Genes and Politics

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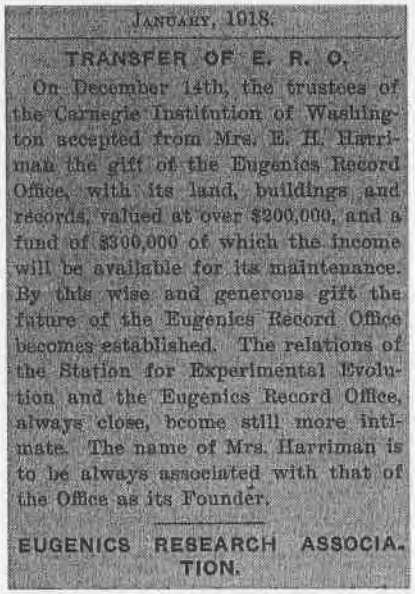
Editors' Note: The quotes below from Davenport show the duality of his desire to know the details of the mechanism of inheritance and his belief that this knowledge and its use was the domain of the State. In this essay, originally published in the 1996 Cold Spring Harbor Laboratory Annual Report, James Watson discusses why scientific justification of political policies just does not work. Dr. Watson puts forth several examples showing the dangers of the co-option of science to political aims—early U.S. immigration law, race hygiene in Germany during World War II, Larmarckism in Soviet Russia, and the more recent Science for the People movement in the United States—as well as how he headed off such a clash when he headed the government-funded Human Genome Project (HGP). From his unique perspective, he also considers issues such as genetic determinism, genetic injustice, and the ethical implications of knowing our genetic futures. He concludes that "In the last analysis, we should accept the fact that if scientific knowledge exists, individual persons or families should have the right to decide whether it will lead to their betterment."



JANUARY, 1918.

TRANSFER OF E. R. O.

On December 14th, the trustees of the Carnegie Institution of Washington accepted from Mrs. E. H. Harriman the gift of the Eugenics Record Office, with its land, buildings and records, valued at over $200,000, and a fund of $300,000 of which the income will be available for its maintenance. By this wise and generous gift the future of the Eugenics Record Office becomes established. The relations of the Station for Experimental Evolution and the Eugenics Record Office, always close, bcome still more intimate. The name of Mrs. Harriman is to be always associated with that of the Office as its Founder.

EUGENICS RESEARCH ASSOCIATION.

Since this essay was written in 1997, the HGP has been completed and many variations of this project are now under way, from sequencing the genomes of hundreds of organisms to studying the nature of variation in the human genome with single-nucleotide polymorphisms (SNPs) and haplo-

types. And now the genomes of individual humans have been sequenced and analyzed at much lower cost in time and money than the HGP, opening the door for anyone to have their genome sequenced and their genetic future revealed—one culmination of Davenport's dream.

> *If one is provided with a knowledge of the methods of inheritance of unit characters it might seem to be an easy matter to state how each human trait is inherited and to show how any undesirable condition might be eliminated from the offspring and any wished for character introduced. Unfortunately, such a consummation cannot for some time be achieved.*
>
> DAVENPORT, PP. 23–24

> *The commonwealth is greater than any individual in it. Hence the rights of society over the life, the reproduction, the behavior and the traits of the individuals that compose it are, in all matters that concern the life and proper progress of society, limitless, and society may take life, may sterilize, may segregate so as to prevent marriage, may restrict liberty in a hundred ways.*
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> DAVENPORT, P. 267

THE SCIENCE OF GENETICS AROSE TO study the transmission of physical characteristics from parents to their offspring. When closely studied, much variation exists for virtually any characteristic, say, in size or color, among the members of all species, be they flies, dogs, or ourselves, the members of the *Homo sapiens* species. The origin of this variability long fascinated the scientific world, which already in the nineteenth century asked how much of this variation is due to environmental causes (nurture) as opposed to innate hereditary factors (nature) that pass unchanged from parents to offspring. That such innate heredity exists could never be realistically debated. One need just look at how characteristics in the shape of the face pass through families. Ascribing, say, the uniqueness of the Windsor face to nurture as opposed to nature goes beyond the realm of credibility.

GENES AS THE SOURCE OF HEREDITARY VARIATION BOTH WITHIN AND BETWEEN SPECIES

The key conceptual breakthrough in understanding the nature component of variation came in the mid-1860s from the experiments of the Austrian monk and plant breeder, Gregor Mendel (1822–1884). In his monastery gardens he created, by self-breeding, strains of peas that bred true for a given character like pea color or pod shape. Then he crossed his inbred strains with each other and observed how the various traits assorted in the progeny pea plants. In his seminal scientific paper, published in 1865, Mendel showed that the origin of this hereditary variability lay in differences in discrete factors (genes) that pass unchanged from one plant generation to another.

Most importantly, he showed that each pea has two sets of these factors, one coming from the male parent, the other from the female. Some of those factors are expressed when present in only one copy (dominant genes), whereas others become expressed only when two copies, one from each parent, are present (recessive genes). Mendel's results later were used by the Danish botanist, Wilhelm Johannsen (1857–1927), to make the important distinction between the physical appearance of an individual (its phenotype) and its genetic composition (genotype). Mere examination of a plant's physical appearance need not reveal its genetic composition. Recessive genes present in only one copy can be identified only by further genetic crosses. Mendel further made the equally important observation that genes do not necessarily stay together when the male and female sex cells are formed. Instead, they often independently assort from each other, giving rise to progeny with sets of features very different from those of either parent.

Mendel's work, done before the behavior of chromosomes during cell division was understood, almost had to lay unappreciated until the turn of the century, when three plant breeders working on the European continent—Correns, de Vries, and Tschermak—independently rediscovered the basic rules for hereditary transmission, which today we call Mendel's laws. It was not until 1890 that the sex cells were found to possess only half the number of chromosomes present in adult cells. Fertilization through combining the haploid N number of chromosomes of the sperm with the haploid N number of the egg restores the $2N$ diploid chromosome number of adult plants and animals. Except

for those special chromosomes that determine sex, adult cells contain two copies of each distinct chromosome, each of which is exactly duplicated prior to the cell division. With the basic facts of chromosome behavior so established for both ordinary cell division (mitosis) and sex cell formation (meiosis), the rediscovered laws of Mendel were given a chromosomal basis by the American, Walter Sutton. Perceptively, he noted in 1903 that the segregation patterns of Mendel's genes exactly parallel the behavior of chromosomes during the meiotic cell divisions that produce the male and female sex cells (the Chromosomal Theory of Heredity). During the next several decades, an ever-increasing number of genes were found to have precise locations along specific chromosomes. In essence, each chromosome came to be seen as a linear collection of genes running between its two ends.

Genes first were of interest because they were the source of the variability between the members of a species, but they soon began to be appreciated more properly as the source of information that gives an organism its unique form and function. Its collection of genes (its genome) is what gives each organism its own unique developmental pathway. A dog is a dog, a bacterium a bacterium, and so on, because of the information carried by their respective genomes. Thus, gene duplication prior to cell division must be based on a very accurate copying process. Otherwise, there would be no constancy of genetic information and of the development processes they make possible. Correspondingly, genetic variation arises when genes are not accurately copied (mutated) and give rise to changed (mutant) genes.

HEREDITARY VARIABILITY GENERATED BY CHANGES IN GENES (MUTATION) UNDERLIES EVOLUTION BY NATURAL SELECTION

As soon as the first spontaneous gene mutations became known, they were perceived as the obvious source of the new genetic variants necessary for Darwinian evolution by "survival of the fittest." Many more dysfunctional than more functional genes, however, resulted from random mistakes in the gene-copying process. Thus, the rate at which the gene-copying process makes mistakes is likely also to be under strong

evolutionary pressure. If too many spontaneous mutations occur, none of the mutant-gene-bearing organisms are likely to develop and produce viable offspring. Correspondingly, too low a mutation rate will not generate sufficient gene variants to allow species to compete effectively with those species evolving faster because of their more frequent generation of biologically fitter offspring.

EUGENIC SOLUTIONS FOR HUMAN BETTERMENT

The coming together of Darwinian and Mendelian thinking immediately raised the question of the applicability of the new science of genetics to human life. To what extent was human success due to the presence in their recipients of good genes that led to useful biological traits like good health, social dependability, and high intelligence? Correspondingly, how many individuals at the bottom of the human success totem pole were there because they possessed gene variants perhaps useful for earlier stages in human evolution but now inadequate for modern urbanized life? Social Darwinian reasoning viewed the sociocultural advances marking humans' ascent from the apes as the result of continual intergroup and interpersonal strife, with such competitive situations invariably selecting for the survival of humans of ever-increasing capabilities. Social Darwinism came naturally to the monied products of the industrial revolution, a most prominent one being the talented statistician, Francis Galton (1822–1911). Early in his career, he wrote the 1869 treatise *Hereditary Genius*, later coining the term "eugenics" (from the Greek meaning wellborn) for studies that would bring about improvements of the human race through the careful selection of parents.

Clever though he was, and able to take comfort that he was Charles Darwin's (1809–1882) cousin, Galton's eugenic prescriptions offered no basic improvement on the long-attempted practice of seeing that offspring from families of attainment married into families of similar high function. In this way, supposed good germ plasm would not be diluted by inputs of putative bad heredity. But whether Galton was promoting reality, as opposed to an unjustified prejudice against the vulgarity of the lower classes, had no way of being even half-tested before the arrival of Mendelian analysis. So the eugenics movement naturally became gal-

vanized by the new laws of Mendelian heredity. But immediately, their hopes had to be tempered by the fact that human genetics never would have the power of other forms of genetics where genetic crosses could be made as well as observed. For better or worse, the eugenicists' main research tool had to be hopefully well-collected, multigenerational pedigrees of physical and mental traits that passed through families from one generation to the next. Toward that end, Galton, then already 84, coauthored in 1906 the book *Noteworthy Families*, an index to kinships in near degrees between persons whose achievements are honorable and have been publicly recorded.

Initially, there were hopes that simple Mendelian ratios would characterize the inheritance of a broad-ranging group of human traits. But in addition to the limitations brought about through the inability to confirm genetic hypotheses through genetic crosses, many of the studied traits appeared in too few families for appropriate statistical analysis. Particularly difficult to analyze were progeny traits not present in either parent. Conceivably, individuals had inherited one copy of the same recessive gene from each parent. Such tentative conclusions became more convincing when the respective traits, like albinism, were found more often in highly inbred, isolated populations where marriages of cousins were frequent.

Easier to assign as bona fide genetic determinants were dominant-acting genes that need be inherited from only one parent for their presence to be felt. Once Mendelian thinking had appeared, the inheritance mode of Huntington's disease, the terrible neurological disease that leads to movement and cognition disorders, was quickly ascertained as a dominant gene disorder. Similar clear genetic attributions could be assigned to traits, such as red–green color blindness and hemophilia, which preferentially appear in males but which are never passed on to their own male offspring. This is the behavior of a trait caused by a gene present on the X sex chromosome, two copies of which are present in females but only one in males, whose sexuality is determined by the Y chromosome.

Important as these diseases of the body were to the individuals and families of those so afflicted, the main focus of early twentieth century eugenicists soon moved to potential genetic causations for disabilities

of the mind, embracing a wide spectrum of manifestations from insanity through mental defectiveness, alcoholism, and criminality, to immorality. With poorhouses, orphanages, jails, and mental asylums all too long prominent features of the most civilized societies, eugenicists with virtually religious fervor wanted to prevent more such personal and societal tragedies in the future. They also desired to reduce the financial burdens incumbent on civilized society's need to take care of individuals unable to look after themselves. But in their evangelical assertions that genetic causations lay behind a wide variety of human mental dysfunctions, the early eugenically focused geneticists practiced sloppy, if not downright bad, science and increasingly worried their more rigorous geneticist colleagues.

AMERICAN EUGENICS: SLOPPY GENETICS FOR THE LEGITIMATION OF CLASS STRATIFICATION

The most notable American eugenicist, whose conclusions went far beyond his facts, was Charles B. Davenport (1866–1944), who parlayed his position as Director of the Genetics Laboratory at Cold Spring Harbor, New York, to establish in 1910 a Eugenics Record Office using monies provided by the widow of the railway magnate E.H. Harriman. In his 1911 book *Heredity in Relation to Eugenics*, pedigrees were illustrated for a wide-ranging group of putative hereditary afflictions ranging from bona fide genetic diseases, such as Huntington's disease and hemophilia, to behavioral traits of much less certain hereditary attribution, such as artistic ability and mechanical ability with reference to shipbuilding. With so little then known about the functioning of the human brain, Davenport's early rush to associate highly specific accomplishments of the human brain to specific genetic determinants could not automatically be dismissed as nonsense. In today's intellectual climate, however, a predilection for genes that predispose individuals to city life as opposed to rural life would not be the way to an academic career. But, even his fellow early eugenicists must have regarded as more wartime patriotism than science his 1917 claim that a dominant gene for thalassophilia predisposed its recipients to careers as naval captains.

In addition to its family pedigree assembly and archival roles, the Cold Spring Harbor Eugenics Record Office frequently counseled individuals with family backgrounds of genetic diseases, particularly when they were considering marriage to blood relatives. Many such seekers of help must have been misled by advice that never should have been given, considering that era's limited power for meaningful genetic analysis. Worries about insanity were a major concern, where manic–depressive disease was seen to move through some families as if it were a dominant trait. In contrast, schizophrenia had more aspects of a recessive disease. Yet, even with today's much more powerful human genetics methodologies, we still do not know the relative contribution of dominant versus recessive genes to these two major psychoses or any other form of mental disease.

The Eugenics Record Office's pre-World War II message was that insanity usually expressed itself only when genes predisposing it were inherited from both parents. If this were so, siblings of individuals displaying mental instability were at risk of being carriers of insanity-provoking genes. Because recessive genes for insanity would be silently passing through many families, marriage to any individual with mentally disturbed siblings was not prudent. Even more certainly, marriage should be avoided between individuals having severe mental illness in both parents. In those days, when no effective medicines existed for any form of psychiatric illness, most families bearing mental disease not surprisingly kept this knowledge as secret as possible. There must have been many couples, perhaps overworried about producing mentally disturbed offspring, who chose not to have children.

The eugenicists predictably were concerned about mentally unstable individuals marrying those with similar disturbances. Also of obsessive concern to them were individuals with feeblemindedness, where Davenport believed that recessive genes were also involved. With his certainty that all children of two feebleminded parents would be defective, he wrote of the "folly, yes the crime, of letting two such persons marry." In his mind, the inhabitants of rural poorhouses were there largely because of their feeblemindedness, and he considered one of our nation's worst dangers to be the constant generation of feebleminded individuals by the unrestrained lusts of parents of similar conditions.

It was to stop such further contaminations of the American germ plasm that Davenport, as early as 1911, saw the need for state control of the propagation of the mentally unstable or defective. Initially, he did not favor adoption of state laws allowing for their compulsory sterilization, an idea then considered wise and humane by much of that era's socially progressive elite. Clearly somewhat sexually repressed (obsessed?), he feared that with pregnancy no longer a worry, the sexual urges of the sterilized, mentally unstable impaired might cause more harm to society than even the procreation of more of their kind. Instead, he wanted mentally impaired women to be effectively segregated (imprisoned?) from the impaired of the opposite sex until after they passed the age of procreation. This prescription, however, was totally unrealistic and the American eugenics movement as a whole enthusiastically promoted the compulsory sterilization legislation that spread to 30 states by the start of World War II.

If the eugenics movement had focused its attention predominately on genetic afflictions that truly disabled its recipients, we might now be able to look back at it as a mixture of sloppy science and well-intentioned but kooky naiveté. Photos of the eugenics booths of the 1920s state farm fairs are virtually laughable. In them can be seen "fitter families" displayed near the pens at which prize cattle were shown. The thought that sights of their earnest faces would lead to preferential procreation of more of the same now stretches our credulity. In contrast, the words and actions of Harry P. Laughlin, Davenport's close associate and Superintendent of the Eugenics Record Office, today can only make our minds flinch.

Pleased that his ancestors were traceable to the American Revolution, Laughlin shared Davenport's belief that the strengths and weaknesses of national and religious groups were rooted in genetic as well as in cultural origins. While, at least in public, Davenport wrote that no individual should be refused admission to the United States on the basis of religious group or national origin, Laughlin stated as scientific fact before appropriate Congressional bodies that the new Americans from Eastern and Southern Europe were marked by unacceptable amounts of insanity, mental deficiency, and criminality. Although he lacked any solid evidence, he nonetheless promoted the belief that the newest immigrants to our shores were much more likely to be found in prisons and insane

asylums than were the descendants of earlier waves of English, Irish, German, and Scandinavian settlers. Even though the then-current postwar hysteria against unrestrained immigration by itself might have led to the 1924 legislation, there is no doubt that Laughlin's testimony tilted the composition of the future immigrants to Northern Europeans.

With legislation in place, Davenport no longer had to fear that "the population of the United States will on account of the great influence of blood (genes) from South-Eastern Europe rapidly become darker in pigmentation, smaller in stature, more mercurial, more attached to music and art, given to crimes of larceny, kidnapping, assault, murder, rape, and sex immorality and less given to burglary, drunkenness, and vagrancy than were the original English settlers." Through propagating such racial and religious prejudices as scientific truths, the American eugenics movement was, in effect, an important ally of the ruling classes, many of whose privileges inevitably came through treating those less fortunate as inherently unequal.

USING THE FIRST IQ TESTS TO JUSTIFY RACIAL DISCRIMINATION WITHIN THE UNITED STATES

The emergence of intelligence measuring reinforced the belief of America's prosperous people that their wealth reflected their respective family's innate intellectual superiority. The French psychologist, Alfred Binet (1857–1911), was the first person to try to systematically measure intelligence, responding to a 1904 request from the French government to detect mentally deficient children. The resulting Binet–Simon tests crossed the Atlantic by 1908, being first deployed in the United States by Henry Goddard in New Jersey at a training school for feebleminded boys and girls. Soon afterward, he went on to test 2000 children with a broad range of mental abilities. Initially, there was considerable public opposition to the testing of "normal" individuals because of the test's first use on the feebleminded. Within only a few years, however, revised Binet–Simon tests, more appropriate for precocious children, were prepared by Lewis Terman (1877–1956) at Stanford University. These so-called IQ (intelligence quotient) tests were soon employed during World War I on hundreds of thousands of army draftees. Their main

function was not to weed out mental defectives, but to assign recruits to appropriate army roles. Those administering the tests, led by the noted psychologist Robert M. Yerkes (1876–1956), claimed they were seeing native intelligence independent of the recruit's environmental history. Yet, clearly, many of the questions or arithmetic problems would be more easily answered by those with extensive schooling and possessing a broad vocabulary. Not surprisingly, the non-English-speaking recruits just off the immigration boats tested badly, allowing a test leader to privately confide to Davenport, "we are well on the right track in our contention that the germ plasm (now) coming into the country does not carry the possibilities of that arriving earlier." Such "objective test data" further convinced the eugenicist world that not only was mental deficiency genetically determined, but so was general intelligence.

Although black men from urban areas tested higher than white southern rural men, their IQ scores were significantly lower than their white equivalents from the same communities. Given today's realization that intelligence measurements virtually by necessity have cultural biases, the comparative data assembled from the army recruits had little real meaning. In many ways, it was like comparing oranges with apples. Nonetheless, the data summarized in *Psychological Examining in the United States Army* were used to justify the discriminatory segregation laws that effectively made America's black population second-class citizens. Genetic inequalities across so-called race boundaries were taken for granted, and 29 states maintained laws against black–white intermarriages, often using the argument that the superior white germ stock would be diluted with inferior genes.

Although eugenics had its origin in England, it never affected the national consciousness there as it did in the United States. With social class stratification so long a characteristic feature of British life, the ruling classes had no need of further justification for their privileged existence. To a lesser but real extent, social inequalities also were taken-for-granted features of most European countries, many of which still had royal families and their attendant aristocracy. Enthusiastic prewar eugenics movements nonetheless sprang up all over the continent, extending even to Southern America and Japan in the 1920s. Everywhere, the chief adherents were the professional middle class, naively prosely-

tized into believing that genetic thinking could soon lead to human beings with heightened hereditary capabilities. Although the continent's eugenicists frequently used the now unacceptable term "race hygiene" for their movement, their ways for the betterment of human heredity for the most part in no way infringed upon preexisting human liberties. Offered as the future panacea was the standard package of marriage between genetically healthy individuals, with correspondingly strong disapproval of marriage for individuals bearing obviously bad genes like those leading to Huntington's disease. Only in two European countries, Germany and Sweden, was legislation enacted for obligatory sterilization of individuals thought to be the bearers of disabling genes.

NAZI EUGENICS (RACE HYGIENE): A MURDEROUS MÉNAGE À TROIS OF BAD GENETICS, RACIAL ANTHROPOLOGY, AND PSYCHIATRY AT THE BECKON OF HITLER AND HIMMLER

Although it was the Hitler-led Nazi government that quickly passed the 1933 Eugenic Sterilization Law, the broadly based German eugenics movement of the 1920s laid the groundwork. Then it was embraced by a spectrum of political thought, much of it totally respectable by the ethical standards of those days. The Germany of that time was a nation undergoing a great moral crisis brought on by its humiliating defeat in the World War. Its four awful years of trench warfare had killed a significant fraction of its better younger men and left it vulnerable to the hyperinflation that wiped out much of the savings of its professional middle class. Unlike England or France, Germany as a world power had only a fleeting existence, and the German people then saw the need to somehow reinvigorate themselves. The eugenicists' vision that human beings' futures lie in their genes struck a receptive chord in the immediate postwar German psyche. Even in the postwar chaos of its Weimar government, human genetics gained strong governmental support. Genetics quickly became a high-quality science in Germany, with Berlin becoming one of the world's leading centers for genetics. Study of supposed genetic differences between the so-called races was vigorously promoted, with it being accepted as fact that the commercial colonization of the world by major countries in Europe

and the United States reflected the inherent superiority of the Nordic people's genes for intelligence and strength of moral purpose. Anthropological-based research had strong genetic components, with genes being perceived as the crucial element determining human behavior.

In total contrast, genetic explanations for human successes were not favorably received in the Soviet Union, whose communist doctrines emphasized social, as opposed to genetic, causation for the currently existing inequalities between humans. Already by the mid-1930s, eugenic thinking had become strongly inimical to Russian Communist policymakers, who increasingly favored the Lamarckian explanations (inheritance of acquired characteristics) of Trofim Lysenko (1898–1976), its homegrown agriculturist, over the foreign-originating Morgan–Mendelian analysis of heredity. Those pursuing genes within the Soviet Union soon were putting not only their careers, but also their lives at risk. The great American geneticist, Hermann J. Muller (1890–1967), whose left-wing views led him to leave Texas and go to Russia in 1933, effectively ended his Soviet career when, in 1936, he compared Lamarckian thinking to alchemy, astrology, and shamanism.

Seeking backing for the putative superiority of the Caucasian race, Adolf Hitler (1889–1945), while imprisoned in 1924 for the failed Munich putsch, read *Menschliche Erblichkeitslehre und Rassenhygiene* (The Principles of Human Heredity and Race Hygiene), a leading German genetic text of the time coauthored by E. Baur, Eugen Fischer, and Fritz Lenz. Enveloped by an uncritical eugenic perspective, it strongly reinforced Hitler's view of Germans as the *master race* that justifiably should rule the world. If, however, the Germans were indeed the master race, the Nazis had to explain their nation's humiliating defeat in the Great War and its subsequent devastating hyperinflation.

A perfidious scapegoat was needed, and here Hitler drew upon the long-existing, anti-Semitic feelings of many German people. Long segregated in rural enclaves dating back to the Middle Ages, Jews became effectively part of Germany's commercial and professional life only by the middle of the nineteenth century. Gravitating especially to the professions where their talents could more easily prevail over still-existing prejudices, Jewish importance in German commerce and professional life soon became disproportionate to their numbers, creating jealousies

that inevitably fanned preexisting anti-Semitism. Clearly, much of this Jewish success reflected its religion and its respect for the intellect as opposed to oft revelatory-based opinions of their Christian equivalency. Their anti-Semitic opponents, however, saw the Jews' upward trajectory as manifestation of inherent immoralities that let them take unfair advantage of the more honest Christian Germans.

Until the arrival of Mendelian thinking, German anti-Semites never consistently decided whether their enemy was the Jews themselves or their religion. If their failure to acknowledge Christ was the problem, Jews who converted posed no further threat to Christian civilization. But if their reputed unscrupulous behavior and sexual licentiousness reflected innate hereditary qualities, their presence within Christian societies threatened their country's moral resolve, if not its very existence. Assertions by eugenicists that gene differences lay behind human behavioral differences were thus made to order for Nazi needs. From the 1933 start of their absolute rule, the Nazi propaganda machine ruthlessly portrayed Jews and Communists as the two main villains blocking the ultimate triumph of National Socialism. No words were vile enough to express their hatred for the genes that supposedly let Germany's one million Jews steal for themselves the monies and jobs of the honest Germans, or their horror of the Communists who wanted to redistribute monies from those who worked hard to those not able or willing to take care of themselves. Treated with equal contempt by the Nazis, but of less importance because of their much smaller numbers (30,000), were the Gypsies. Because of their wandering, supposed sexually unrepressed lifestyles, and their lack of respect for property, the German Gypsies were regarded by Nazi anthropologists as descendants of peoples of primitive etiological origin who had mated repeatedly with the German criminal, asocial subproletariat. So considered, the further breeding of this mixed-blood people must be stopped.

STERILIZATION OF THE MENTALLY UNFIT AS A PRELUDE TO MORE BROADLY BASED WARTIME GENOCIDE

Gypsies, however, were not specifically targeted under the 1933 Eugenics Law that mandated compulsory sterilization for schizophrenia,

manic–depressive psychoses, hereditary epilepsy, Huntington's chorea (disease), hereditary blindness, hereditary deafness, severe physical deformity, and severe alcoholism. Tribunals of Hereditary Health, consisting of a judge, a government medical officer, and an "independent" physician, made the resulting decisions where the individuals concerned often knew they were at risk only when called before its members. With appeals extremely difficult, these psychiatrist-led verdicts between 1934 and 1939 led to some 400,000 compulsory sterilizations, many to noninstitutionalized persons. These reputedly hereditary-damned individuals were further subjected to a subsequent 1934 law forbidding persons with serious mental disturbances from marrying. A year later, legislation specifically affecting Jewish marriages came through the 1935 "Nuremberg Decrees" for the protection of German blood and health. They forbade not only marriages, but also sexual intercourse, between the so-called German and Jewish races.

Concomitant with these eugenic actions was the assembly of vast record collections documenting individual hereditary–biological characteristics. To the Reich Kinship Bureau were referred decisions as to the origin of individuals with potential partial Jewish blood. Many such anthropological "expert conclusions" were made using only photos of the putative fathers. However, with the census of 17 May 1939 providing supposed "confidential" information of any Jewish grandparent, the Nazis, as the war started, felt they had a firm handle on the Jewish blood within their midst. So encouraged, later that year Professor Eugen Fischer, this time responding to coal barons of the Ruhr, wrote, "When a people wants somehow or other to preserve its own nature, it must reject alien racial elements and when they have already insinuated themselves, it must suppress and then eliminate them. The Jew is such an alien... ."

With the war on, the German government, seeing no reason to waste scarce resources to keep what they considered genetically inferior peoples alive, proceeded to what it termed a "euthanasia policy of mercy killing." In a one-sentence letter postdated 1 September 1939, Hitler himself wrote, "Reichleiter Bouhler and Dr. Brandt are entrusted with responsibility of extending the rights of specifically designated physicians such that patients who are judged incurable after the most

thorough review of their condition which is possible can be granted mercy killing." So authorized, 3000 mental patients in occupied Poland were summarily shot by storm troopers. In the Reich itself, where German citizens were involved, somewhat more formal procedures were used. Questionnaires were distributed to the mental hospitals, where they were completed in their capacity as experts by nine Professors of Psychiatry assisted by 39 other medical doctors. For their labors, they were paid 5 pfennigs (the cost of a cigarette) per questionnaire when they processed more than 3500 per month, but up to 10 pfennigs when fewer than 500 questionnaires per month were processed. The patients so selected for "euthanasia" had their respective questionnaires marked with a cross. Subsequently, carbon monoxide supplied by I.G. Farben was used for the elimination process. Before the killings stopped in the fall of 1941, some 94,000 mental patients had been killed. Subsequently, covert "euthanasia" by starvation, drugs, and failure to treat infectious diseases led to only 15% (40,000 persons) of Germany's prewar mental hospital population remaining alive at the war's end.

The primary reason for the supposed stopping of mental patient "mercy killings" was the need to transfer the personnel trained in killing by gas to the concentration camps, primarily in Poland (e.g., Auschwitz), to which most German Jews and gypsies had already been deported. With the decision already taken to invade the Soviet Union, a conference was held in March 1941 in Frankfurt at the Institute for the Investigation of the Jewish Question. At this conference, Dr. Gross, the head of the Race Policy Institute of the Nazi party, stated, "The definitive solution must involve the removal of Jews from Europe and he demands sterilization of quarter Jews." In an October letter to Himmler, Oberdiensleiter Brack of the Fuhrer's chancellery wrote that there are no objections to doing away (gassing) Jews who are unfit for concentration camp work. Less than a month later, Rosenberg, theoretician and minister of the occupied eastern territories, before representatives of the German press, announced the Final Solution of the Jewish Question, revealing plans, still to be kept secret, for the eventual mass murder of all European Jews, including the six million then living in the Soviet Union. The gas chambers so used were in no way restricted to Jews and Gypsies, with Soviet prisoners of war being victims of the

first uses of Zyklon B (hydrocyanic acid) at Auschwitz. Anxious to give their racial extermination policies "scientific" justification, Himmler later in 1943 specified in a decree that only physicians trained in anthropology should carry out selection for killing and supervise the killings themselves in extermination camps. Some quarter Jews were to be spared, but not those with Jewish facial features who should be treated as half Jews. By the war's end, five to six million European Jews were so killed, the majority by the gassing procedures that the Nazis' co-opted human geneticists, psychiatrists, and anthropologists thought appropriate for individuals bearing genes inimical to the best interests of the German people.

With the liberation first of Poland and then Germany, the full horror of the racially based genocide policies of National Socialism quickly became known, generating even further disgust for the pseudoscientific theories of race superiority and purity that underpinned Nazi ideology. Anyone subsequently calling himself a eugenicist put his reputation as a decent moral human at risk. In fact, before the war even started, eugenics in the United States already was being perceived more as a social than a scientific movement. Already in 1930, the leaders of the Carnegie Institute of Washington had been told that its Cold Spring Harbor Eugenics Record Station practiced sloppy, if not dishonest, science. But with its founder Charles Davenport nearing retirement, it was allowed to expire more slowly than in retrospect it should have. Its doors closed only when Miloslav Demerec became director of the Department of Genetics in 1942. There thus was the embarrassment of Harry Laughlin's receipt in 1936 of an honorary degree from the University of Heidelberg in recognition of his contributions to racial hygiene. Undoubtedly pleased that eugenics, then fading in the United States, was becoming even more ascendant in Germany, Laughlin went to New York to receive his diploma from the German Diplomatic Counsel.

EUGENICS, A DIRTY WORD, AS THE SEARCH FOR THE CHEMICAL NATURE OF THE GENE BEGINS

By the time I first came to Cold Spring Harbor for the summer of 1948, accompanying my Ph.D. supervisor Salvador Luria, then a professor

at Indiana University, the Eugenics Record Office had been virtually expunged from its consciousness. Only in the library was its ugly past revealed through the German journals of the 1920s and 1930s on human genetics and race hygiene. No one that summer showed any interest in human genetics as a science or toward the general question of how much of human behavior reflects nature as opposed to nurture. Instead, genetic research there focused on the fundamental nature of genes and their functioning. It was not that human genetic diseases had suddenly become unimportant to its director, Miloslav Demerec. But there was general agreement both by the year-round staff and the many summer visitors that until the chemical identity of the gene was elucidated and the general pathways by which it controlled cell structure and functioning were known, it was premature to even speculate how genes contributed to human development and behavior.

Then, much sooner than anyone expected, the gene was revealed in 1953 to be DNA. The genetic code was established by 1966, and gene expression was seen to be controlled by DNA-binding regulatory proteins between 1967 and 1969. Genetics, happily then, had no reasons to intersect politics, except in Russia, where the absurdity of its Lamarckian philosophy became painfully more clear to its intelligentsia with every new major advance in molecular genetics. These major genetic breakthroughs were largely accomplished using the simple genetic systems provided by bacteria and their viruses that go under the name phages. By 1969, phage had become so well understood genetically that it became possible to create specific phage strains cleverly engineered to carry specific bacterial genes from one bacterial strain to another. Yet, seeming more ashamed than pleased with their neat science, James Shapiro and Jonathan Beckwith of Harvard Medical School held with much fanfare a press conference to announce that their new way to isolate specific genes was on the pathway to eugenically motivated genetic engineering of human beings. Knowing of the left-wing views of their "Science for the People" group, I, like most of my colleagues in the Boston region, saw their self-denunciations as manifestations of unrepentant leftist fears that further genetic research would render inviable the Communist dogma that assigned all social inequalities to capitalistic selfishness. Shapiro then moved (temporarily) to Cuba to regain his ideological purity.

Although the phage transductional system developed by Shapiro and Beckwith proved not to be a forerunner for eventual human genetic engineering, this was not true for the much more powerful and general "recombinant DNA" methodologies that Herbert Boyer and Stanley Cohen developed 4 years later, in 1973, just 20 years after the discovery of the double helix. Their new procedures allowed the isolation (cloning) of specific genes, through their insertion into tiny chromosomes (plasmids) that could be moved from one cell to another. At roughly the same time, unexpectedly powerful new ways to determine the exact sequences of the four letters (A, G, T, and C) of genetic messages were worked out by Fred Sanger in Cambridge, England, and by Walter Gilbert and Allan Maxam at Harvard. Together, using these two new techniques, the exact structure of any gene could eventually be determined, given the appropriate facilities and resources.

The resulting recombinant DNA era, however, despite all the promises it held for major scientific advances, did not immediately take off. It initially stalled because of fears that among the many new forms of DNA created in the laboratory would be some that would pose unacceptable dangers to life as it now exists. In particular was the fear that highly pathogenic new forms of viruses and bacteria would be created. To give time to assess such potential dangers scientifically, a scientist-initiated moratorium on recombinant DNA research was declared in 1975. Effectively, it blocked virtually all recombinant DNA research for the next 2 years; and research concerned with cancer, where worries were expressed that a cancer gene might become bacterially transmitted, was held up for 2 more years.

During the moratorium, governmental committees were set up in the United States and in various European countries to assess the potential dangers from recombinant DNA experimentation in relation to its potential benefits for biology, medicine, and agriculture. No plausible scientific reasons for stopping such research emerged, and such committees, often containing public as well as scientific representatives, invariably concluded that in the absence of any quantifiable potential dangers, it would be irresponsible not to move ahead with experiments that could dramatically change the nature of biology. In retrospect, these decisions to move ahead were always the correct ones.

For example, cancer research and our knowledge of the genetic basis of the immune system would effectively be back in the scientific middle ages if the enlightenments made possible through recombinant DNA had not occurred.

To my knowledge, moreover, not one case of recombinant DNA-induced illness has since occurred. No person has been so killed, nor has even one case of serious illness been attributed to recombinant DNA, nor do we know of any case where the release into nature of any recombinant DNA-modified organism has led to any known ecological disaster. This is not to say that someday a recombinant DNA-induced disease or ecological upset will not occur. Today, however, there is certainly no logical reason for not exploiting recombinant DNA procedures as fast as possible for human betterment.

IDEOLOGICAL AND VALUE-BASED OPPOSITIONS TO RECOMBINANT DNA RESEARCH

Although there was no evidence of danger from recombinant DNA, there soon arose much visible and sometimes regretfully effective opposition to recombinant DNA research. Here the distinction should be made between objections from scientists who understand the technical issues involved and opposition from groups of public citizens who, though not understanding the science involved, nonetheless oppose much to all recombinant DNA research. Although some initial opposition arose from scientists whose own DNA research was not going well, virtually all the continuing scientific opponents at their heart had political hang-ups. As leftists, they did not want genes involved in human behavioral differences and feared that the onslaught of scientific advances that would follow from the unleashing of recombinant DNA might eventually allow genes affecting mental performance to be isolated and studied.

As a member of the Harvard Biology Faculty between 1975 and 1977, I watched in despair when "Science for the People" successfully assisted the public members of the Cambridge, Massachusetts, City Council to block recombinant DNA research at our Biological Laboratories. Later, I asked Salvador Luria, who was then at Massachusetts

Institute of Technology and who knew that his left-wing friends were putting forth scientifically dishonest statements, why he never publicly criticized them. His reply was that politics was more important than science. This remark has long haunted me, because my own career owes much to the generous way he shared his great scientific talents with me at the beginning of my scientific career. But as a Jew who had to flee first his native Italy and then France for the eventual safety of the United States, Luria's left-wing political affinities were understandable, and I'm lucky I never had to so choose.

Specific political ideologies, however, are not the cause of the prolonged and sometimes effective opposition to recombinant DNA from parts of the general public, particularly in German-speaking regions. With professional agitators like Jeremy Rifkin playing important roles in heightening these public fears, such leadership would never have been effective if their audiences were at emotional ease with the gene and the geneticists who study it. The concept of genetic determinism is inherently unsettling to the human psyche, which likes to believe that it has some control over its fate. No one feels comfortable with the thought that we, as humans, virtually all contain one to several "bad" genes that are likely to limit our abilities to fully enjoy our lives. Nor do we necessarily take pleasure in the prospect that we will someday have gene therapy procedures that will let scientists enrich the genetic makeups of our descendants. Instead, there has to be genuine concern as to whether our children or their governments decide what genes are good for them.

Genetics as a discipline must thus strive to be the servant of the people, as opposed to these governments, working to mitigate the genetic inequalities arising from the random mutations that generate our genetic diseases. Never again must geneticists be seen as the servants of political and social masters who need demonstrations of purported genetic inequality to justify their discriminatory social policies. On the whole, I believe that genetics still commands broad respect in the United States and in much of Europe, despite the efforts of the recombinant DNA opponents to portray the genetic manipulations underlying the biotechnology industry as money-driven actions done at the expense of the public's health and the world's environment. Unfortunately, genetics and geneticists remain much less highly respected in Germany. There

even today the most benign of recombinant DNA experiments remain controversial and subject to needless regulation. Propagation of genetically engineered plants is routinely sabotaged, with the mere practice of human genetics regarded as a criminal act by extremists on the left.

This German dislike for the gene and its human-directed manipulations is easily assignable to their Nazi eugenics past. The vile actions then done in the name of the gene hover as almost permanent nightmares never erasable from their national identity. As human beings, never sure that the world is immune from further such depraved behavior, we should never let this awful past slip from our consciousness. At the same time, the whole civilized world will suffer if today's German geneticists are unfairly thought to be cut from the same material that clothed those German geneticists, anthropologists, and psychiatrists who not only assisted the Nazi eugenic efforts, but promoted them as scientific-based necessities for German progress.

Part of today's problem may lie in the postwar fate of Hitler's biological conspirators. Naively as outsiders we long assumed that they would have all been treated as potential if not real war criminals, with even those of only slight guilt losing all further opportunities for academic existence. But as the German geneticist Benno Müller-Hill courageously pointed out in his 1984 book, *Todlicel Wissenschaft* (*Murderous Science*, Cold Spring Harbor Laboratory Press, 1998), there was no attempt by the German academic community to find out what truly happened. Instead, it was academically dangerous in Germany to explore the half-truths that allowed many key practitioners of Nazi eugenics to resume important academic posts. A number of professors who early joined the Nazi Party or SS and were directly involved with its genocide programs committed suicide, but there were many Nazi-assisting scientists, successfully claiming that they were only apolitical advisors, who slid quietly back into academic prominence.

The most damning example was that of Professor Otmar von Verschuer, who actively helped the Nazis—first at the Kaiser Wilhelm Institute of Anthropology under Professor Eugen Fischer and later at his own Institute of Human Genetics in Frankfurt. Involved in distinguishing Jews and part-Jews, he later closely collaborated with his former assistant, the now notorious Josef Mengele, then doing "scientific"

research at Auschwitz. After the war, he nonetheless was appointed to be Professor of Human Genetics at the University of Münster. Equally disturbing was the postwar appointment of Fritz Lenz as head of an institute for the study of human heredity at the University of Göttingen, Germany's most distinguished university. Although clearly a very competent scientist, he was a major advisor for laws on euthanasia between 1939 and 1941, as well as author of a 1940 memorandum, "Remarks on resettlement from the point of view of guarding the race."

The postwar 1949 exoneration of von Verschuer occurred despite knowledge of the 1946 article in *Die New Zeit* accusing him of studying eyes and blood samples sent to him from Auschwitz by Josef Mengele. Yet a committee of professors, including Professor Adolf Butenandt, later the head of the Max Planck Gesellschaft (the postwar name for the Kaiser Wilhelm Gesellschaft), concluded that von Verschuer, who possessed all the qualities appropriate for a scientific researcher and teacher of academic youth, should not be judged on a few isolated events of the past. I find it difficult to believe that the Butenandt committee had gone to the trouble of reading his article published in the *Volkischer Beobachter* 1-8-42. In it he wrote, "Never before in the course of history has the political significance of the Jewish question emerged so clearly as it does today. Its definitive solution as a global problem will be determined during the course of this war." Now there may be more reason to remember Professor Butenandt for his part in the von Verschuer whitewash than for his prewar Nobel Prize for research on the chemistry of the estrogen sex hormone.

GENUINE HUMAN GENETICS EMERGES FROM RECOMBINANT DNA METHODOLOGIES

Long holding back the development of human genetics as a major science was the lack of a genetic map allowing human genes to be located along the chromosomes on which they reside. As long as conventional breeding procedures remained the only route to gene mapping, the precise molecular changes underpinning most human genetic diseases seemed foreordained to remain long mysterious. The key breakthrough opening a path around this seemingly insuperable obstacle came in the

late 1970s when it was discovered that the exact sequence (order of the genetic letters A, G, T, and C) of a given gene varies from one person to another. Between any two individuals, roughly 1 in 1000 bases are different, with such variations most frequently occurring within the noncoding DNA regions not involved in specifying specific amino acids. Initially most useful were base differences (polymorphisms) that affected DNA cutting by one of the many just discovered "restriction enzymes" that cut DNA molecules within very specific base sequences.

Soon after the existence of DNA polymorphisms became known, proposals were made that they could provide the genetic markers needed to put together human genetic maps. In a 1980 paper, David Botstein, Ron Davis, Mark Skolnick, and Ray White argued that human maps could be obtained through studying the pattern through which polymorphisms were inherited in the members of large multigenerational families. Those polymorphisms that stay together were likely to be located close to each other on a given chromosome. During the next 5 years, two groups, one led by Helen Donis-Keller in Massachusetts, the other led by Ray White in Utah, rose to this challenge, both using DNA from family blood samples stored at CEPH (Centre d'Étude du Polymorphisme Humain), the mapping center established in Paris by Jean Dausset. By 1985, the mutant genes responsible for Huntington's disease and cystic fibrosis (CF) had been located on chromosomes 4 and 7, respectively.

By using a large number of additional polymorphic markers in the original chromosome 7 region implicated in CF, Francis Collins' group in Ann Arbor and L.C. Tsui's group in Toronto located the DNA segment containing the responsible gene. Its DNA sequence revealed that the CF gene coded for a large membrane protein involved in the transport of chloride ions. The first CF mutant they found contained three fewer bases than its normal equivalent and led to a protein product that was nonfunctional because of its lack of a phenylalanine residue.

THE HUMAN GENOME PROJECT: RESPONDING TO THE NEED FOR EFFICIENT DISEASE GENE MAPPING AND ISOLATION

Although the genes responsible for cystic fibrosis and Huntington's disease were soon accurately mapped using only a small number of

DNA polymorphic markers, the genes behind many other important genetic diseases quickly proved to be much harder to map to a specific chromosome, much less assign to a DNA chromosomal segment short enough to generate hopes for its eventual cloning. All too obviously, the genes behind the large set of still very badly understood diseases like Alzheimer's disease, late-onset diabetes, or breast cancer would be mapped much, much sooner if several thousands more newly mapped DNA polymorphisms somehow became available. Likewise, the task of locating the chromosomal DNA segment(s) in which the desired disease genes reside would be greatly shortened if all human DNA were publicly available as sets of overlapping cloned DNA segments (contigs). And the scanning of such DNA segments to look for mutationally altered base sequences would go much faster if the complete sequence of all the human DNA were already known. However, to generate these importantly new resources for human genetics, major new sources of money would be needed. So, by early 1986, serious discussions began as to how to start, soon, the complete sequencing of the 3×10^9 base pairs that collectively make up the human genome (the Human Genome Project or HGP).

Initially, there were more scientific opponents than proponents for what necessarily would be biology's first megaproject. It would require thousands of scientists and the consumption of some $3 billion-like sums. Those disliking its prospects feared that, inevitably, it would be run by governmental bureaucrats not up to the job and would employ scientists too dull for assignment to this intellectually challenging research. Out of many protracted meetings held late in 1986 and through 1987, the argument prevailed that the potential rewards for medicine as well as for biological research itself would more than compensate for the monies the Human Genome Project would consume during the 15 years then thought needed to complete it. Moreover, completion of each of the two stages—the collection of many more mapped DNA markers and the subsequent ordering of cloned DNA segments into long overlapping sets (contids)—would by themselves greatly speed up disease gene isolation.

Always equally important to point out, the 15 years projected to complete the Human Genome Project meant that its annual cost of

$200 million at most would represent only 1–2% of the money spent yearly for fundamental biomedical research over the world. There was also the realization that some 100,000 human genes believed sited along their chromosomes would be much easier to find and functionally understand if genome sequences were first established for the much smaller, well-studied model organisms such as *Escherichia coli, Saccharomyces cerevisiae, Caenorhabditis elegans*, and *Drosophila melanogaster*. Thus, the biologists who worked with these organisms realized that their own research would be speeded up if the Human Genome Project went ahead.

The American public, as represented by their congressional members, proved initially to be much more enthusiastic about the objectives of the Human Genome Project than most supposedly knowledgeable biologists, with their parochial concerns for how federal monies for biology would be divided up. The first congressionally mandated monies for the Human Genome Project became available late in 1987, when many intelligent molecular geneticists still were sitting on the fence as to whether it made sense. In contrast, Congress, being told that big medical advances would virtually automatically flow out of genome knowledge, saw no reason not to move fast. In doing so, they temporarily set aside the question of what human life would be like when the bad genes behind so many of our major diseases were found. Correctly, to my mind, their overwhelming concern was the current horror of diseases like Alzheimer's, not seeing the need then to, perhaps prematurely, worry about the dilemmas arising when individuals are genetically shown at risk for specific diseases years before they show any symptoms.

GENOME ETHICS: PROGRAMS TO FIND WAYS TO AMELIORATE GENETIC INJUSTICE

The moment I began in October 1988 my almost 4-year period of helping lead the Human Genome Project, I stated that 3% of the NIH-funded component should support research and discussion on the ethical, legal, and social implications (ELSI) of the new resulting genetic knowledge. A lower percentage might be seen as tokenism, while I then could not see wise use of a larger sum. Under my 3% proposal, some $6 million (3% of $200 million) would eventually be so available, a much larger sum than ever before provided by our government for the ethical implications of biological research.

In putting ethics so soon into the genome agenda, I was responding to my own personal fear that all too soon critics of the Genome Project would point out that I was a representative of the Cold Spring Harbor Laboratory that once housed the controversial Eugenics Record Office. My not forming a genome ethics program quickly might be falsely used as evidence that I was a closet eugenicist, having as my real long-term purpose the unambiguous identification of genes that lead to social and occupational stratification as well as to genes justifying racial discrimination. So I saw the need to be proactive in making ELSI's major purpose clear from its start—to devise better ways to combat the social injustice that has at its roots bad draws of the genetic dice. Its programs should not be turned into public forums for debating whether genetic inequalities exist. With imperfect gene copying always the evolutionary imperative, there necessarily will always be a constant generation of the new gene disease variants and consequential genetic injustice.

The issues soon considered for ELSI monies were far-ranging. For example, how can we ensure that the results of genetic diagnosis are not misused by prospective employers or insurers? How should we try to see that individuals know what they are committing themselves to when they allow their DNA to be used for genetic analyzing? What concrete steps should be taken to ensure the accuracy of genetic testing? And when a fetus is found to possess genes that will not allow it to develop into a functional human being, who, if anyone, should have the right to terminate the pregnancy?

From their beginnings, our ELSI programs had to reflect primarily the needs of individuals at risk of the often tragic consequences of genetic disabilities. Only long-term harm would result in the perception of genetics as an honest science if ELSI-type decisions were perceived to be dominated either by the scientists who provided the genetic knowledge or by the government bodies that funded such research. And because women are even in the distant future likely to dispropor-

tionately share the burden of caring for the genetically disabled, they should lead the discussions of how more genetic knowledge is to come into our lives.

HUMAN HESITATIONS IN LEARNING THEIR OWN GENETIC FATE

With the initial distribution of American genome monies and the building and equipping of the resulting genome centers taking 2 years, the Human Genome Project in its megaphase did not effectively start until the fall of 1990. Decisions to go ahead by funding bodies in the United States helped lead to the subsequent inspired creation of Généthon outside Paris by the French genetic disease charity, Association Française contre les Myopathies (AFM), as well as the building of the now immense Sanger Centre, just south of Cambridge, England, by the British medically oriented charity, the Wellcome Trust. Now effectively 7 years into its projected 15-year life, the Human Genome Project has more than lived up to its role in speeding up genetic disease mapping and subsequent gene cloning. It quickly made successful the search for the gene behind the Fragile X syndrome that leads to severe mental retardation in boys preferentially affected by this sex-linked genetic affliction. The molecular defect found was an expansion of preexisting three-base repetitive sequences that most excitingly increase in length from one generation to the next. The long mysterious phenomenon of anticipation, in which the severity of a disease grows through subsequent generations, was thus given a molecular explanation. Then at long last, in 1994, the gene for Huntington's disease was found. Its cause was likewise soon found to be the expansion of a repetitive gene sequence.

While the mapping to a chromosome per se of any disease gene remains an important achievement, the cloning of the disease gene itself is a bigger milestone. Thus, the 1990 finding by Mary-Claire King that much hereditary breast cancer is due to a gene on chromosome 17 set off a big gene-cloning race. With that gene in hand, there was a chance that its DNA sequence would reveal the normal function of the protein it codes for. In any case, it gives its possessors the opportunity to examine directly the DNA from individuals known to be at risk for a disease to see whether they had the unwanted gene. Thus, when in 1993 the chromosome 17 breast cancer gene (*BRCA1*) was isolated by Myriad, the Utah disease gene-finding company, it could inform women so tested for *BRCA1* whether or not they had the feared gene.

Initially, concerns were voiced that unbridled commercialization of this capability would all too easily give women knowledge they would not be psychologically prepared to handle. If so, the ethical way to prevent such emotional setbacks might be to regulate both how the tests were given and who should be allowed to be tested. I fear, however, that a major reason behind many such calls for regulation of genetic testing is the hidden agenda of wanting to effectively stop widespread genetic testing by making it so difficult to obtain. Now, however, calls for governmental regulation may fall on increasingly deaf ears. To Myriad's great disappointment, it appears that the great majority of women at 50% risk of being breast cancer gene carriers don't want to be tested. Rather than receive the wrong verdict, they seem to prefer living with uncertainty. Likewise, a very large majority of the individuals at risk for Huntington's disease are also psychologically predisposed against putting themselves at risk of possibly knowing of their genetic damnation.

Although we are certain to learn in the future of many individuals regretting that they subjected themselves to genetic tests and wishing they had been more forewarned of the potential perils of such knowledge, I do not see how the state can effectively enter into such decisions. Committees of well-intentioned outsiders will never have the intimate knowledge to assess a given individual's psychological need, or not, for a particular piece of scientific or medical knowledge. In the last analysis, we should accept the fact that if scientific knowledge exists, individual persons or families should have the right to decide whether it will lead to their betterment.

INARGUABLE EXISTENCE OF GENES PREDISPOSING HUMANS TO BEHAVIORAL DISORDERS

The extraordinarily negative connotations that the term eugenics now conveys are indelibly identified with its past practitioners' unjustified

statements that behavioral differences, whether between individuals, families, or the so-called races, largely had their origins in gene differences. Given the primitive power of human genetics, there was no way for such broad-ranging assertions to have been legitimatized by the then-current methods of science. Even the eugenically minded psychiatrists' claims that defective genes were invariably at the root of their mental patients' symptoms were no more than hunches. Yet, it was by their imputed genetic imperfection that the mentally ill were first sterilized and then, being of no value to the wartime Third Reich, released from their lives by subsequent "mercy killings."

But past eugenic horrors in no way justify the "not in our genes" politically correct outlook of many left-wing academics. They still spread the unwarranted message that only our bodies, not our minds, have genetic origins. Essentially protecting the ideology that all our troubles have capitalistic exploitative origins, they are particularly uncomfortable with the thought that genes have any influence on intellectual abilities or that unsocial criminal behavior might owe its origins to other than class or racially motivated oppression. However, whether these scientists on the left actually believe, say, that the incidence of schizophrenia would seriously lessen if class struggles ended is not worth finding out.

Instead, we should employ, as fast as we can, the powerful new techniques of human genetics to find soon the actual schizophrenia predisposing genes. The much higher concordance of schizophrenia in identical versus nonidentical twins unambiguously tells us that they are there to find. Such twin analysis, however, reveals that genetics cannot be the whole picture. Because the concordance rates for schizophrenia, as well as for manic–depressive disease, are more like 60%, not 100%, environmental predisposing factors must exist and, conceivably, viral infections that affect the brain are sometimes involved.

Unfortunately, still today, the newer statistical tricks for analyzing polymorphic inheritance patterns have not yet led to the unambiguous mapping of even one major schizophrenic gene to a defined chromosomal site. The only convincing data involve only the 1% of schizophrenics whose psychoses seemingly are caused by the small chromosome 22 deletions responsible also for the so-called DiGeorge

facial syndrome. Manic–depressive disease also has been more than hard to understand genetically. Only last year did solid evidence emerge for a major predisposing gene on the long arm of chromosome 18. This evidence looks convincing enough for real hopes that the actual gene involved will be isolated over the next several years.

Given that over half the human genes are thought to be involved in human brain development and functioning, we must expect that many other behavioral differences between individuals will also have genetic origins. Recently, there have been claims that both "reckless personalities" and "unipolar depressions" associate with specific polymorphic forms of genes coding for the membrane receptors involved in the transmission of signals between nerve cells. Neither claim now appears to be reproducible, but we should not be surprised to find some subsequent associations to hold water. Now anathematic to left-wing ideologues is the highly convincing report of a Dutch family, many of whose male members display particularly violent behavior. Most excitingly, all of the affected males possess a mutant gene coding for an inactive form of the enzyme monoamine oxidase. Conceivably having too little of this enzyme, which breaks down neurotransmitters, leads to the persistence of destructive thoughts and the consequential aggressive patterns. Subsequent attempts to detect in other violent individuals this same mutant gene have so far failed. We must expect someday, however, to find that other mutant genes that lead to altered brain chemistry also lead to asocial activities. Their existence, however, in no way should be taken to mean that gene variants are the major cause of violence. Nonetheless, continued denials by the scientific left that genes have a role in how people interact with each other will inevitably further diminish their already tainted credibility.

KEEPING GOVERNMENTS OUT OF GENETIC DECISIONS

No rational person should have doubts whether genetic knowledge properly used has the capacity to improve the human condition. Through discovering those genes whose bad variants make us unhealthy or in some other way unable to function effectively, we can fight back in several different ways. For example, knowing what is wrong at the mo-

lecular level should let us sometimes develop drugs that will effectively neutralize the harm generated by certain bad genes. Other genetic disabilities should effectively be neutralized by so-called gene therapy procedures restoring normal cell functioning by adding good copies of the missing normal genes. Although gene therapy enthusiasts have promised too much for the near future, it is difficult to imagine that they will not with time cure some genetic conditions.

For the time being, however, we should place most of our hopes for genetics on the use of antenatal diagnostic procedures, which increasingly will let us know whether a fetus is carrying a mutant gene that will seriously proscribe its eventual development into a functional human being. By terminating such pregnancies, the threat of horrific disease genes continuing to blight many families' prospects for future success can be erased. But even among individuals who firmly place themselves on the pro-choice side and do not want to limit women's rights for abortion, opinions frequently are voiced that decisions obviously good for individual persons or families may not be appropriate for the societies in which we live. For example, by not wanting to have a physically or mentally handicapped child or one who would have to fight all its life against possible death from cystic fibrosis, are we not reinforcing the second-rate status of such handicapped individuals? And what would be the consequences of isolating genes that give rise to the various forms of dyslexia, opening up the possibility that women will take antenatal tests to see if their prospective child is likely to have a bad reading disorder? Is it not conceivable that such tests would lead to our devoting less resources to the currently reading-handicapped children whom now we accept as an inevitable feature of human life?

That such conundrums may never be truly answerable, however, should not concern us too much. The truly relevant question for most families is whether an obvious good to them will come from having a child with a major handicap. Is it more likely for such children to fall behind in society or will they through such affliction develop the strengths of character and fortitude that lead, like Jeffrey Tate, the noted British conductor, to the head of their packs? Here I'm afraid that the word handicap cannot escape its true definition—being placed

at a disadvantage. From this perspective, seeing the bright side of being handicapped is like praising the virtues of extreme poverty. To be sure, there are many individuals who rise out of its inherently degrading states. But we perhaps most realistically should see it as the major origin of asocial behavior that has among its many bad consequences the breeding of criminal violence.

Thus, only harm, I fear, will come from any form of society-based restriction on individual genetic decisions. Decisions from committees of well-intentioned individuals will all too often emerge as vehicles for seeming to do good as opposed to doing good. Moreover, we should necessarily worry that once we let governments tell their citizens what they cannot do genetically, we must fear they also have power to tell us what we must do. But for us as individuals to feel comfortable making decisions that affect the genetic makeups of our children, we correspondingly have to become genetically literate. In the future, we must necessarily question any government that does not see this as its responsibility. Thus, will it not act because it wants to keep such powers for itself?

THE MISUSE OF GENETICS BY HITLER SHOULD NOT DENY ITS USE TODAY

Those of us who venture forth into the public arena to explain what genetics can or cannot do for society seemingly inevitably come up against individuals who feel that we are somehow the modern equivalents of Hitler. Here we must not fall into the absurd trap of being against everything Hitler was for. It was in no way evil for Hitler to regard mental disease as a scourge on society. Almost everyone then, as still true today, was made uncomfortable by psychotic individuals. It is how Hitler treated German mental patients that still outrages civilized societies and lets us call him immoral. Genetics per se can never be evil. It is only when we use or misuse it that morality comes in. That we want to find ways to lessen the impact of mental illness is inherently good. The killing by the Nazis of the German mental patients for reasons of supposed genetic inferiority, however, was barbarianism at its worst.

Because of Hitler's use of the term *master race*, we should not feel the need to say that we never want to use genetics to make humans more capable than they are today. The idea that genetics could or should be used to give humans power that they do not now possess, however, strongly upsets many individuals first exposed to the notion. I suspect that such fears in some ways are similar to concerns now expressed about the genetically handicapped of today. If more intelligent human beings might someday be created, would we not think less well about ourselves as we exist today? Yet anyone who proclaims that we are now perfect as humans has to be a silly crank. If we could honestly promise young couples that we knew how to give them offspring with superior character, why should we assume they would decline? Those at the top of today's societies might not see the need. But if your life is going nowhere, shouldn't you seize the chance of jump-starting your children's future?

Common sense tells us that if scientists find ways to greatly improve human capabilities, there will be no stopping the public from happily seizing them.

Charles Benedict Davenport, 1866–1944

Jan A. Witkowski
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Editors' Note: Charles Davenport was a complex character—he was one of the earliest human geneticists, who was quick to pick up on and accept Mendelism and who recognized the relationship between genetics and evolution. Yet, his original biographer E. Carleton MacDowell described Davenport as having "a deep lack of confidence," and stated that he had a "defensive attitude which led to exaggerated emphasis and dulled objective thinking"—weaknesses that are reflected in his role in the U.S. eugenics movement. Dr. Witkowski describes the arc of Davenport's life and puts into context his strengths and weaknesses, as well as his legacy at Cold Spring Harbor.