# Syllabus for BIOL 47115. An Investigation into Nobel Prize-Winning Research

Fall 2021

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Office Hours: by appointment on Zoom

## Weekly expectations:

**Read** all of assigned papers and importantly, **look up** terms and experiments you are unfamiliar with. There will be much to look up in each paper, so start early, take your time, and take notes on what you research. You will be handing in a concise write-up about each paper.

**Participation** is the key to active learning. I expect participation from \*each\* of you during \*every\* session; not just to ask questions, but to answer questions, provide context, analyze data, etc. Participation is how you will become more comfortable speaking about research!

**Presentation** of papers: I will ask two of you to take the lead each week and present an introduction to the topic and the selected paper(s) and take us through each of the figures. Explaining why particular research was Nobel prize-worthy often requires a historical context for the work, and a thorough introduction will include this context. Each pair of presenters must be able to explain the research techniques found within their papers. A quick powerpoint presentation, short (!) instructional videos from youtube, etc. are welcome but not necessary. Be prepared to answer questions.

**Watch** the Nobel lectures of the laureates (if available) or **read** the transcript of their speeches. While the lectures may include data not found in the papers we are analyzing, these presentations give you context, history and greater understanding. I also believe that hearing laureates (investigators) talk about their research is important for your training as scientists. Nobel Transcripts and Nobel lectures are available on the official Nobel website: www.nobelprize.org

### Grading:

Your assigned papers and weekly participation will count for 60% of your grade. Quizzes/exams will count for 40%. We will likely have 2 - 3 exams over the course of the semester. Attendance in this class is mandatory.

# Learning Goals\*

- Students will be able to apply critical thinking and analytical skills to interpreting scientific data sets.
- Students will be able to demonstrate written and oral presentation skills to communicate scientific knowledge.
- Students will be able to acquire and synthesize scientific information from a variety of sources.

<sup>\*(</sup>Taken from Stamford.edu)

#### Please note:

There is NO class on Sept. 8<sup>th</sup>.

There is NO class on Sept 15<sup>th</sup>.

We will hold class remotely on October 27<sup>th</sup>.

December 8<sup>th</sup> is our last class.

December 15<sup>th</sup> we will do 10' presentations!

- 1. The Nobel Prize in Physiology or Medicine 2005 was awarded jointly to Barry J. Marshall and J. Robin Warren "for their discovery of the bacterium Helicobacter pylori and its role in gastritis and peptic ulcer disease"
- R. Warren. B. Marshall. Unidentified Curved Bacilli on Gastric Epithelium in Active Chronic Gastritis. The Lancet. June, 1983. 1273-1275.
- B. Marshall and R. Warren. Unidentified Curved Bacilli in the Stomach of Patients With Gastritis and Peptic Ulceration. The Lancet., Sept. 1984. Pp 1311-1315
- B. J. Marshall, J.A. Armstrong, D.B. McGechie, R. J. Glancy. Attempt to Fulfill Koch's Postulates for Pyloric Campylobacter. The Medical Journal of Australia. 142: Pp 436- 439. 1985.

### Discover article:

http://discovermagazine.com/2010/mar/07-dr-drank-broth-gave-ulcer-solved-medical-mystery#.Uxgeyn-9KSM

2. The Nobel Prize in Physiology or Medicine 1945 was awarded jointly to Sir Alexander Fleming, Ernst Boris Chain and Sir Howard Walter Florey "for the discovery of penicillin and its curative effect in various infectious diseases".

A. Fleming. On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to Their Use in the Isolation of B. Influenzae. British Journal of Experimental Pathology 10:226–236. (Now International Journal of Experimental Pathology.) 1929.

- E. Chain, H. W. Florey, A. D. Gardner, N. G. Heatley, M. A. Jennings, J. Orr-Ewing, And A. G. Sanders. Penicillin as a Chemotherapeutic Agent. Lancet ii:226–228. 1940.
- E. P. Abraham and E. Chain. An Enzyme from Bacteria Able To Destroy Penicillin. Nature 146:837. 1940.

(Nobel lecture of Fleming is helpful - better pictures.) Penicillin. Nobel Lecture, December 11, 1945

3. The Nobel Prize in Physiology or Medicine 1923 was awarded jointly to Frederick Grant Banting and John James Rickard Macleod "for the discovery of insulin"

Banting, Best, Collip, Campbell, and Fletcher. Pancreatic Extracts in the Treatment of Diabetes Mellitus. Canadian Med. Assoc. Journ., March, 1922.

F. G. Banting, W. R. Campbell and A. A. Fletcher. Further Clinical Experience With Insulin (Pancreatic Extracts) In The Treatment Of Diabetes Mellitus. The British Medical Journal, Vol. 1, No. 3236 (Jan. 6, 1923), pp. 8-12.

Ralph H. Major, M.D.The Treatment Of Diabetes Mellitus With Insulin. JAMA. 1923; 80(22).1597-1600.

4. The Nobel Prize in Physiology or Medicine 2012 was awarded jointly to Sir John B. Gurdon and Shinya Yamanaka "for the discovery that mature cells can be reprogrammed to become pluripotent"

Takahashi, K., and Yamanaka, S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 126, 663–676. 2006.

Takahashi, K. et al. Induction of pluripotent stem cells from adult human fibroblasts by defined factors. Cell 131, 861–872. 2007.

Shinya Yamanaka & Helen M. Blau. Nuclear reprogramming to a pluripotent state by three approaches. Nature. Vol 465. 704 -712. 2010. (Good review)

5. Nobel Prize in Physiology or Medicine 2008 was divided, one half awarded to Harald zur Hausen "for his discovery of human papilloma viruses causing cervical cancer", the other half jointly to Françoise Barré-Sinoussi and Luc Montagnier "for their discovery of human immunodeficiency virus". (Focus on HIV)

F. Barré-Sinoussi, J. C. Chermann, F. Rey, M. T. Nugeyre, S. Chamaret, J. Gruest, C. Dauguet, C. Axler-Blin, F. Vézinet-Brun, C. Rouzioux, W. Rozenbaum and L. Montagnier. Isolation of a T-Lymphotropic Retrovirus from a Patient at Risk for Acquired Immune Deficiency Syndrome (AIDS). Science, Vol. 220, No. 4599, pp. 868-871. 1983.

Good perspective (for both HPV and HIV) in the Nobel Assembly information: Advanced- medicine prize 2008. The discoveries of human papilloma viruses that cause cervical cancer and of human immunodeficiency virus

(From Gallo)

M. G. Sarngadharan, Mikulas Popovic, Lilian Bruch, Jörg Schüpbach and Robert C. Gallo. Antibodies Reactive with Human T-Lymphotropic Retroviruses (HTLV-III) in the Serum of Patients with AIDS. Science, Vol. 224, No. 4648, pp. 506-508. 1984.

Mikulas Popovic, M. G. Sarngadharan, Elizabeth Read and Robert C. Gallo. Detection, Isolation, and Continuous Production of Cytopathic Retroviruses (HTLV-III) from Patients with AIDS and Pre-AIDS. Science, Vol. 224, No. 4648, pp. 497-500. 1984.

Jon Cohen and Martin Enserink. HIV, HPV Researchers Honored, but One Scientist Is Left Out. Science, Vol. 322, No. 5899. pp. 174-175. 2008.

6. Michael S. Brown and Joseph L. Goldstein for their discoveries concerning "the regulation of cholesterol metabolism".

Joseph L. Goldstein and Michael S. Brown

Familial Hypercholesterolemia: Defective Cultured Fibroblasts Associated with Imp 3-Hydroxy-3-Methylglutaryl Coenzyme A.Proc. Nat. Acad. Sci. USA Vol. 70, No. 10, pp. 2804-2808, October 1973

Michael S. Brown and Joseph L. Goldstein. Familial Hypercholesterolemia: Defective Cultured Fibroblasts Associated with Imp 3-Hydroxy-3-Methylglutaryl Coenzyme A Reductase Activity. Proc. Nat. Acad. Sci. USA Vol. 71, No. 3, pp. 788-792, March 1974.

Joseph L. Goldstein, Michael S. Brown. History of Discovery. The LDL Receptor. Arterioscler. Thromb. Vasc. Biol. 2009;29:431-438. (Good history of LDL receptor. paper written by prize winners)

7. The Nobel Prize in Physiology or Medicine 1990 was awarded jointly to Joseph E. Murray and E. Donnall Thomas "for their discoveries concerning organ and cell transplantation in the treatment of human disease".

E. Donnall Thomas, C. Dean Buckner, Meera Banali, Reginald A. Cliff, Alexander Fefer, Nancy Flournoy, Brian W. Goodell, Robert O. Hickman, Kenneth G. Lerner, Paul E. Neiman, George E. Sale, Jean E. Sanders, Jack Singer, Mary Stevens, Rainer Storb, and Paul L. Weiden. One Hundred Patients With Acute Leukemia Treated by Chemotherapy, Total Body Irradiation, and Allogeneic Marrow Transplantation. Blood, Vol. 49, No. 4 (April), 1977 511

Recent Bone Marrow Transplant review: http://www.stembook.org/node/746

8. The Nobel Prize in Physiology or Medicine 1999 was awarded to Günter Blobel "for the discovery that proteins have intrinsic signals that govern their transport and localization in the cell".

Günter Blobel and Bernhard Dobberstein. Transfer of Proteins across Membranes I. Presence of Proteolytically Processed and Unprocessed Nascent Immunoglobulin Light Chains on Membrane-Bound Ribosomes of Murine Myeloma. The Journal of Cell Biology. Vol. 67, 1975. pages 835-851.

Günter Blobel and Bernhard Dobberstein. Transfer of Proteins across Membranes II .Reconstitution of Functional Rough Microsomes from Heterologous Components. The Journal of Cell Biology. Vol. pages 852-862.

Günter Blobel. Intracellular Protein Topogenesis. Proc. Natl. Acad. Sci. USA Vol. 77, No. 3, pp. 1496-1500, March 1980.

# 9. The Nobel Prize in Physiology or Medicine 1997 was awarded to Stanley B. Prusiner "for his discovery of Prions - a new biological principle of infection".

S. Prusiner. Novel Proteinaceous Infectious Particles Cause Scrapie. Science, New Series, Vol. 216, No. 4542, pp. 136-144. 1982

*Review from 2013*: S. Prusiner. Biology and Genetics of Prions Causing Neurodegeneration. Annu. Rev. Genet. 2013. 47:601–23

# 10. The Nobel Prize in Physiology or Medicine 2010 was awarded to Robert G. Edwards "for the development of in vitro fertilization".

Steptoe, PC and Edwards, RG. Birth After The Reimplantation Of A Human Embryo. The Lancet, August 12, 1978. P. 366

Edwards, RG, Bavister, BD. and Steptoe, PC. Early Stages of Human Fertilization In Vitro of Human Oocyte Matured in Vitro. Nature, Vol. 221, February 15, 1969. pp.632-635.

Edwards, RG, Steptoe, PC, and Purdy, JM. Fertilization and Cleavage In Vitro of Preovulator Human Oocytes. Nature Vol. 227, September 26, 1070.

Background paper: Edwards, RG. "The Bumpy Road to In Vitro Fertilization. NATURE MEDICINE Vol. 7, No. 10, October 2001. Pp. 1091-1094

# 11. The Nobel Prize in Physiology or Medicine 2016 was awarded to Yoshinori Ohsumi "for his discoveries of mechanisms for autophagy".

Kazuhiko Takeshige, Misuzu Baba, Shigeru Tsuboi, Takeshi Noda, and Yoshinori Ohsumi Autophagy in Yeast Demonstrated with Proteinase-deficient Mutants and Conditions for its Induction. The Journal of Cell Biology. Vol. 119, Number 2, October 1992 . pages 301-311.

Review from 2007:

Noboru Mizushima. Autophagy: Process and Function. GENES & DEVELOPMENT 21:2861–2873. 2007

12. The Nobel Prize in Physiology or Medicine 2013 was awarded jointly to James E. Rothman, Randy W. Schekman and Thomas C. Südhof "for their discoveries of machinery regulating vesicle traffic, a major transport system in our cells".

Peter Novick and Randy Schekman

Secretion and cell-surface growth are blocked in a temperature-sensitive mutant of Saccharomyces cerevisiae. Proc. Nati. Acad. Sci. USA Vol. 76, No. 4, pp. 1858-1862, April 1979 Cell Biology

Background recent review:

http://www.nature.com/nm/journal/v8/n10/full/nm769.html

13. The Nobel Prize in Physiology or Medicine 1968 was awarded jointly to Robert W. Holley, Har Gobind Khorana and Marshall W. Nirenberg "for their interpretation of the genetic code and its function in protein synthesis".

Marshall Nirenberg and Philip Leder

RNA Codewords and Protein Synthesis Science, New Series, Vol. 145, No. 3639 (Sep. 25, 1964), pp. 1399-1407

(Background 1962 paper)

Marshall W. Nirenberg J. Heinrich Matthae, and Oliver W. Jones

An Intermediate In The Biosynthesis Of Polyphenylalanine Directed By Synthetic Template RNA, Proc. Natl. Acad. Sci. U.S. 48, 104 (1962).

Quick sum on Nobelprize.org: http://www.nobelprize.org/educational/medicine/gene-code/history.html

(In same session)

14. The Nobel Prize in Physiology or Medicine 1962 was jointly awarded to Francis Harry Compton Crick, James Dewey Watson and Maurice Hugh Frederick Wilkins "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".

J.D Watson and F.H.C Crick. Molecular Structure of Nucleic Acids. Nature. Vol 171, April 25, 1953. Pp 737-738.

(Some perspectives on the discovery of DNA structure:)

Robert Olby. Quiet Debut for the Double Helix. Nature. Vol. 421. 23 January 2003. Pp. 402-405.

Brenda Maddox. The Double Helix and the 'Wronged Heroine'. Nature. Vol. 421. 23 January 2003. Pp. 407-408.

15. The Nobel Prize in Physiology or Medicine 1930 was awarded to Karl Landsteiner "for his discovery of human blood groups".

Landsteiner, K. On Agglutination of Normal Human Blood. Wiener Klinische Wochenschrift. (translation) 1132-1134. 1901

Owen, R. Anecdotal, Historical and Critical Commentaries on Genetics. Karl Landsteiner and the First Human Marker Locus. Genetics 155: 995- 998 (July 2000).

As ABO paper was very short, decided to cover Landsteiner's discovery of M and N glycoproteins on blood cells.

Landsteiner, K. And Levine, P. On Individual Differences in Human Blood.

On Rh from NYT: http://www.nytimes.com/2011/01/04/health/04first.html

Background information on Rh: <a href="https://www.ncbi.nlm.nih.gov/books/NBK2269/?report=reader">https://www.ncbi.nlm.nih.gov/books/NBK2269/?report=reader</a>

16. The Nobel Prize in Physiology or Medicine 2011 was divided, one half jointly to Bruce A. Beutler and Jules A. Hoffmann "for their discoveries concerning the activation of innate immunity" and the other half to Ralph M. Steinman "for his discovery of the dendritic cell and its role in adaptive immunity".

Nussenzweig MC, Stein-man RM, Gutchinov B, Cohn ZA. 1980. Dendritic cells are accessory cells for the development of anti-trinitrophenyl cytotoxic T lymphocytes. J. Exp. Med. 152:1070–84 (Very difficult paper).

Steinman RM Decisions About Dendritic Cells: Past, Present, and Future Annual Review of Immunology, VOL 30 2012; 30:1-22

17. The Nobel Prize in Physiology or Medicine 2001 was awarded jointly to Leland H. Hartwell, Tim Hunt and Sir Paul M. Nurse "for their discoveries of key regulators of the cell cycle."

Melanie G. Lee & Paul Nurse. 1987. Complementation used to clone a human homologue of the fission yeast cell cycle control gene cdc2. Nature 327. 31-35.

Nurse, P. 1975. Genetic control of cell size at cell division in yeast. Nature 256, 547–551 (1975).

18. The Nobel Prize in Physiology or Medicine 1984 was awarded jointly to Niels K. Jerne, Georges J.F. Köhler and César Milstein "for theories concerning the specificity in development and control of the immune system and the discovery of the principle for production of monoclonal antibodies."

Georges J.F. Köhler and César Milstein. Continuous cultures of fused cells secreting antibody of predefined specificity. Nature 256. 495-497 (1975).

## Review paper:

Justin K.H. Liu. The history of monoclonal antibody development - Progress, remaining challenges and future innovations. `annals of Medicine and Surgery 3. (2014) 113-116.

19. The Nobel Prize in Physiology or Medicine 2018 was awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation".

Yoshiko Iwai, Masayoshi Ishida, Yoshimasa Tanaka, Taku Okazaki, Tasuku Honjo, and Nagahiro Minato. Involvement of PD-L1 on tumor cells in the escape from host immune system and tumor immunotherapy by PD-L1 blockade. PNAS.vol. 99.no. 19, 12293–12297. (2002)

Dana R. Leach, Matthew F. Krummel, James P. Allison. Enhancement of Antitumor Immunity by CTLA-4 Blockade. Science. Vol. 271 . 1734-1736. (1996)

- J.D. Wolchok, V. Chiarion-Sileni, R. Gonzalez, P. Rutkowski, J.-J. Grob, C.L. Cowey, C.D. Lao, J. Wagstaff, D. Schadendorf, P.F. Ferrucci, M. Smylie, R. Dummer, A. Hill, D. Hogg, J. Haanen, M.S. Carlino, O. Bechter, M. Maio, I. Marquez-Rodas, M. Guidoboni, G. McArthur, C. Lebbé, P.A. Ascierto, G.V. Long, J. Cebon, J. Sosman, M.A. Postow, M.K. Callahan, D. Walker, L. Rollin, R. Bhore, F.S. Hodi, and J. Larkin. Overall Survival with Combined Nivolumab and Ipilimumab in Advanced Melanoma. N. engl j med 377;14. nejm.org. 1345-1356. 2017
- 20. The Nobel Prize in Physiology or Medicine 1959 was awarded jointly to Severo Ochoa and Arthur Kornberg "for their discovery of the mechanisms in the biological synthesis of ribonucleic acid and deoxyribonucleic acid."
- I. R. Lehman, Steven B. Zimmerman, Julius Adler, Maurice J. Bessman, E. S. Simms, and Arthur Kornberg. Enzymatic Synthesis of Deoxyribonucleic Acid. v. Chemical Composition of Enzymatically Synthesized Deoxyribonucleic Acid. PNAS. Vol. 44. Pp 1191-1196. 1958.

M Goulian, A Kornberg, R L Sinsheimer. Enzymatic synthesis of DNA, XXIV. Synthesis of infectious phage phi-X174 DNA.. Proceedings of the National Academy of Sciences of the United States of America, Volume 58, Number 6 (December 1967), pp. 2321-2328,

#### Good Reviews:

I. R. Lehman. Discovery of DNA Polymerase. JBC Papers in Press, June 5, 2003, DOI 10.1074/jbc.X300002200

A.Kornberg. The early history of DNA polymerase: a commentary by Arthur Kornberg. Biochimica et Biophysica Acta, 1000 (1989)pp. 53-56.

### (Possible alternatives:

Lehman, I.R., Bessman, M.J., Simms, E.S. and Kornberg, A. (1958) J. Biol. Chem. 233, 163-170. Or

Bessman, M,J., Lehman, I.R., Simms, E.S. and Kornberg, A. (1958) J. Biol. Chem. 233, 171-177.)

21. The 2019 Nobel Prize in Physiology or Medicine was awarded jointly to William G. Kaelin Jr., Sir Peter J. Ratcliffe and Gregg L. Semenza for their discoveries of how cells sense and adapt to oxygen availability.

Gregg I. Semenza, Mary K. Nejfelt, Suzie M. Chi, and Stylianos E. Antonarakis. Hypoxia-inducible nuclear factors bind to an enhancer element located 3' to the human erythropoietin gene. Pro. Natl. Acad. Sci. USA Vol. 88, pp. 5680-5684, 1991.

Mircea Ivan, Keiichi Kondo, Haifeng Yang, William Kim, Jennifer Valiando, Michael Ohh, Adrian Salic, John M. Asara, William S. Lane, William G. Kaelin. . HIF aTargeted for VHL-Mediated Destruction by Proline Hydroxylation: Implications for 0₂ Sensing. Science. Vol. 292. 2001.

Review (from 2012)

Gregg L. Semenza. Hypoxia-Inducible Factors in Physiology and Medicine. Cell. 2012 February 3; 148(3): 399–408. doi:10.1016/j.cell.2012.01.021

22. The Nobel Prize in Physiology or Medicine 2015 was divided, one half jointly to William C. Campbell and Satoshi Ōmura "for their discoveries concerning a novel therapy against infections caused by roundworm parasites" and the other half to Tu Youyou "for her discoveries concerning a novel therapy against Malaria."

W. C. Campbell, M. H. Fisher, E. O. Stapley, G. Albers-Schönberg and T. A. Jacob. Ivermectin: A Potent New Antiparasitic Agent. Science, New Series, Vol. 221, No. 4613 (Aug. 26, 1983), pp. 823-828

#### Review:

Roz Laing, Victoria Gillan, and Eileen Devaney. Ivermectin – Old Drug, New Tricks? Trends in Parasitology, June 2017, Vol. 33, No. 6 http://dx.doi.org/10.1016/j.pt.2017.02.004. Pages 463-472.

Andy Crump and Satoshi Ōmura. Ivermectin, 'Wonder drug' from Japan: the human use perspective. Proc. Japan. Acad., Ser. B 87 (2011). Pages 13-28.

23. The Nobel Prize in Physiology or Medicine 1952 was awarded to Selman Waksman "for his discovery of streptomycin, the first antibiotic effective against tuberculosis".

Schatz, A., Bugie, E. And Waksman ,S.A. Streptomycin, a substance exhibiting Antibiotic activity against gram-positive and gram-negative bacteria. Proc.Soc. Exptl.Biol.Med.,55. 1944. Pages 66-69.

## Concerning the controversy:

H. Boyd Woodruff. Selman A. Waksman, Winner of the 1952 Nobel Prize for Physiology or Medicine Applied and Environmental Microbiology. January 2014. Volume 80, Number 1. Pages 2-8.

Peter Pringle. Notebooks Shed Light on an Antibiotic's Contested Discovery. The New York Times. June 12, 2012, on Page D3 of the New York edition.

Nan Waksman Schanbacher. Defense of a Scientist. - The New York Times. June 19, 2012, on Page D4 of the New York edition.

24. The Nobel Prize in Physiology or Medicine 1987 was awarded to Susumu Tonegawa "for his discovery of the genetic principle for generation of antibody diversity."

Nobumichi Hozumi and Susumu Tonegawa. Evidence for somatic rearrangement of immunoglobulin genes coding for variable and constant regions. Proc. Natl. Acad. Sci. USA Vol. 73, No. 10, pp. 3628-3632, October 1976.

Christine Brack, Minoru Hirama, Rita Lenhard-Schuller and Susumu Tonegawa. A Complete Immunoglobulin Gene Is Created by Somatic Recombination. Cell, Vol. 15, 1-14, September 1978. (Difficult paper. Enough material in first paper.)

25. The Nobel Prize in Physiology or Medicine 1971 was awarded to Earl W. Sutherland, Jr. "for his discoveries concerning the mechanisms of the action of hormones".

T.W. Rall, Earl W. Sutherland, and Jacques Berthet. Relationship of epinephrine and glucagon to liver phosphorylase. IV Effect of epinephrine and glucagon on the reactivation of phosphorylase in liver homogenates. Biol. Chem. 1957 224: 463- 475.

26. Nobel Prize in Physiology or Medicine 2008 was divided, one half awarded to Harald zur Hausen "for his discovery of human papilloma viruses causing cervical cancer", the other half jointly to Françoise Barré-Sinoussi and Luc Montagnier "for their discovery of human immunodeficiency virus". (Focus on HPV -zur Hausen)

Matthias Durst, Lutz Gissmann, Hans Ikenberg, and Harald Zur Hausen. A papillomavirus DNA from a cervical carcinoma and its prevalence in cancer biopsy samples from different geographic regions. Proc. Natl Acad. Sci. USA Vol. 80, pp. 3812-3815, June 1983.

Michael Boshartb, Lutz Gissmann, Hans Ikenberg, Andreas Kleinheinz, Wolfram Scheurlen and Harald zur Hausen. A new type of papillomavirus DNA, its presence in genital cancer biopsies and in cell lines derived from cervical cancer. The EMBO Journal vol.3 no.5 pp.1151-1157, 1984.

Good perspective (for both HPV and HIV) in the Nobel Assembly information: Advanced- medicine prize 2008. The discoveries of human papilloma viruses that cause cervical cancer and of human immunodeficiency virus