7. The Human Genome Initiative and Human Responsibility

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The Human Genome Initiative is a massive government undertaking designed to determine the structure of every gene in the human body. It has been presented to the public as a concentrated scientific effort aimed directly at knowledge that will cure disease. In reality it is a controversial multiagency set of programs with unclear medical implications but with a growing impact on how we think of ourselves as individuals.

From its scientific origins to the present, the Human Genome Initiative has illustrated the fundamental relationship between science and society. At the outset, the basic research that made the initiative possible was typical in that it followed an erratic course driven by scientific norms and resistance to political controls.

The Development of Modern Genetics

The story of modern genetics began over a century ago and proceeded with discoveries that followed anything but a straight line.[1] In 1866, the Austrian monk Gregor Mendel published a paper concerning the breeding of sweet peas. Presumably few people in history have failed to notice that living organisms pass on traits to their offspring, but Mendel made an unusually systematic inquiry into the process. When he bred tall peas with tall and short with short, the offspring were true to type—the tall begat tall and the short begat short. When he bred tall and short, the offspring were all tall. But when these mixed ancestry tall plants were

crossed, 75 percent of their offspring were tall and 25 percent were short. From these and similar results, Mendel was able to deduce that inherited traits were determined by two heredity units, one from each parent, and that the agents of inheritance might turn out to be dominant or recessive.

Mendel did not, however, know the mechanism through which inheritance took place; indeed, the word *gene* did not exist in his day, nor did he coin it. Unbeknownst to Mendel, at the same time he was crossing sweet peas, the Swiss scientist Friedrich Miescher was determining that what we now call deoxyribonucleic acid (DNA) was found in the nucleus of cells. Miescher was unaware of Mendel's work, and, even if he had been, it is unlikely that any connection between them would have been made. Although Miescher sensed that his work had implications concerning cellular growth, the science and technology of his day were unable to uncover the basic structure of DNA, let alone its relationship to the mechanism of inheritance.

These modest beginnings of modern genetics demonstrate the folly of efforts to force basic research to produce precisely defined social ends. Imagine a regulatory agency that somehow had jurisdiction over farflung researchers such as Mendel and Miescher and that sought to shape all science for specific social ends such as better medicine. Even if such hypothetical masterplanners were indifferent to both the freedom of the researcher and the value of knowledge for its own sake, they would founder on the sheer unpredictability of scientific progress. After Mendel and Miescher it simply was not knowable which characteristics of human beings were inherited, how if at all such characteristics could be changed, and at what cost such changes could be made. It was not even immediately clear if their work related to health or if it had any practical implications at all. Although as research progresses its technological implications become more evident, at the very beginning the future is nearly invisible.

Indeed, the next steps in the unraveling of the human genetic code were not even inspired by Mendel's work, which was published but lay unread for decades. Instead it was Charles Darwin's theory of evolution that sparked the rediscovery of Mendel's ideas and subsequent progress. Darwinian evolution required, of course, that organisms pass on certain traits; otherwise the survival of the fittest would last exactly one generation. Yet Darwin, unaware of Mendel's research, wrote that "[t]he laws

governing inheritance are for the most part unknown. No one can say . . . why the child often reverts in certain characteristics to its grandfather or grandmother or more remote ancestor."[2]

In the latter part of the nineteenth century, controlled experiments in botany confirmed Darwin's idea that mutations leading to fitness enhanced survival. Finally, in 1900, unknown to each other and unaware of Mendel, three botanists rediscovered Mendel's laws. Each of the three—Karl Correns of Germany, Erich von Tschermak of Austria, and Hugo de Vries of Holland—searched the literature, found Mendel's paper, and credited him for the discovery. Thus we speak today of Mendel's laws and Mendelian inheritance rather than Correns's laws or de Vries's inheritance.

Not every scientist has been as gracious as Correns, von Tschermak, and de Vries, but their reference to Mendel does illustrate the fundamental role priority plays in the value system of science. It's coming in first that counts—not how well-written your paper is or even how clever you may be. An independent rediscovery might take as much sheer brilliance as the original discovery, but it does not generate equal fame. Indeed, even if the trio of researchers in 1900 had not cited Mendel, we still might invoke the monk's name if later research had uncovered his work. By rewarding priority science puts progress first. A researcher seeking recognition within the scientific establishment is on notice that repeating old work will not lead to the greatest rewards. Finally, the emphasis on priority supports the cumulative nature of science. One reads earlier work to avoid repetition, and one is then in a position to build on that work.

The contrast with law is striking. Consider the development of the idea of privacy, a concept that, as we will see, has important implications for individuals' control over information about their genetic makeup. Most lawyers and legal scholars associate the early development of modern privacy law with U.S. Supreme Court Justice Louis D. Brandeis. It was, after all, Brandeis who wrote the famous dissent in the 1928 *Olmstead* case in which he called for extending the constitutional protection against unreasonable searches and seizures to wiretapping,[3] a position the Supreme Court ultimately adopted in 1967.[4] In the most famous passage in *Olmstead*, Brandeis said that the makers of our Constitution "conferred, as against the Government, the right to be let alone—the most comprehensive of rights and the right most valued

by civilized men."[5] Thus we associate Brandeis with "the right to be let alone."

Careful scholars have noted that when Justice Brandeis discussed the "right to be let alone" he was drawing on a law review article, "The Right to Privacy," he had coauthored in 1890 while practicing law.[6] But even here there often seems to be an assumption that it was Brandeis rather than the coauthor, Samuel D. Warren, who was the primary force behind the article. In fact it was Warren, whose marriage to a prominent woman had led magazines to report on his life "in lurid detail," who proposed to Brandeis that the piece be written.[7] In any event, it was neither Brandeis nor Warren who first spoke of privacy as the right to be let alone. As they noted in their article,[8] this idea was drawn from a passage in Thomas Cooley's 1888 *Treatise on the Law of Torts:* "The right to one's person may be said to be a right of complete immunity: to be let alone."[9]

Now Cooley was not an obscure man in his day. He served on the Supreme Court of Michigan, he was a professor of law, and he was a prolific writer on legal topics.[10] If scientific conventions governed, law students today would speak of Cooley's right to privacy. But there is nothing surprising or inappropriate about the use of Brandeis's name instead. Brandeis wrote more powerfully, he applied the idea more broadly, and his position on the U.S. Supreme Court gave his words special importance. Priority alone is hardly decisive in the law.

After the rediscovery of Mendel's laws in 1900, the focus shifted to finding the chemical basis for heredity. By 1940 a series of scientists had established that the units of heredity were contained in sausage-shaped structures called chromosomes in the nucleus of every cell. These chromosomes carried genes that determined an organism's biochemical characteristics. Chromosomes, it had been determined, came in pairs, with each parent providing one of each pair. Genes were known to produce proteins and enzymes, the source of the structure and chemistry of living matter.

In the early 1940s researchers at the Rockefeller Institute in New York found evidence that genes were made of DNA, the substance found decades earlier by Friedrich Miescher in the nucleus of cells. The puzzle was that DNA seemed too simple to carry out genetic instructions while replicating itself for the next generation. The mystery was solved by the 1953 publication of James Watson and Francis Crick's paper setting

forth the double helical structure of DNA. A rapid series of later discoveries filled in the precise nature of the genetic code.

The discovery of the double helix is a classic example of the role of aesthetics in science: the double helix was an elegant structure, inspiring Watson to write that he and Crick were convinced that "a structure this pretty just had to exist."[11] A scientist cannot force the world to fit his image of beauty. But that image can inspire his efforts to find something that will later stand up—as the double helix did—to verification by others.

The discovery of the double helix also points up again the centrality of priority in the scientific endeavor, although it is an aspect of priority that is less attractive than the trio of researchers independently crediting Mendel's earlier work. Priority can also mean winning a close race against someone you know is working in your area. Watson was aware that the great scientist Linus Pauling was also seeking to find the structure of DNA. When Watson, immediately after the discovery of the double helix, wrote to professor Max Delbrück about his breakthrough, he urged Delbrück not to tell Pauling:

> I was still slightly afraid something would go wrong and did not want Pauling to think about hydrogen-bonded pairs until we had a few more days to digest our position. My request, however, was ignored. Delbrück wanted to tell everyone in his lab. . . . Then there was the even more important consideration that Delbrück hated any form of secrecy in scientific matters.[12]

Watson's experience with the tension between priority and secrecy is typical. Trying to keep matters secret is, if nothing else, difficult. In the end, prompt publication is typically the best guarantee of priority.

As we have seen, the role of priority changes radically when one moves from science to law. Indeed, it is not simply a matter of crediting Brandeis rather than Cooley for the right to privacy because of the former's greater eloquence and prestige. At times, coming in second is better for a judge or a lawyer. Being the first to confront an issue can happen by chance and a result initially reached often has to be amended in light of experience.

Consider, for example, the admissibility in criminal trials of evidence from what has come to be called DNA typing.[13] Apart from identical twins, any two people differ, albeit very slightly, in terms of their DNA. Criminals often leave behind hair follicles, blood stains, or other sub-

stances from which DNA can be extracted. A suspect's DNA can then be compared with the crime scene evidence to see if they match. The system is not foolproof. Typing the DNA in the laboratory must be done very carefully so that errors do not creep in. Moreover, with present technology, it is only possible to type a portion of an individual's DNA, so there is a small chance that when two samples match they are, in fact, from different people—the match is simply a coincidence. The odds of such a match between samples from two different individuals' DNA are higher if the two are related, or of the same race, or otherwise more closely linked genetically than two people chosen at random from the world's population.

The first appellate decision ruling on the admissibility of DNA evidence in a criminal trial was a 1988 Florida judgment upholding the use of such evidence.[14] But just being first hardly granted this court any special status. The case reached the court when it did because of the size of the appellate docket, not because of any wisdom on the part of anyone. Moreover, a judge's decision that a certain kind of evidence is admissible does not resolve an issue in the way that a scientific discovery does. In our federal system, other states can take other views and a given court can even reverse itself if relevant value choices or social mores change.

In fact, the 1988 Florida decision has been strongly criticized, particularly on the grounds that the court did not consider thoroughly enough the possibility of laboratory errors or the chances of a coincidental match.[15] A later New York decision that was more careful on these points and excluded the evidence before it has been better received.[16] The point is not that it was a mistake to admit DNA evidence—at present such evidence is admissible in most jurisdictions if it is carefully obtained and analyzed.[17] The point is that the first judicial decision is often the recipient of potshots rather than praise.

In the decades following the discovery of the double helix, the model of inheritance that underlies the Human Genome Initiative came into sharp focus.[18] The term *genome* is used to refer to all the genetic material in the chromosomes of a particular organism. Each human has twenty-three pairs of chromosomes; one in each pair from the father, one from the mother. Each chromosome contains a long strand of DNA, the chemical that makes up the genes. The DNA is a two-stranded chemical polymer with each strand composed of four nucleotides: A

(adenine), G (guanine), C (cytosine), and T (thymine). DNA, as Watson and Crick found, is a double helix in that each nucleotide on one strand is precisely paired with another nucleotide on the other strand: A will only bond with T and G will only bond with C. During cell division the double helix "unzips" and each strand can serve as a template for the creation of a complementary strand. Because of the specific bonding between nucleotide pairs, precise replication of the DNA is assured, resulting in two perfect copies.

A given chromosome contains an average of about four thousand genes whereas a given gene consists of anywhere from two thousand to two million nucleotide pairs. Thus a complete description of the human genome would contain about three billion nucleotide pairs. It would appear to be a long list, filling over a million pages in a book, made up entirely of the letters A, T, G, and C.

This list is valuable because gene sequences are consistent within species. Thus a particular gene on a particular human chromosome controls the same trait in all humans. In genetic terms we are more alike than we are different; according to current estimates, the DNA sequences for two randomly selected individuals are likely to be over 99 percent identical—the remainder accounts for the genetic differences between the two.[19] Indeed, the current belief is that human and chimpanzee sequences are about 98 percent identical.[20]

The Human Genome Initiative is not going to actually take a single person and list his or her three billion nucleotide pairs—it will instead be a composite drawn from cell lines of people around the world over several decades. The effort, which is underway but will require further advances in technology to be practical, is expected to cost about $3 billion over the next ten years. The result will be in essence a reference set, enabling, for example, comparisons to be drawn with people suffering certain ailments in an effort to find a genetic cause.

The Political History of the Genome Initiative

It would be hard to imagine a more unitary goal than mapping the human genome. One might expect that here at least a single federal agency would do the job. But fragmentation, not unity, is central to American science spending, and that truth holds true here.

The political history of the Human Genome Initiative reveals the

strengths and weaknesses of our decentralized approach to government science.[21] As early as the 1970s there were discussions concerning whether it would be sensible to map the human genome. At first, the federal government did not show much interest. Those efforts that did take place were found largely in the private sector, particularly at the philanthropic Howard Hughes Medical Institute.

In 1984, however, the Department of Energy held a conference in Alta, Utah, which began substantial federal involvement. As a successor agency to the Atomic Energy Commission, the Department of Energy had a special interest in the effects of radiation. The Alta meeting focused on whether advances in DNA research could improve the government's ability to detect increases in mutations among survivors of the atomic bombings of Hiroshima and Nagasaki. Participants in the meeting discussed the possibility that a reference sequence of the human genome could be helpful in this endeavor. By the time of a 1986 conference in Santa Fe, New Mexico, enthusiasm for sequencing the genome had grown; shortly thereafter, officials at the Department of Energy reallocated a few million dollars of previously appropriated money to begin the Human Genome Initiative. Support was then sought and won for congressional appropriations to keep the project going. The initial reallocation was not unusual in terms of the reality of how large agencies, particularly in the technical field of science spending, operate and, as we have seen, it is not the sort of decision typically subject to judicial oversight.

As word spread in the scientific community about the Department of Energy effort, officials at the National Institutes of Health inevitably became interested. The NIH, after all, is the leading supporter of biomedical research in the United States, and it could see implications of the genome initiative in health areas far removed from mutations caused by radiation. By 1987, NIH had created its own office of genome research and had begun to receive federal funding.

In its early stages, both in the Department of Energy and in NIH, the genome initiative was pushed by research scientists. As one commentator has noted:

> The history of the genome project makes it clear that scientists played a crucial role in starting it, and they were the sources to which policymakers turned for advice along the way. . . . A few pivotal scientific figures—the scientists who took the trouble to learn about the policy process and to interact with it—

clearly had enormous influence. Watson was preeminent among these, but Hood, Gilbert, Bodmer, Baltimore, Berg, Dulbecco, Alberts, Cantor, Olson, and others had major effects at critical junctures.[22]

The attraction of scientists to the genome project stems in part from adherence to purely scientific values. If it is desirable, as many scientists believe, simply to know as much as possible about the way the world is, then knowing the genetic makeup of humans is a worthy goal. There is a kind of elegance in a finite list of four letters in various combinations representing the complete genetic identity of the human species. Surely this helps explain the desire of many scientists to map and sequence the entire human genome, even though 90 percent of the base pairs appear to have no genetic function and the money used in this endeavor could obviously be used in other ways.[23]

Today the Department of Energy and NIH coordinate their genome efforts, and seek to coordinate as well with efforts in the private sector and overseas. Nonetheless there is unavoidable inefficiency in having two major agencies working together in this fashion. This is most dramatically demonstrated in Congress. Because no one agency (let alone a Department of Science) runs the genome show, no one committee has jurisdiction over authorizing the spending of the taxpayers' money. Thus in the House of Representatives, authorization for the Department of Energy's genome program goes through the Science, Space, and Technology Committee, whereas the NIH seeks genome money from the Labor, Health, Human Services, and Education Committee. On the Senate side, things are no better organized: the Department of Energy genome project answers to the Energy and Natural Resources Committee, whereas NIH genome requests are analyzed by the Health and Environment Committee. Indeed, even this catalogue is not exhaustive; some genome money is spent by still a third federal agency, the National Science Foundation, which answers to its own pattern of oversight on Capitol Hill.

To someone new to American science, this approach would seem at least odd, and almost surely controversial. But here as in other areas of science we are comfortable with inefficiency because of our fear of centralization. Different agencies means different approaches, and new technologies for analyzing genetic material will have to be developed if the Human Genome Initiative is to be finished without unreasonable expense. Moreover, disparate funding sources provide some protection

against sudden reductions in government support. Thus the Congressional Office of Technology Assessment rejects even designating a lead agency for the genome effort: "if there were a single lead agency controlling genome projects, the choices would be limited, diminishing the pluralistic funding that has been a mainstay of American biology."[24]

And so the Human Genome Initiative moves forward in typical American fashion: in an array of agencies the scientific community, motivated in large part by the ethos of pure science, shapes the direction of research. Supervision by Congress is limited, and control by the judiciary is essentially nonexistent. The result is that the Human Genome Initiative, like much of American science, lumbers forward a bit slowly but it does keep moving; indeed, it becomes close to unstoppable once it is fully underway.

Big Science versus Little Science in Genome Research

This account should not be taken to suggest that there are no divisions in the scientific community concerning the genome initiative. In general, scientists support large budgets for scientific research more or less across the board. Most would rather see cuts in nonscientific programs before cuts are made in science. This approach enabled the scientific community to remain largely unified concerning federal support for research in the decades following World War II. But the budgetary pressures that began to grow in the 1980s brought increasing pressure on scientists to pick and choose concerning which projects they would support before Congress. A key event in this process was a 1988 speech by Frank Press, president of the National Academy of Sciences and former head of the Office of Science and Technology Policy, in which he explicitly called on scientists to provide guidance to politicians on research priorities so that important work could be protected as budgets tightened.[25]

It was in this environment that the Human Genome Initiative began to take shape. Moreover, the initiative was subject to a very specific complaint within the scientific community—it was said to represent "big science" over "little science," a criticism that requires a bit of explanation.

Whereas scientific research may once have been largely the province of the individual or small teams, the twentieth century has seen the growth of activities (such as the Manhattan Project and the space pro-

gram) that involve hundreds, even thousands, of people and vast sums of money. The classic description and analysis of this trend is *Little Science, Big Science* by Derek J. de Solla Price.[26] Of course, there is a continuum between large and small projects, and there is no reason science programs of various sizes cannot be simultaneously funded, as indeed they are today. But at the extreme ends of the spectrum, undertaking one gigantic project may in reality foreclose funding for hundreds of smaller research grants, while bestowing money on a wide array of small research programs may make it impossible to undertake one or more big ones.

The little science, big science controversy has been largely fought out within the scientific community itself. From the beginning, the Human Genome Initiative has been attacked by some scientists, particularly younger ones, as a misguided intrusion of big science into biomedical research, a field that has been characterized by small initiatives heading in many directions.[27]

A key supporter of these concerns in the early days of the initiative was Ruth Kirschstein, director of the National Institute of General Medical Sciences, a branch of the National Institutes of Health and the largest source of funds in the world for small-scale genetic research.[28] But the initiative was not sidetracked by these concerns, in part because of the important scientists who supported it, and in part because it was not big science in the same way as the superconducting supercollider. The initiative is a centralized effort, but it is carried out in numerous laboratories around the country. Moreover, it involves the development of automated technologies for mapping the gene and of computerized approaches to information problems, both of which are techniques of broad value to biologists doing other, smaller scale research jobs.[29] In the end, the arguments for the initiative carried the day within the scientific community; indeed, the initiative ultimately won the public support of Ruth Kirschstein.[30]

So the scientific community, as is typical, called the shots in the formation and execution of this major research effort. Of course, a continued refrain that helped keep the genome initiative politically palatable was the promise of a payoff down the road, in particular an "immense benefit to the field of medicine."[31] Such claims are certainly plausible. But, as always, these payoffs will be slower in coming and more piecemeal than it appears when the basic research is underway,

because it is here that the regulatory gap inevitably comes in. When science leads to technology—when biomedical research leads to medicine—the road is not smooth. In the case of the Human Genome Initiative, the medical payoffs will be slow in coming and controversial, and even the increases in our knowledge about ourselves will lead to problems concerning personal privacy.

Science Counselors at Work

Before turning to these difficulties, however, it must be noted that the gap between science and social impact has been narrowed in the genetics area, at least as compared with our experience with nuclear power. Indeed, the nuclear experience made a difference. In the early 1970s, before there was any Human Genome Initiative, DNA researchers began to work in the related area of recombination. Scientists began to understand that they could alter genetic material and create new biological entities. These scientists themselves saw the possibility not only of better medicines or crops, but of new diseases and new threats to the public safety. One reason they had this level of concern was their sense that they were working in the shadow of nuclear power and nuclear bombs. Thus as early as 1971 cancer researcher Robert Pollack believed that lax safety standards in laboratories doing recombinant DNA research posed a " 'pre-Hiroshima condition—It would be a real disaster if one of the agents now being handled in research should in fact be a real human cancer agent.' "[32] In 1974, future Nobel laureate David Baltimore explained his concerns about biohazards by noting that "we all grew up with the question of the correctness of using the atomic bomb as one of the great moral dilemmas of the second part of the twentieth century. And I don't think that any of us are untouched by that."[33]

The analogy between atomic bombs and recombinant DNA is hardly precise. The first involved a conscious decision by government and scientific leaders to build a weapon of war, and a subsequent decision by the president to use that weapon. By contrast, the main early concern with genetic engineering was that an accident might lead to tragedy; although recombinant DNA research presumably could be used in warfare, that was not the concern Pollack and Baltimore were addressing.

In a larger sense, however, the nuclear experience was relevant. It pointed up the inevitable social consequences when science becomes

technology and it dramatized the ways in which those consequences could be negative. Moreover, the debate over the civilian uses of nuclear power, a debate that had already begun by the 1970s, made clear to many scientists and others that weapons were not the only unwelcome consequence of science.

In the recombinant DNA field these heightened concerns had real results. For about seven months in 1974 and 1975, scientists themselves observed an international moratorium on certain DNA research.[34] Subsequently, the scientific community drafted voluntary research safety guidelines that became the basis of later government regulations.[35] In helping to shape the restrictions under which their own research would take place, scientists acted as science counselors, shoring up public acceptance of their work and attempting to pave the way for greater public use of technology.

And this is the way it will be for genetic engineering from now on. Not a moratorium by any means, but a lengthy back-and-forth process in the agencies, courts, and legislatures as the new technology simultaneously adjusts to and alters existing rights and values. The result has been a small but growing industry built on the results of DNA research; a promising field for some investors, but not an instantaneous boom stemming directly from the work of Watson and Crick.[36]

Science counselors have been at work as well with the Human Genome Initiative, and thus, here too, we can expect steady if relatively undramatic commercial progress. In 1989 the government created a working group of scientists and others on the ethical, legal, and social issues related to the initiative, and the government has continued to fund conferences and studies undertaken by this group.[37] These endeavors have undoubtedly illuminated the future to some extent. But even advance warning cannot make the road ahead completely smooth, as the following survey of issues identified by the working group makes clear.[38]

The Regulatory Issues Ahead: Gene Therapy and Privacy

Consider first the matter of gene therapy, the most highly publicized benefit from compiling genetic information. As our knowledge of the human genome has increased, there have been discoveries relating to the genetic basis of disorders such as cystic fibrosis, Huntington's disease, and amyotrophic lateral sclerosis (Lou Gehrig's disease). These discover-

ies are generally accompanied by the statement that genetic engineering may someday lead to therapies, either for the affected individual or for that person's offspring.[39] But the key word here is "someday." Our actual experience with gene therapy suggests that patience should be the watchword.

The key figure in the first use of human gene therapy was Dr. W. French Anderson, who conceptualized and brought into play a treatment at the National Institutes of Health for two children with severe combined immunodeficiency (SCID).[40] People with SCID are born with a genetic defect that destroys their immune systems and leaves them vulnerable to countless infections. At one time, SCID victims were put in plastic bubbles to protect them from the world around them; more recently, drugs and other treatments provided some relief. Dr. Anderson's approach involved removing blood cells from the victims, using retroviruses to insert normal genes into them, cultivating the repaired cells and then reintroducing them into the body.

This procedure avoided the most controversial application of gene therapy because it did not involve the patient's germline cells; in other words, the changes in the patient would not be passed on to children. Still, when the proposal was formally put forward in 1990, it had to undergo an arduous process of review. There was, after all, the background debate over genetic engineering led by Jeremy Rifkin, as well as the ordinary concerns about the risks of a new treatment. The proposal had to be approved by the Recombinant DNA Advisory Committee of the National Institutes of Health, as well as by the Food and Drug Administration. Dr. Anderson's test received approval and has proceeded with encouraging results. Other proposals have since received approval from the same federal agencies.

Thus the current situation with gene therapy is one where a cautious case-by-case approach is in place for a list of genetic ailments. As the Human Genome Initiative moves forward, new information will be gained that will increase the list of potential defects subject to gene therapy. But as Dr. Anderson himself has explained, this type of therapy as presently practiced will hardly revolutionize modern medicine—it simply is too cumbersome to reach far into the lives of most people:

> How much impact will gene therapy have on medical practice in the future? Not a great deal so long as the technique is carried out as it is today, where cells are removed from patient, the desired gene is inserted, and the gene-corrected cells

are returned to the patient. This procedure is too dependent on specialized technologies, is too expensive, and requires too much scientific and medical expertise to be used extensively except in major medical centers. . . . [G]ene therapy will be applied to a broad range of diseases over the next several years, but only thousands, not millions, of patients are treatable by current techniques.[41]

Dr. Anderson speculates that gene therapy will become more widespread when we develop a way to inject vectors that will repair cells into patients just as drugs like insulin are injected now, although he cautions, as a science counselor should, that "[a]lthough the medical potential is bright, the possibility for misuse of genetic engineering technology looms large, so society must ensure that gene therapy is used only for the treatment of disease."[42] Thus gene therapy will move forward slowly, given not only the complex technology involved, but the absence of a societal consensus on what needs to be repaired. Huntington's disease is an easy case, but extreme lack of height, for example, is not.

But what about the benefits the Human Genome Initiative will bring apart from therapy? Surely there is much to be gained in simply knowing one's own genetic code, completely apart from the question of changing that code. The initiative holds out the possibility that someday individuals will be able to find out their own susceptibility and that of their children not only to ailments like cystic fibrosis, but to syndromes like heart disease and certain types of cancer. Even if we assume there are environmental components to these illnesses, and even if we assume there is no magic genetic therapy, surely people would want to know what they are facing so they can, to the extent possible, take precautions.

Actually, we already have evidence that many people simply will not want to know. Consider the case of Huntington's disease, a genetic condition for which the symptoms do not become visible until the carrier reaches middle age. The symptoms are devastating, including dementia, a severe loss of physical control over oneself, and a wasting away as dramatic as that caused by cancer.[43] At present, with Huntington's disease being detectable but not treatable, over half of the at-risk adults advised of the test for its presence decline to take it.[44] Moreover, most geneticists will not test children at all for this ailment, given the possibility that the child, when grown, may not wish to know.[45] In general, with a variety of genetic ailments, researchers have found that revealing the

existence of the ailment can cause anxiety, depression, and a feeling that one has been stigmatized.[46]

Even those individuals who want to know all they can about their own health prospects may hesitate before undergoing genetic screening. The reasons are not hard to fathom. First of all, if your genetic information is knowable, insurance companies will want to know it. They will want to charge higher premiums for those likely to get heart attacks than for those who are not predisposed to heart disease. Most importantly, insurance companies will not want to sell their product at all to people who know a lot more than they do about their odds of getting sick. Insurance company representatives have quite predictably and quite appropriately been involved in the discussions to date of the initiative. They and others have already begun to debate whether genetic testing should be required, allowed, or forbidden in the insurance world and how all of these issues intersect with questions relating to national health insurance. No one can presently predict the outcome of any of this, but clearly there are important reasons why society may want to go slowly in gathering and disseminating genetic information.

And insurance issues are small compared to those surrounding employment. Should an airline be able to look at the genetic profile of a potential pilot? What about a school board interested in whether a prospective teacher is likely to contract cancer in the next ten years? Here notions of individual privacy and autonomy will militate strongly against those seeking to gain genetic information about others. Working out the appropriate boundaries will take decades of legislation and litigation. In the meantime, the safest course for many individuals will be to avoid obtaining information about themselves.

So the practical impact of the Human Genome Initiative—the technology that flows from it—will not quickly reshape society. Gene therapies for diseases are likely to remain rare for decades, and those that are proposed will have to undergo years of testing and regulatory approvals before use. The initiative will yield information that can lead to predictions of disease if not cures for many individuals, and this information will have an impact when people plan their careers and their childbearing decisions. But even here concerns about insurance and employment will retard the acquisition and dissemination of information as our legal culture slowly works out an accommodation between privacy and efficiency concerns.

Determinism and Human Values

Yet the Human Genome Initiative already has had an impact on our society. For if the regulatory gap means a delay in technology, the road between basic research and the formation of values remains wide open. Stressing the most dramatic implications of basic research serves the funding goals of science administrators and the professional norms of popular journalists. Thus the mainstream media have already seen the initiative as opening up the possibilities of the most dramatic sort of manipulation of human nature. *Time* magazine headlined a story on the initiative, "Seeking a Godlike Power: Science Promises to Deliver the Blueprint for Human Life."[47] The story referred to genetic technology as giving humankind the "awesome ability," indeed, the "almost godlike power to improve its condition."[48] In another story, *Time* told us that genetic research will give us "the genetic tool kit for building such intellectual traits as musical talent, mathematical genius and, above all, personality."[49] A book reviewer in *Fortune* magazine was no less modest: "In essence, genetic engineering will make humanity mutable. . . . Our great-grandchildren may be more like designed artifacts than random genetic mixes like ourselves."[50]

There are more than a few problems with these formulations; indeed most geneticists recoil from the simplistic determinism that underlies these ideas.[51] Even the terminology is misleading, because most popular accounts seem to assume there will be "a gene" for some trait, when, in fact, monogenic disorders are rare—most common genetic disorders involve the interaction of several genes, often genes on different chromosomes. More importantly, most traits, whether monogenic or multigenic, are shaped by both heredity and environment. Even when Mendel bred tall peas with tall, the offspring would not do very well if they were tossed in vats of acid. All we can typically say is that certain traits are likely to be inherited in an appropriate environment. Most human diseases are genetically linked only in the sense that genes make us more or less susceptible to them; whether we actually get them depends on a host of environmental factors. That is why the periodic discoveries of a "gene for alcoholism" are misleading; some genetic factors may explain why some people drink too much, but many other factors, including everything from family structure to religious practice, play a role in countless cases.[52] This is all the more true with personality traits, not to mention

complex ideas like "intelligence." One group of scientists and policymakers concluded that "[t]he number of combinations that 100,000 genes can form interacting with one another and with the environment is essentially infinite, so we do not now foresee [the Human Genome Initiative], at any rate, leading to fundamental changes in what we regard as the nature of the self."[53]

The notion that our knowledge of the gene can lead to "a genetic tool kit" to remake humanity enjoys currency in part because it plays into deep-seated American ideas about the inevitability and desirability of progress—ideas that closely fit with scientific norms. Americans have always tended to believe that our condition can be bettered, including the condition of ourselves. In an earlier era improving the human species was called eugenics, an idea with considerable influence in this country.[54] Indeed, it is precisely the science counselors involved in the Human Genome Initiative who are trying to perform the important function of calming down public expectations about what genetics can do and of pointing up some of the dangers in pushing genetic capabilities to their limits. After all, even if a trait is controllable by genetic manipulation, that hardly means it should be so controlled. Curing Huntington's disease is one thing; "curing" "shortness" is another. As one commentator put it, a "counterattack of technically knowledgeable" voices has tended to subdue "the new eugenics."[55]

Finally, at the deepest level, the public debate about genetic explanations of human nature reflects the extraordinary impact of scientific models on the formation of our values. Keep in mind that, for many, the "moderate" position is to temper genetic theories with a recognition of the importance of the environmental factor in human behavior. But even to accept a complex interaction of environment and genes as an explanation of what it is to be human is to accept what remains deeply problematic from nonscientific perspectives. Attributing behavior to genes plus environment is still inherently deterministic. It may make human behavior hard to predict, it may mean that certain behavior can only be explained probabilistically or as the result of chance, but it means that free choice is out of the picture. For the work of scientists that is certainly understandable, and that work has illuminated human actions along with the actions of planets and electrons. But for humans the possibility of free will remains, and the related ideas of responsibility, praise, and blame remain as well. The public discourse

about what it is to be human should not be restricted to the scientific world view.

From a philosophical perspective, the Human Genome Initiative adds little if anything to the age-old debate about free will and determinism. It has always been possible to imagine physical causes for human actions, and it has always been possible to argue that nonetheless our sensations of freedom and choice are real and meaningful. Determinists have had their champions, from Hobbes to Hume, as have the opponents of determinism, from Aquinas to Kant to the present.[56] Long before the Human Genome Initiative, the determinist Robert Fearey argued that "[m]an's variegated character and wide capacities have blinded us to the fact that he is in fact as passive to his creation and development, and hence as unaccountable for his actions, as an inanimate machine."[57] Long after the implications of modern genetics became clear, a secular philosopher, Stuart Hampshire, argued that "[o]ne may say that the sense of freedom that men undoubtedly have is to be identified with their power of reflection and with the self-modifying power of thought. The intuition that when we are thinking of ourselves as thinking beings, we are excluding deterministic explanations of our performances, can be justified, so far at least."[58] And these hardly exhaust the positions of what remains a lively area of philosophical debate. Theological scholars continue to analyze the ideas of freedom and responsibility, with some contending, for example, that Christianity holds an individual "responsible for his actions not only to secular authorities and his fellowman, but also to God,"[59] whereas a secular school of thought called compatibilism maintains that deterministic causation is not incompatible with ideas of responsibility. As Michael Moore has argued, when you show that glaciers caused Lake Michigan, you are not showing that Lake Michigan does not exist.[60]

Our public consideration of who we are as humans should be open to purely scientific perspectives, but it should not and it need not be limited to those perspectives. Nothing in the substance of the Human Genome Initiative or in the structure of American law is to the contrary. There is nothing in our ban on established religion or in our settled traditions that prevents discussion of the secular and theological dimensions of the issue of free will in our classrooms as well as in our media. The pathway for scientific influence on our value formation is wide open, but the pathway for other influences can be just as inviting.