori received the Garvan Medal (1948), the St. Louis Award (1948), the Sugar Research Prize (1950), the Borden Award (1951) and honorary Doctor of Science degrees from Boston University (1948), Smith College (1949), Yale (1951), Columbia (1954), and Rochester (1955). Carl Cori, a Member of the Royal Society ( London) and the American Association for the Advancement of Science, also received the Willard Gibbs Medal (1948), the Sugar Research Foundation Award (1947, 1950) and honorary Doctor of Science degrees from Western Reserve University (1946), Yale (1946), Boston (1948), and Cambridge (1949). He was President of Fourth International Congress of Biochemistry (Vienna, 1958).  Carl and Gerty Cori married in 1920 and had one son. They became naturalized Americans in 1928. They have always been fond of outdoor hobbies.  Dr Gerty Cori died on October 26th, 1957. |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0678** |
| Interview |  |
|  |  |
| ID | **0679** |
| Biographical | Bernardo Alberto Houssay was born in Buenos Aires, Argentina, on April 10, 1887, one of the eight children of Dr. Albert and Clara (*née* Laffont) Houssay, who had come to Argentina from France. His father was a barrister. His early education was at a private school, the Colegio Británico. He then entered the School of Pharmacy of the University of Buenos Aires at the exceptionally early age of 14, graduating in 1904. He had already begun studying medicine and, in 1907, before completing his studies, he took up a post in the Department of Physiology. He began here his research on the hypophysis which resulted in his M.D.-thesis (1911), a thesis which earned him a University prize.  In 1910 he was appointed Professor of Physiology in the University’s School of Veterinary Medicine. During this time he had been doing hospital practice and, in 1913, became Chief Physician at the Alvear Hospital. In addition to this he was also in charge of the Laboratory of Experimental Physiology and Pathology in the National Department of Hygiene from 1915 to 1919. In 1919 he became Professor of Physiology in the Medical School at Buenos Aires University. He also organized the Institute of Physiology at the Medical School, making it a centre with an international reputation. He remained Professor and Director of the Institute until 1943. In this year the Government then in power deprived him of his post, as a result of his voicing his opinion that there should be effective democracy in the country. Although receiving many invitations from abroad, he continued his work in an institute which he organized with the support of funds contributed by the Sauberan Foundation and other bodies. This was the *Instituto de Biología y Medicina Experimental,* where he still remains as Director. In 1955 a new Government reinstated him in the University.  He has worked in almost every field of physiology, having a special interest in the endocrine glands. He has made a lifelong study of the hypophysis and his most important discovery concerns the role of the anterior lobe of the hypophysis in carbohydrate metabolism and the onset of diabetes. He has worked on many other topics in physiology and pharmacology, including the physiology of circulation and respiration, the processes of immunity, the nervous system, digestion, and snake and spider venoms.  Apart from his research, he has been active in promoting the advancement of university and medical education, and of scientific research, in Argentina.  Dr. Houssay is the author of over 500 papers and of several books. He has won many prizes ranging in time from that of the National Academy of Sciences, Buenos Aires, in 1923, to the Dale Medal of the Society of Endocrinology (London) in 1960.  He holds honorary degrees of twenty-five universities and is a member of the Argentine National Academy of Medicine, the Academy of Letters, the National Academy of Sciences of Buenos Aires, the Academy of Moral and Political Sciences of Buenos Aires, and of the Pontifical Academy of Sciences. He is honorary professor of 15 universities, foreign associate of 11 academies or learned societies, member (honorary or correspondent) of 38 Academies, 16 Societies of Biology, 11 of Endocrinology, 7 of Physiology and 5 of Cardiology. He has been decorated by the governments of several countries.  He married Dr. Maria Angelica Catan, a chemist, who died in 1962. They have three sons, Alberto, Hector, and Raul.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). To cite this document, always state the source as shown above.  *Bernardo Houssay died on September 21, 1971.* |
| Autobiographical |  |
| Podcast |  |
| Telephone  interview | **0679** |
| Interview |  |
|  |  |
| ID | **0680** |
| Biographical | Hermann Joseph Muller was born in New York City on December 21, 1890. His grandparents on his father’s side were of artisan and professional background and, though at first Catholics, had emigrated from the Rhineland during the wave of reaction of 1848 to seek the greater freedom of America. His father, born in New York, had continued the grandfather’s art metal works (the first in the U.S.A.), but was not by inclination a business man, and, although he died in 1900, he early awoke in the boy a lively interest in the nature of the universe and in the process of evolution, as well as in the welfare of men in general. The boy’s mother, Frances Lyons Muller, had also been born in New York City. Her parents had come from Britain, but were in the main descended from Spanish and Portuguese Jews who, as an after-effect of the Inquisition, had settled generations earlier in England and Ireland. She, as well as the father, encouraged in the boy a broad sympathy, an interest in living things, and a love of nature.  He was brought up in Harlem, first attending public school there and later Morris High School (also public) in the Bronx. There he and his classmates Lester Thompson and Edgar Altenburg founded what was perhaps the first high-school science club. Though his family (mother, sister Ada, and himself) had very limited means, they were fortunate in usually being able to spend their summers in the country while he was of school age. But he was enabled to attend a first class college – Columbia – only through the unexpected award of a scholarship (the Cooper-Hewitt), automatically granted to him in 1907 on the basis of entrance examination grades. He spent his summers, during his college years, at such jobs as bank runners and hotel clerk (the latter at $25 a month, plus board, for a 14-hour work-day).  At Columbia College he was before the end of his first year fascinated by the subject of biology. Reading by himself in the summer of 1908 R.H. Lock’s (1906) book on genetics, his interests became centered in that field. Courses soon afterwards taken under E. B. Wilson influenced him profoundly, as did also his reading, independently of courses, of works by Jacques Loeb and by other writers on experimental biology and physiology. In I909 he founded a students’ biology club, which was participated in, among others, by Altenburg, and by two students, Bridges and Sturtevant, who had entered Columbia a year later.  For his first two years of graduate work, since there was no opening offered to him in zoology, he managed to obtain a scholarship (1910-1911) and then a teaching fellowship (1911-1912) in physiology, the latter at Cornell Medical College, while keeping up with genetics on the side and doing various extra jobs, such as teaching English to foreigners in night school. Finally, however, he obtained a teaching assistantship in zoology at Columbia (1912-1915). The first summer (1911) of graduate work was spent in studies at Woods Hole, the rest in laboratory teaching at Columbia. During these five years he was seriously overworked. In all this period he was chiefly interested in the *Drosophila* work which [Morgan](https://www.nobelprize.org/nobel_prizes/medicine/laureates/1933/index.html) had opened up, and from 1910 on he closely followed this research and was an intimate member of the group, although he did not have opportunity for much experimental work of his own on this material until 1912. Then he was able to begin his investigation of the simultaneous inter-relationships of many linked genes, which supported the theory of crossing-over and constituted his thesis. At the same time he undertook his analysis of variable, multiple-factor, characters by means of the device of «marker genes». This extended the validity both of chromosomal inheritance and of gene stability, and led later (1916) to his theory of balanced lethals.  Called to the Rice Institute, Houston, as Instructor, by Julian Huxley, he taught varied biological courses (1915-1918), and began studies on mutation. During this time and the two years following, when he was again at Columbia (1918-1920), now as instructor, he elaborated methods for quantitative mutation study. Altenburg, who had meanwhile moved to the Rice Institute, and he, partly in collaboration, obtained the first results in this field (1918-1919), including evidence that made probable an effect of temperature. He then (1920) returned to Texas, this time to the University, at Austin, as Associate Professor, and from 1925 on as Professor, teaching mainly genetics and evolution, and doing research mainly on mutation. He formulated in 1918, 1920, 1921, and 1926 the chief principles of spontaneous gene mutation as now recognized, including those of most mutations being detrimental and recessive, and being point effects of ultramicroscopic physico-chemical accidents arising in the course of random molecular motions (thermal agitation). At the same time he put forward the conception of the gene as constituting the basis of life, as well as of evolution, by virtue of its possessing the property of reproducing its own changes, and he represented this phenomenon as the cardinal problem of living matter.  In late 1926 he obtained critical evidence of the abundant production of gene mutations and chromosome changes by X-rays (published 1927). This opened the door to numerous researches, many of them carried on with the aid of students and co-workers, both at his own and other institutions, in the twenty years that followed. These have been briefly outlined in his Nobel Lecture, since they, together with the first discovery of the effect, constitute the work for which the Nobel Award was granted. They include studies on the mechanisms of the gene mutation effects and of the structural changes, on the roles which each kind of changes, when spontaneously occurring, play in evolution, and on the properties of genes and of chromosome parts (e.g. eu- versus hetero-chromatin), as disclosed by studies in which the chromosomes were broken and rearranged.  This later work was carried on at a succession of places. In 1932 he was awarded a Guggenheim Fellowship and for a year worked at Oscar Vogt’s institute in Berlin, in Timoféeff’s department of genetics. At the request of N. I. Vavilov, he then spent 3 1/2 years as Senior Geneticist at the Institute of Genetics of the Academy of Sciences of the U.S.S.R., first in Leningrad later (1934-1937) in Moscow, with a considerable staff of co-workers. With the rise of the Lysenko anti-genetics movement, he moved to the Institute of Animal Genetics, University of Edinburgh (1937-1940); here numerous graduate students, largely from India, took part. Then, from 1940 to 1945, I he did both teaching and research at Amherst College, being professor ad I interim there from 1942 to 1945. At Amherst he completed a large-scale experiment showing the relationship of ageing to spontaneous mutations. Finally, in 1945, he accepted a professorship in the Zoology Department at Indiana University, Bloomington, Indiana. Here he is again devoting his time chiefly to work on radiation-induced mutations, using them on the one hand for purposes of genetic analysis and on the other hand in the study of how radiation produces its biological effects.  One group of studies, participated in by J. I. and Ruby M. Valencia, I. H. Herskowitz, I. I. Oster, S. Zimmering, S. Abrahamson, A. Schalet, J. D. Telfer, Helen U. Meyer, Sara Frye, Helen Byers, and others, has been concerned with the influence on mutation frequency in the fruit fly *Drosophila* of diverse conditions and agents, when these were used before, after, or with radiation, or without radiation, on the influence of dose-rate and total dose of the radiation, and on the relative sensitivities of different cell stages to induced or natural mutagenesis. The types of mutations studied included «point» changes and both minute and gross structural changes of chromosomes. In another group of studies, since carried much further by E. A. Carlson, the interrelations among independently arisen mutations of the same gene were studied intensively, their intra-genic arrangement determined, and principles governing their functional interactions worked out.  The incidence of radiation damage to the bodies of the individuals that have themselves been exposed, as manifested in a long-term mortality or, in other words, life-span shortening or accelerated «ageing», was also investigated, first by I. I. Oster and then by W. Ostertag and Helen U. Meyer in collaboration with Muller. Evidence was obtained that these effects are for the most part consequences of losses of chromosomes from dividing somatic cells, after these chromosomes have been broken by the radiation. Natural ageing, however, gave evidence of not being caused in this way.  Another group of researches, also carried out with cooperation from students, more especially Margaret Lieb and S. L. Campbell, had concerned itself with problems of dominance and related subjects. It was shown that most mutant genes are incompletely recessive (not «overdominant») and are acted upon by selection while heterozygous. Studies of dominance in relation to «dosage compensation» disclosed that selection usually acts with high precision, tending to establish homozygous «normal» types. Most genetic variation within populations was deduced to depend on the recurrence of detrimental mutations which, balanced by selective elimination, constitute a «load». Estimates of this load were formed for both *Drosophila* and man (in the latter case in cooperation with Drs. Newton E. Morton and James F. Crow of the University of Wisconsin).  Included in the studies were calculations concerned with both the «spontaneous» and the radiation-induced mutation frequencies, and of the consequences of selection. Estimates were made of the effects of changes in mutation frequency, on the one hand, and of selection pressure, on the other hand, on the load. It was shown that eugenic policies are needed to avoid genetic degeneration in man as well as to bring about the genetic enhancement called for by his advances in technology and in other aspects of his culture. It was pointed out that modern reproductive technologies, such as germ-cell banks, and liberalized mores now make possible the exercise of voluntary germinal choice in human reproduction, and that this procedure affords the practical solution necessary to enable cultural evolution to promote the biological evolution of man instead of perverting it.  Prof. Muller will retire from Indiana University, in June, 1964, to take an appointment at the Institute for Advanced Learning in the Medical Sciences, The City of Hope, Duarte, California – for one year.  Muller has contributed over 300 articles on biological subjects to the scientific publications of learned societies. His principal books are *The Mechanism of Mendelian Heredity* with T. H. Morgan and others, 1915 and 1922, *Out of the Night – a Biologist’s View of the Future,* 1935, 1936, and 1938, and *Genetics, Medicine and Man* with C. C. Little and L. H. Snyder, 1947.  He was President of the 8th International Congress of Genetics in 1948 and of the American Humanist Association during 1956-1958. He has received Doctor of Science degrees from the Universities of Edinburgh (1940), Columbia (1949) and Chicago (1959), the honorary Doctor of Medicine from Jefferson Medical College (1963), the Annual Award of the American Association for Advancement of Science (1927), the Kimber Genetics Award (1955) and the Darwin-Wallace Commemoration Medal (1958). He was Pilgrim Trust Lecturer (Royal Society) and Messenger Lecturer (Cornell University) in 1945, and was designated Humanist of the Year by the American Humanist Association in 1963. He has also received honorary memberships and fellowships of many learned societies in the United States, England, Scotland, Sweden, Denmark, India, Japan, Italy, etc.  Muller married his first wife, formerly Jessie M. Jacobs, in 1923 – they had one son, David Eugene. In 1939 he married Dorothea Kantorowicz – they have one daughter, Helen Juliette.  From [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html)*, Physiology or Medicine 1942-1962*, Elsevier Publishing Company, Amsterdam, 1964  This autobiography/biography was written at the time of the award and first published in the book series [*Les Prix Nobel*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lesprix.html). It was later edited and republished in [*Nobel Lectures*](https://www.nobelprize.org/nobel_organizations/nobelfoundation/publications/lectures/index.html). 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