Annu. Rev. Anthropol. 1998. 27:473–502

LEGAL, ETHICAL, AND SOCIAL ISSUES IN HUMAN GENOME RESEARCH

Henry T. Greely
Stanford Law School, Stanford University, Stanford, California 94305-8610;
e-mail: hgreely@stanford.edu

KEY WORDS: genetics, ethics, law, society, project

ABSTRACT

In the past several decades, biological sciences have been revolutionized by their increased understanding of how life works at the molecular level. In what ways, and to what extent, will this scientific revolution affect the human societies within which the science is situated? The legal, ethical, and social implications of research in human genetics have been discussed in depth, particularly in the context of the Human Genome Project and, to a lesser extent, the proposed Human Genome Diversity Project. Both projects could have significant effects on society, the former largely at the level of individuals or families and the latter primarily at the level of ethnic groups or nations. These effects can be grouped in six broad categories: identity, prediction, history, manipulation, ownership and control, and destiny.

INTRODUCTION

> It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.
> Watson & Crick (1953)

Watson & Crick did not announce the discovery of DNA in their famous, understated paper. Nor did they invent molecular biology or human genetics. But the now-familiar double helix they discovered, with its embedded sequence of nucleotides coding for proteins, has combined with the so-called "Central

0084-6570/98/1015-0473$08.00

Dogma"—that genetic information passes from DNA to RNA to protein—to transform biology (Judson 1979). The result has been a vision of DNA molecules, and the genomes they constitute, as the "blueprints" of life with vast consequences for science.

Nor did it escape the notice of others that the science of DNA, when applied to humans rather than bacteria or fruit flies, immediately suggested many and varied applications to human affairs. As the tools for analyzing and understanding the human genome improved, the possible value of those tools for understanding human lives captured the attention of many publics, academic, political, and popular. Forty-five years later, the implications of human genome research for human societies, though still largely in the future, are becoming clearer.

These implications have also become the subject of what is nearly a discipline: ELSI—ethical, legal, and social implications. The social effects of increased knowledge of human genetics probably have been speculated about—and studied—more than those of any ongoing social change in history. Some of this attention derives from the fascination, sometimes tinged with horror, humans have with any technology that offers—fairly or not—to teach us about our pasts, our futures, and our essences. Although substantial scholarly attention was paid to these issues before 1990 (Andrews 1987; Fletcher 1988; Milunsky & Annas 1975, 1980, 1985; President's Comm. Study Ethical Probl. Med. Biomed. Res. 1982, Reilly 1977), some of the attention stems from the decision, apparently made on the spur of the moment by James Watson as director of the United States Human Genome Project, to commit at least 3% of the project's budget to ELSI (Cook-Deegan 1994). The results include myriad conferences, symposia, books, and articles, as well as grants for anthropologists, lawyers, philosophers, physicians, psychologists, sociologists, students of religion, and others (Annas 1992, Cranor 1994, Frankel & Teich 1993, Kevles & Hood 1992, Kitcher 1996, Murray & Lappé 1994, Murray et al 1996, Pollock 1994, Weir & Lawrence 1994, Wertz & Fletcher 1989).

This chapter does not seek to summarize or synthesize all that work. Instead, it seeks to point out the more interesting legal and social issues raised by human genome research and to group them into some analytically useful categories. The Human Genome Project (Natl. Res. Counc., Comm. Mapp. Seq. Hum. Genome 1988; US Congr., Off. Technol. Assess. 1988a; Cook-Deegan 1994) and the proposed Human Genome Diversity Project (Weiss 1998; Natl. Res. Counc., Comm. Hum. Genome Divers. 1997) are especially useful for this effort because their effects fall largely at different levels of social organization. The Human Genome Project (HGP), with its effort to find and understand the full set of human genes, speaks primarily to the implications of genetic knowledge for individuals or families. The more controversial proposed Human Genome Diversity Project (HGDP) (Greely 1997b), with its effort to

collect and assess samples of human genomes from throughout the world, speaks primarily to the implications of genetic knowledge for larger human groups (and, of course, for the people within them).

This chapter first examines specific concerns arising from human genetic research, which are grouped into six categories:

1. Human genomes and identity
2. Human genetics and predicting the future
3. Human genetics and revealing the past
4. Manipulating human genomes
5. Ownership and control of human genes and genetic information
6. Genomes, souls, and destiny

The chapter then points out some common strands in many of these issues. Some of those strands point to ways in which human genetic research has social implications similar to those of other kinds of science or technology. Other strands identify ways in which those implications are unique. Both sets are crucial to viewing the possible consequences of human genetic research in perspective.

And perspective is vital. Discussions of the ethical, legal, and social implications of human genetic research are usually alarming. The foreseen social implications are usually threatening to some or all people, and the likelihood that they will occur is unknown. The foreseen benefits, although also largely speculative, fall mainly in the medical and scientific realms. Both the uncertainties and the differences in the nature of these kinds of implications make it difficult to weigh the long-term human benefits against the long-term human costs. Most discussions of the social consequences of human genetic research do not even make the attempt. This chapter is no exception, so, like similar discussions, it could be read as a litany of plausible horrors. That is not my goal. I want to alert the reader to the consequences I think are most plausible and most significant.

ETHICAL, LEGAL, AND SOCIAL ISSUES: SPECIFIC CONCERNS

The six categories discussed below do not begin to exhaust the implications of human genome research. The possible direct consequences of genome research for medicine are ignored, yet genomics-based interventions that either increase the average life span or decrease morbidity during life could have enormous social implications. Issues arising within the research community itself—corporate, university, and public—are diverse and fascinating (Rabinow 1996, Greely 1995) but are ignored here. Instead, I want to look at the possible implications of these technologies for ordinary people in nonmedical situations.

The following discussion attempts both to expose the reader to many of those implications and to classify them into a few analytically useful categories. The first three categories focus on the effects of information available as a result of genetic research on individuals, groups, and societies. The fourth category deals with the intentional manipulation of human genomes. The fifth deals with issues relating to the acquisition, control, and use of genetic information. The final category deals with the possibly profound implications of human genetic research for our perceptions of ourselves.

Human Genomes and Identity

The use of genetic information for identification gives rise to concerns in at least three areas: individual identification, cloning, and group membership.

INDIVIDUAL IDENTITY The use of DNA tests for individual identification has been most discussed in the context of criminal law. DNA testing has been used since the mid-1980s to try to match suspects to DNA-containing residues left at the scene of a crime. The forensic uses of DNA technology for identification have prompted concerns about competence, overimpressiveness, ethnic discrimination, privacy, and implicit coercion (Lander 1989; US Congr., Off. Technol. Assess. 1990a; Billings 1992; Natl. Res. Counc. 1992, 1996).

The first concern is a straightforward fear that the technology may not be effective or that it may not be done well by average practitioners. This concern is similar to that faced with any new forensic procedure, but it is a continuing worry, as new and more sensitive types of DNA analysis are regularly introduced as the technology improves. The second concern is a fear that jurors would be overly swayed by the apparent scientific proof implied by DNA testing.

A third concern has been with ethnic discrimination. The markers used to analyze the DNA may not be distributed randomly across the population. Certainly, when a suspect has an identical twin, the odds of someone matching are good. Similarly, the odds that family members will match are higher than the odds of a random match. And it is possible that the variations that were examined in a suspect's DNA are found more commonly in the suspect's ethnic group than among the rest of the population. Failure to take that into account might produce overly low estimates of the possibility of a random match. This issue was debated extensively in the late 1980s and early 1990s; the controversy appears to have been resolved with the techniques now being used by forensic labs to calculate the odds of a match (Natl. Res. Council 1996).

Another concern revolves around privacy (McEwen 1997; Am. Soc. Hum. Genet., Ad Hoc Comm. DNA Technol. 1988). The possible value of DNA for forensic purposes has led to the creation of databases that could invade privacy. Some states have created databases of DNA "fingerprints" for those im-

prisoned or those convicted of certain crimes. These databases are used to investigate other crimes. The US military is creating a database of DNA samples for all uniformed personnel for use in identifying remains if necessary. These kinds of databases raise concerns about who may get access to the DNA or its analysis, the uses to which the samples might be put, and the coercive nature of such laws. (Of course, if the database contains only the analysis of DNA samples, checked against a panel of common markers, the possible abuses of the database are much more limited because those markers usually do not have health consequences.)

Finally, coercion may be present apart from mandatory participation in databases. The first use of DNA testing in a criminal context occurred in a rural area of England after a rape and murder. Young men in the nearby villages were asked to volunteer to provide DNA samples to be matched against DNA left on the victim. One man paid an acquaintance to provide a sample in his name; the acquaintance told the police, leading to the suspect's arrest and conviction (Cook-Deegan 1994). It may be worth worrying about how voluntary participation in such a screening program would truly be, when failure to participate could reasonably be expected to draw the attention of the police. Without sympathizing with the guilty, one may be concerned for all those not guilty who are effectively forced to provide a DNA sample.

Convicting the guilty does not normally raise ethical concerns, but the issues raised above can affect the rights and interests of both the guilty and innocent. As the technologies improve and their implementation becomes more routine, some of the concerns about false matches will fade, but that increased accuracy may only increase the pressure for invasions of individual privacy. It is, however, worth noting that DNA testing rules out suspects about as often as it incriminates them—it is much easier to say that there is no match between two samples than to compute the odds that a false match has occurred by chance (US Dep. Justice 1996).

Also, DNA identification has been used for other purposes, such as paternity testing, reuniting separated families, and identifying human remains. The latter two functions have been used in recent years in situations of political interest. DNA analysis has brought together the parents and children of people "disappeared" by the military during the junta's rule in Argentina, and it has been used in Central America to identify the remains of victims of government massacres.

CLONING The birth of Dolly has made it seem possible that new human babies might be created with genes taken solely from one adult parent. Rather than resulting from the random mixing of genes from mother and father, the child would have the entire nuclear genome of one parent. It remains unclear whether humans can be cloned from adult cells—thus far, no one has even cloned a second sheep from adult sheep cells. But the possibility of human

cloning has raised concerns about the physical, and psychological, identity of the resulting child (Silver 1997, Kolata 1998, Pence 1998).

Some of these concerns may have stemmed from a naive, Hollywood understanding of clones as photocopies—one 30-year-old person suddenly becoming five identical 30-year-olds. Clones would begin life as babies. The clone and the "donor" would be no more identical than, at most, identical twins. If the donor nucleus came from an adult cell, the clone would necessarily grow up in an environment different from that of his or her "older twin." Perhaps more important, the clone would develop before birth in a different environment, either an entirely different womb or the same womb but of a much older mother. These are reasons to suspect that clones would be substantially less similar than identical twins, but at this point that remains speculative. That the confusion of identical genomes with identity (Brock 1992)—making a copy of one's self—is a major thread in the negative reaction to cloning seems clear.

GROUP MEMBERSHIP Population genetics and the HGDP raise another possible concern about identity. It is possible that membership in various tribal or ethnic groups might be defined on the basis of an individual's genetic variations (Cavalli-Sforza et al 1994). Thus, for example, the Basques or Euskadi, who constitute the population with the highest known frequency of the Rh-negative blood type, could conceivably require Rh-negative blood as a condition for recognition as a community member.

Such a method for determining group membership would be extremely arbitrary. Groups generally are defined culturally, frequently with provisions for "adoption" into a group. Even for group members who share recent common ancestry, genetic variations will not provide a sensible method for defining a group. It is highly unlikely that any genetic variation is found, in the entire human species, in only one particular population. It is even less likely that it is found in all members of that population. Population genetics deals, as its name indicates, with populations, not with individuals. Although Basques are the people most likely to be Rh negative, most Rh-negative people are not Basque and most Basques are not Rh negative. The group frequencies, unless they are absolutely 100% or 0%, cannot be used logically to determine whether an individual is a group member.

That a membership criterion is arbitrary does not, of course, mean that it might not be used. The ethical implications of the use of such an arbitrary criterion are likely to hinge on the circumstances—including whether the criterion is chosen by the group or imposed externally—regardless of whether the criterion is genetic. Use of a genetically based group membership criterion could, however, have the negative effect of reinforcing false ideas that ethnic groups or races can be scientifically defined through genetics.

Human Genetics and Predicting the Future

Probably the most important immediate issues concerning these new technologies revolve around their ability to predict future expressed characteristics. The strength of the link between the human gene sequence, or genotype, and the functioning person, or phenotype, is often exaggerated, but in some cases genotype does determine phenotype and in other cases strongly influences it. Genetic tests look for genotypes that help predict phenotypes. To the extent that such tests allow medical interventions that benefit the tested person, they are rarely controversial. But the predictions from genetic tests can be problematic in at least four respects: (*a*) through parental decisions about childbearing, (*b*) through individual and familial reactions to prediction, (*c*) through private third-party discrimination based on the predictive information, and (*d*) through government action. Many of these effects could take place as a result of research on either individual or population genetics.

CHILDBEARING Genetic counseling for any patient raises complex issues (Capron & Lappé 1979; President's Comm. Study Ethical Probl. Med. Biomed. Res. 1983; Rapp 1988; Holtzman 1989; Bosk 1992; Caplan et al 1993; Inst. Med., Natl. Acad. Sci. 1993; Nelkin & Tancredi 1994; Wertz et al 1994), perhaps especially in childbearing. Genetic tests are already in use to predict a couple's chances of having fetuses with particular characteristics or the actual characteristics of an already created embryo or fetus. Pre-conception analysis of the possible parents can lead to decisions about marriage or bearing children; analysis of embryos or fetuses can be used to determine which embryos or fetuses will be allowed to survive to birth.

Prospective parents can be tested to determine if the couple is at risk for bearing a child with some genetic diseases. Such pre-conception testing for the risk of Tay-Sachs disease is common in the Ashkenazi Jewish community. This kind of testing can raise conflicts between an individual's possible duty to disclose genetic risks to a potential partner and his or her own privacy and protection from discrimination.

Prenatal fetal diagnosis evokes a spectrum of responses. At one end, some question whether parents should allow a genetically diseased infant to be born; at the other, some attack the morality of elective abortion. An intermediate position, allowing or encouraging abortions for some kinds of genetic diseases but not others, raises difficult questions of drawing lines. Abortion for Tay-Sachs disease, in which children inevitably die after short, unpleasant lives, might raise fewer concerns than would abortion for late-onset Alzheimer's disease, with which people lead normal lives until old age, or for BRCA1 mutations, which confer a 50–80% chance of a breast cancer diagnosis sometime in life. Although under current US constitutional law the issue would not be whether abortion for a given disease would be allowed, one might regulate

whether certain genetic tests could legally or ethically be used for prenatal testing (Capron 1990; Robertson 1990, 1994; Rothenberg & Thomson 1994; Rothman 1986).

One twist on this issue could come from parents with unusual preferences for their children, preferences for what many would view as a genetic disease. Thus, two people with achondroplasia, one of the common forms of very short stature, might want to use prenatal diagnosis to select a fetus with achondroplasia. If society allows prenatal testing for genetic diseases, who defines "disease?"

These latter issues may pose even greater concerns if and when genetic tests can predict phenotypic characteristics that are not generally viewed as diseases. Thus far, only one such characteristic is readily tested—sex. The ethics of parental sex selection by abortion, and the ethics of telling parents fetal sex when sex-selective abortion may be a possibility, are controversial. Some other nondisease characteristics of interest to some parents, such as skin, hair, and eye color and possibly potential height, seem likely to be heavily influenced by genetics and hence eventually testable.

It remains unclear whether other, more complex—and more interesting—traits, such as various aspects of intelligence or personality, will be amenable to genetic testing. If so, they could raise not only issues of the propriety of parents using such traits to abort fetuses (or to decide not to implant embryos), but also broader social issues of "parental eugenics." The ability to select children for particular characteristics may confer on those children cultural advantages. If such selection is allowed but restricted by financial considerations or religious beliefs, some parents—but not others—would be able to give their children a prenatal, genetic advantage or even just a valuable *perception* of genetic advantage. Such a result may have effects significantly greater than the effects of different environments available to children based on their family's wealth, class, or beliefs, but it would be an extension of those kinds of advantages, with possible implications for class structure and distributive justice (Duster 1989).

INDIVIDUAL AND FAMILIAL REACTIONS The personal, psychological, and familial consequences of predictive genetic information are often overlooked, but they may well raise ethical or legal concerns. Apart from the actual health risks revealed by a genetic test, new knowledge of a risk or a perceived flaw can affect a person's self-perception and happiness (King et al 1993, Natl. Soc. Genet. Couns. 1997). Similarly, genetic tests can have significant effects within a family by affecting relationships with spouses, parents, siblings, and children. Also, when one family member tests positive for a disease-related gene, that person's parents, siblings, and children all have a 50% chance of carrying that version of the gene. Whether a physician or genetic counselor has legal or moral obligations to inform other family members of their risks remains uncertain (Andrews 1997).

PRIVATE THIRD-PARTY DISCRIMINATION Concerns about discrimination in health insurance and employment are often reported in the United States as major deterrents to genetic testing. These issues have also been raised for disability insurance, life insurance, and adoption (as to genetic tests both of the child and of the potential adoptive parents). Only a few anecdotal cases of employment and insurance discrimination have been reported (Billings et al 1992; US Congr., Off. Technol. Assess. 1988b, 1990b), but concern is nonetheless high.

These situations share the characteristic that private actors seek to use genetic information about a person to make decisions concerning that person. The information may be used in a rational manner, where the genetic information really does provide data significant for the decision. In other situations, the information could be used inaccurately and irrationally, on the basis of misunderstandings about the nature of the genetic condition.

The legal questions surrounding employment and health insurance discrimination are murky (Gostin 1991; Greely 1992; Alper & Natowicz 1993; Rothstein 1993; Task Force Genet. Inf. Ins., Natl. Inst. Health/Dep. Energy Work. Group Ethical, Legal, Soc. Implic. Hum. Genome Res. 1994). First, it is not clear whether the federal Americans with Disabilities Act prohibits employment discrimination on the basis of genetic characteristics. The issue would turn largely on whether a genetic characteristic actually is a disability, defined by the statute as a mental or physical impairment that significantly affects a major life activity, or is merely regarded as a disability by the employer. No judicial decisions have interpreted that language with regard to genetic characteristics; the Equal Employment Opportunity Commission, which has the power to enforce the employment discrimination provisions of the act, has stated that genetic characteristics may be disabilities, but that conclusion does not have the force of law (Equal Employ. Oppor. Comm. 1995). Many states have statutes similar to the Americans with Disabilities Act; the application of these statutes to genetic characteristics generally also remains unclear.

The situation surrounding health insurance is even more confusing. The issue revolves around medical underwriting and preexisting condition limitations. Insurers and health maintenance organizations medically underwrite consumers when they decide whether to issue coverage based in part on information about consumers' predicted future health (and hence future covered health costs). Most Americans with health coverage are not subject to medical underwriting, as they receive coverage from large employers, who rarely use medical underwriting, or from Medicare and Medicaid, public programs that do not medically underwrite. People purchasing their own health coverage or receiving it from a small employer, however, may be subject to medical underwriting with respect to their past health and known health risks. Similarly, individual coverage, small-employer coverage, and some large-employer cover-

age can include preexisting condition limitations that exclude, for a fixed period of time or forever, payments for conditions that the insured had at the time the coverage began.

In insurance markets where they are used, medical underwriting and preexisting condition limitations can be used to reject for insurance people with a record of many conditions, such as cancer, hypertension, diabetes, obesity, or smoking. Genetic testing would add another class of factors (and another group of people) to those affected by these practices: genetic factors that predict future illness without causing substantial present symptoms.

Federal law does not generally prohibit either medical underwriting or preexisting condition limitations (Greely 1992, Hudson et al 1995). The Americans with Disabilities Act largely exempts health insurance from its coverage, even when the insurance is related to employment. The recently passed Kassebaum-Kennedy bill, however, prohibits most employers from providing health coverage for some employees but not others based on medical conditions. It does not, however, regulate what prices can be charged and what conditions can be covered. The act also puts a complicated time limit on the length of preexisting condition limitations imposed by most employers and restricts the ability of covered employers to classify genetic characteristics as preexisting conditions.

About 20 states have now prohibited insurers from using genetic information in medical underwriting, although those statutes generally do not deal with genetic characteristics as preexisting conditions. The meaning of "genetic information" in these statutes is variable and somewhat uncertain. The scope of these statutes is limited because state jurisdiction over employer-provided health coverage is, to a large extent, prohibited by a federal statute called the Employee Retirement and Income Security Act (ERISA) (Rothenberg 1995, Greely 1992).

Beyond the surprisingly unclear questions of the current legal status of employment and health insurance discrimination based on genetic information lies the normative question of whether such discrimination should be legal. Employers, insurers, and others discriminate among people on many grounds; are genetic grounds inherently inappropriate? Some argue that they are, analogizing them to other characteristics over which individuals have no control, such as their race, sex, or age. Others argue that the propriety of genetic discrimination depends on the importance of the good that could be denied. Under that kind of analysis, discrimination might be banned in health insurance but allowed in life insurance, which could be seen as less important. One could also point out that singling out genetic characteristics for protection tends to emphasize a view of genetic characteristics as inherently immutable, which is often not true. Thus, a person with a genetic predisposition to a given condition might be able either to avoid the condition altogether or to mitigate its effects, through, for example, using eyeglasses to counteract myopia.

All of these concerns can be the result of either individual or population genetic research. Although individuals carry alleles, some kinds of genetic conditions, and hence some varieties of alleles, are more common in some groups than others. Sickle-cell anemia is found at unusually high levels among people from parts of Africa and the Mediterranean; Tay-Sachs disease is disproportionately common among Jews and French Canadians; cystic fibrosis is unusually frequent in people from northern Europe. Research that revealed a high rate of a particular genetic characteristic in certain populations could be used to stigmatize the entire population, leading insurers to reject all its members without examining the genetic makeup of individuals in that group. Of course, to the extent that this kind of stigmatization of an entire group exists already, based on epidemiological evidence, the development of individual genetic tests could be used to protect individuals from the discriminatory consequences. Even if some individual members of the group escape discrimination, however, the stigma may still have negative consequences for the group as a whole (Duster 1989).

Finally, one must note that these issues will present themselves to different people and in different cultural settings. Americans over the age of 65 almost always can receive health coverage through Medicare, with no medical underwriting. Health insurance discrimination should be of little concern to them, as, if they are retired, should employment discrimination. In the United Kingdom, health coverage is universal through the National Health Service, but medically underwritten credit life insurance is important for those seeking home or automobile loans. The use of genetic tests in health insurance is not a major issue there; the use of genetic tests in life insurance is.

GOVERNMENT ACTION Governments could also use genetic predictions to make distinctions among individuals or groups. The history of the eugenics movement looms over this issue. This movement viewed with alarm what it considered the increase in "genetically defective" people caused by what it perceived as a greater rate of reproduction among the "genetically inferior" (Kevles 1986, Müller-Hill 1988, Proctor 1988, Paul 1992). Many countries, including the United States, Germany, Sweden, and the United Kingdom forcibly sterilized people on grounds of genetic predispositions to such traits as criminality and feeblemindedness. The US Supreme Court, in an opinion by Justice Holmes, upheld one such statute (Buck v. Bell 1927) with the famous words "three generations of imbeciles are enough," although it later applied constitutional restrictions to a similar statute (Skinner v. Oklahoma ex rel. Williamson 1942). Arguments from the eugenics movement were also used to support immigration legislation that greatly favored northern Europeans.

State-sponsored eugenics is not simply a matter of history. The People's Republic of China recently adopted legislation that requires all couples to re-

ceive a medical certificate before being allowed to marry; the legislation also requires prenatal testing for pregnancies involving those with "serious" genetic diseases (Gewirtz 1994). The statute at the very least encourages long-term contraception, sterilization, and abortion for those affected. In other countries, the concern that the genetically less favored are "overreproducing" continues to resonate.

The original eugenics movement collapsed with the revelations of the lengths to which Germany took these arguments during the Third Reich, but its demise was aided by an increased scientific understanding of the complex genetic and environmental roots of the conditions at which eugenicists took aim. As knowledge of genetic influences on those kinds of complex conditions increases, some form of more scientifically based, and hence more limited, eugenics can take shape. Required abortion or sterilization is one extreme, but incentives short of requiring abortion might be imposed, such as a refusal to provide health coverage for infants born after such a prenatal diagnosis. Such efforts would raise constitutional questions in the United States and ethical and moral questions everywhere.

Government action based on the predictive power of genetics would not necessarily be limited to eugenics, however. The press occasionally reports the discovery of a "violence gene." A government might decide to take preventive criminal action against someone carrying that genotype. Similarly, a government might use genetic evidence of low intelligence or learning disabilities to limit the education and life opportunities of certain children. On the other hand, such information might be useful in identifying children who would benefit from special attention.

Finally, although the discussion above has been about government action against individuals, data from population genetics could be used to cast an entire ethnic group as genetically inferior. There is no evidence from existing genetic studies that such an outcome is scientifically plausible. All human populations seem to contain nearly all the same genetic variants, albeit at somewhat different frequencies. Levels of particular genetic disorders higher than the overall species average can be found in almost any group. Nonetheless, the absence of good arguments to be drawn from population genetic data does not mean that bad but politically attractive arguments will not be made. Misused data might be cited to argue that governments should take action against "genetically inferior" peoples, action up to and including genocide.

Human Genetics and Revealing the Past

The "fortune-telling" aspects of human genetics have received the most attention, but in some circumstances that information can look backward as well, to provide evidence about the past. These uses of genetic data can raise less obvious social concerns, with respect to both individuals and groups.

INDIVIDUAL ANCESTRY One of the most straightforward uses of human genetic information is to trace family relationships. Parenthood can usually be established readily, as can more distant relationships. Although such analyses have long been done with blood types (based on proteins that are themselves genetically determined), additional genetic data can make the conclusions even more certain.

Whether establishing "true" genetic family ties is a good or bad thing may depend on the circumstances. When used to reunite the children of victims of the Argentinean junta with their grandparents, its advantages seem clear. But if it is used without the consent of those involved, it could have serious implications for their privacy, their social relationships, and even their lives. Genetic counselors can encounter this problem when testing for a familial disorder. They have often discovered that the putative father was not, in fact, the genetic father. In that situation, they had to decide whom, if anyone, to tell about the true parentage. Similarly, use of genetic tests to establish paternity for child-support purposes, though justifiable, would violate the privacy of both a nonconsenting father and a nonconsenting mother, with possibly serious effects on their lives.

HISTORICAL FIGURES Writers have long speculated on the medical and psychological ailments and characteristics of famous people. DNA testing has provided another method to learn more about individuals who have died. Genetic tests on remains can sometimes be used to determine whose remains they really are, as with the Romanovs and Jesse James. Some have urged that remains from Abraham Lincoln be analyzed to determine whether he had Marfan's syndrome, as has often been speculated. Genetic tests, in such circumstances, provide just one more way of analyzing the past, but one that may garner greater attention because of the high status of genetic information. The spread of such testing has implications for the privacy of the dead historical figures, with surviving family members probably experiencing the strongest effects. It also could have broader social implications, if, for example, the identification and reburial of the Romanov remains were used as weapons in Russian politics.

THE HISTORY OF PEOPLES—AND PEOPLE The HGDP raises another set of issues about the past, centering on particular populations. With enough data, population geneticists can estimate how closely related different populations of humans are to each other. This information could then be used, with linguistic, anthropological, archeological, and historical analysis, as one line of evidence to help trace the history of human migrations across the globe (Cavalli-Sforza et al 1991, Cavalli-Sforza et al 1994, Weiss 1998).

For some cultures, that evidence might be unwelcome. Many societies have their own creation stories, one of which is the Garden of Eden. Although belief

in the literal truth of the Bible's creation story remains strong in the United States in spite of much scientific evidence to the contrary, for some peoples additional inconsistent scientific evidence might disrupt their own historical beliefs or self-image. In some situations, such information could disrupt an entire culture.

Genetically based historical information could have modern political implications. In the American Southwest, for example, the Hopi and Navajo peoples have long disputed ownership of certain land. Genetic evidence as to whether the Navajo are relatively recent immigrants to the region, as the Hopi maintain, could have political consequences for that land dispute. Of course, the genetic evidence would be only one additional strand of evidence, but it could be an important strand.

More broadly, evidence from population genetics could help confirm, or rebut, understandings of overall human evolution. The "out of Africa" and multiregional hypotheses certainly could be affected by more genetic data, which in turn could change scientific and popular views about human creation or evolution.

Even more broadly, one of the most striking findings from research into genomes is how much genetic material is shared by very different kinds of life. Genes found in humans can almost always be found in substantially similar form in mice; they can often be found in fruit flies, nematodes, and even yeast. "Human" genes are often just slight variants on "mammalian" genes or "vertebrate" genes or genes that are universal to all life on earth. A broad public appreciation of this reality might affect our understanding of nature and humanity's place in it. Not only would all humans be cousins, but all life would be demonstrably related.

Manipulating Human Genomes

Thus far, the implications discussed have arisen from information derived from existing (and inferred past and future) human genomes. The manipulation of human genomes may also raise ethical issues.

Moving DNA bearing genes from one species into another species in order to create chimeras—organisms that, genetically, are part one species and part another—is a mainstay of research in molecular biology and is also used extensively in biotechnology. Moving human DNA into non-human animals strikes some as a profanation of humanity; mixing DNA from non-human species can be perceived as a violation of a perceived natural order. The creation of mixes of humans and other animals that are apparent at a non-molecular level—chimpanzees with near-human brains, humans with feline fur—remains in the realm of science fiction, but if accomplished would raise serious questions about the meaning of "human" for various laws and cultural norms.

Finally, supporters of animal rights would also raise concerns about the purposeful use of members of other species for human ends, especially when the human gene caused harm or discomfort to the animal or when the animal ultimately was killed for human use, as would be the case with organ transplants.

HUMAN GENE THERAPY Moving genes from one human to another for therapeutic purposes is less controversial. The paradigm of gene therapy, as originally conceived, was to insert a "proper" gene into the relevant cells of a person with a genetic disease so that the gene would produce a protein necessary for health. Thus, gene therapy for cystic fibrosis would provide lung cells with genes making functional copies of the CTFR1 gene (Lyon & Gorner 1996).

Because of its direct connection to human health, gene therapy aimed at inserting functioning genes into the relevant cells of the body has caused little ethical controversy. This approach to treatment, however, has produced little success in spite of major funding; the appropriate level of support has thus become controversial. Some have also questioned the ethics of human gene therapy research in offering highly experimental treatments to often desperate patients.

HUMAN GERM LINE GENE MANIPULATION The somatic cell gene therapy discussed above would affect only the patient who received it; it would not normally have any effects on the genes of the patients' descendants. Particular variants of genes could also be inserted into eggs and sperm, thus making intentional changes in the genomes of the patients' descendants indefinitely. This could be done for the purpose of avoiding a genetic disease or, possibly, for "enhancing" the characteristics of the child. The alleles that are added might come from the parents or from other humans. In theory, at least, they could also come from other species or come, newly made, from laboratories. It is not clear how realistic these scenarios are. All these technologies would be technically difficult and of uncertain safety for the fetus; the desire for alleles found in the parents or in other humans could also be met by preimplantation diagnosis and sperm or egg donation.

Germ line genetic manipulation raises all the issues of prenatal genetic selection, through preimplantation diagnosis or otherwise. It is not clear whether it raises others. Some might argue that the affirmative act of inserting alleles not otherwise present is different from the sorting through of genetic combinations produced by the merger of eggs and sperm, perhaps paralleling the action/inaction distinction. The social implications of the two technologies, whether voluntarily chosen by parents with the opportunity (and the money) to make the choice or imposed by the state, seem largely identical.

Ownership and Control of Human Genes and Genetic Information

The next set of issues moves from how human genetic material and information could be used to who should control those materials and their uses. Control might be exercised in several ways: through property rules, through privacy protections, through informed consent, or through direct government regulation.

OWNERSHIP OF HUMAN BIOLOGICAL MATERIALS AND HUMAN GENETIC INFORMATION Human genetic research raises issues as to appropriate legal and ethical ownership of both human biological materials and the information they contain. Human bodies and their parts have long been subject to special treatment under the law of property. Anglo-American law, at least after the abolition of slavery, does not recognize property interests in human bodies, living or dead. The next of kin of a decedent have a long-recognized quasi-property right over the corpse, but only for the purpose of arranging for its proper disposition. While living, people are viewed as having control over their bodies and bodily integrity, but not as a result of the laws of property. Thus, in the United States, competent adults are not legally able to exercise one of the prime characteristics of a property right with respect to their organs: They are not allowed to sell them.

On the other hand, some kinds of body parts can be sold: human hair, blood and blood products (in some states), and eggs and sperm. Other organs may be donated and, where they come from a living donor, may be designated for donation to a specific person. The donors are entitled to get their expenses but no price for the organs themselves.

Biological materials sought primarily for their genetic information do not fit easily into this framework. Who owns—or should own—chromosomes or genes, or, indeed, cells contained within human tissues, once they have been separated from the person in whom they grew? (US Congr., Off. Technol. Assess. 1987; Knoppers 1997; Knoppers et al 1996a; Gold 1996). Only one court decision has addressed this issue—*Moore v. Regents of the University of California*—and *Moore*'s importance is unclear (Moore v. Regents of the Univ. Calif. 1991). The California Supreme Court in *Moore* rejected a claim that a patient owned a cell line derived from his surgically removed tissue, although it allowed Moore to try to prove at trial a claim that he had not given true informed consent to the procedure. Because of its facts, *Moore* may not apply to anything other than cell lines or other substantially modified human biological materials; in any event, at this point it has not been adopted—or rejected—by any other court. It remains the express law in California only, leaving the property status of human biological materials in other contexts legally uncertain.

The ethical discussion of ownership of human biological materials has two major aspects. The most prominent argument revolves around the effects such ownership would have on our views of humans, on whether humans would become commodities. This view has been expressed forcefully with respect to surrogate motherhood and the selling of organs for transplantation purposes; the connection between individual cells, molecules, or parts of molecules from human bodies to humans seems more tenuous but can still be asserted.

The second argument, raised clearly by John Moore's suit, is the fairness of the distribution of benefits from human tissue: If any profit is made as a result of research with human biological materials, how should it be shared between the source of the materials and the researchers? Individual donors of materials rarely will be able to show that their contributions played a crucial role, as most human genetic research depends on contributions from many individuals. The argument, however, becomes stronger when the entire group that has contributed to the research—extended families, people who share a genetic disease, or communities—asserts such a claim (Greely 1997a; North Am. Reg. Comm., Hum. Genome Divers. Proj. 1997).

The legal status of intellectual property in the *information* in human genetic material seems clear, except at the margins. The ethical status of that kind of property is much more controversial (Eisenberg 1990).

The United States, Europe, and Japan have all issued patents for "inventions" that include human genetic information. These patents follow from the long-standing patent treatment of complex organic chemicals. Even though the chemical might be found in nature, a method for producing a useful compound at greater purity or higher effectiveness than found in nature can be patented. For the patent offices, human DNA has largely been just another complex organic chemical.

Patents issued on human DNA confer on the holder a monopoly on the right to use that invention for a limited amount of time, now usually 20 years from the date of the patent application. The patent holder cannot claim control over naturally occurring DNA with that sequence—it could not demand royalties from all humans for their normal use of "its" DNA—but it can control commercial uses of that DNA sequence during the patent's term. (There is a statutory exception for some research uses in the patent statutes of many countries; the United States has no statutory research exception but there is some unclear support for one in court opinions.)

Some "inventions" involving human DNA, such as expressed sequence tags, may not qualify for patent protection because they lack some of the essential attributes of patentability, notably utility, enablement, and novelty. And in many countries, but not the United States, the patent statutes contain an exception for inventions that are "against public morality;" this might be used against some patents on biotechnology. The core concept that useful stretches

of human DNA sequence can be patented is not, however, in substantial legal doubt in the United States, Europe, or Japan.

Whether such DNA patents are ethical is, however, controversial. Patents on human DNA have attracted opposition from many directions. Some opponents object, on religious grounds, to any claim of human ownership to divinely created creatures or their DNA. Others view the human genome, in particular, as a common heritage of mankind that should belong to all humanity. This position, adopted by the UNESCO International Bioethics Committee in its Universal Declaration of Rights in the Human Genome, rejects the idea that some should profit from the human genome. Others object to the possibility of genetic engineering generally and view the elimination of DNA patents as a useful instrument for slowing or stopping the entire technology. Still others, equating parts of the human genome with humans themselves, see gene patents as a commodification of humanity. Finally, even some biotechnology companies and academic researchers object to certain patents or the scope of some patents, such as patents on expressed sequence tags or on single nucleotide polymorphisms, as likely to interfere unduly with research.

Thus far, the movement against gene patents has led to some relatively minor modifications in a European patent directive; otherwise it seems to have had little influence on the constantly increasing number of patents issued on DNA sequences.

PRIVACY The concept of genetic privacy has great appeal (Andrews & Jaeger 1991; Annas et al 1995a,b; Rothstein 1997; Gostin 1993a). It is the subject of much proposed and enacted legislation throughout the United States, in part as a means of avoiding the kinds of employment and insurance discrimination discussed above and in part as an end in itself. When examined closely, however, genetic privacy becomes complex and difficult (Greely 1998b).

First, privacy itself has many meanings. Privacy can refer to the ability to make particular decisions without governmental intrusion, as in abortion. It can mean a claimed right to choose with whom to associate, as in marriage or certain residential situations. It can refer to a right to avoid unwanted publicity, even if accurate. It can denote a right against unwanted physical intrusion into one's body or one's home, as in the Fourth Amendment's protection from unreasonable governmental search and seizure. Finally, it can mean confidentiality—the right to insist that information, conveyed to one party for a particular purpose, not be retransmitted to another. Most of these forms of privacy are subject to some degree of constitutional or statutory protection in the United States. Discussion of genetic privacy has focused on intrusion and confidentiality, with some discussion of a decisional privacy right in making decisions about childbearing (Robertson 1990, 1994).

Protection against intrusional privacy would involve prohibitions on the collection of genetic information on people without their consent. At one level, this is not difficult. One cannot normally force someone to provide a blood sample, cheek swab, or other source of genetic material. On the other hand, people constantly shed biological materials that contain cells from which DNA can be recovered, in sloughed skin, fallen hairs, saliva, urine, and feces. There seems to be little legal protection for such, often unintentionally, discarded materials; nor does there seem any practical way to enforce a prohibition on the collection of such materials.

The intrusion, however, could be viewed not as the collection of biological materials but their analysis for genetic information. In that case, a ban on analysis for genetic information of materials collected without consent might be plausible. Such a rule would, however, raise problems both in the definition of genetic information and in the situation of partial consent: If a person authorizes the collection and analysis of a blood sample for medical purposes, would all genetic information have to be the subject of specific consent? At least one US court has ruled that testing voluntarily provided blood samples for "intimate" medical information—information on pregnancy, syphilis infection, and carrying an allele for sickle-cell anemia—without specific consent may violate the law (*Norman-Bloodsaw v. Lawrence Berkeley Lab. 1998*).

That kind of limitation on the unconsented genetic analysis shares a second problem with attempted protection of the confidentiality of genetic information. "Genetic information" may be a meaningless term because a great deal of information, medical and otherwise, provides evidence, conclusive or weak, about genes. For example, a person's ABO blood group is determined by a test of certain molecules found on the surface of red blood cells. Those molecules are determined by the variations in specific genes; knowing that a person is blood type O gives an observer specific information about the person's genetic sequence. Knowing that a couple had a child with sickle-cell anemia provides the observer with definite knowledge of the sequence of a hemoglobin gene found in each parent. Even knowing that people are male or female provides information about their genomes. If genetic information is defined narrowly, as the result of analyses of a gene's sequence, it misses family history or protein tests that would provide strong evidence about the person's genome. If genetic information is defined broadly, it encompasses nearly all medical information.

Medical information is currently protected by various legal doctrines, but that protection is generally considered woefully inadequate (US Congr., Off. Technol. Assess. 1993; Gostin 1993b, 1995). The difficulty of defining "genetic information" could argue for more effective protection of all medical information. Unfortunately, trends in both medicine and the financial management of health care in the United States are pushing for broader collection and

easier dissemination of medical information. The practical scope for legislation improving the privacy of medical information is unclear (Holtzman 1995, Reilly 1995, Greely 1998b).

Genetic privacy also has a corollary in population genetics. Communities studied by population genetic researchers may not want to be identified for fear of various negative consequences, such as discrimination or weakening a political argument. It may be possible to blur the identity of such groups by referring to them only as members of a broader group of people. Thus, instead of identifying research as being done in a particular village of a particular Apache nation, published accounts might speak of research in an Apache village or, more broadly, a village of speakers of a language in the Na Dene language family. This technique, if chosen by the group, is feasible to some extent, but the greater the imprecision in the description of the group, the less useful the published data would be for fine-scale research.

INFORMED CONSENT In the past 40 years, the requirement of informed consent of a patient to medical intervention has become an important part of US law governing the doctor-patient relationship. During the same period, the principle of requiring informed consent of human participants in research has become enshrined in international and US law. Both kinds of informed consent have important implications in human genetics.

In the clinical setting, the law of informed consent may well be insufficient to protect patients adequately with respect to genetic testing. States have taken two approaches to determining when informed consent is necessary. In some states, informed consent is required only when the standards of professional practice require it—that is, doctors have to get their patients' informed consent for a particular intervention only if doctors usually get informed consent in that situation. Other states have adopted a "reasonable patient" standard: Doctors have to get their patients' informed consent when the intervention involves risks that a reasonable patient would want to know about.

Under either standard, it is not clear that informed consent would be required for genetic tests. There is no established standard for most genetic tests, and most kinds of clinical tests are not currently the subject of informed consent. More fundamentally, the risks to a patient from genetic tests are not the kinds of direct medical risks, such as death or paralysis, that informed consent usually covers. Indeed, the risks of the "procedure" could be said to be limited to the trivial risks of drawing a blood sample.

If informed consent were required, what kind of information should be given? The main risks of genetic tests are usually the risks of psychological consequences, familial disturbances, and employment and insurance discrimination that test results might bring. These are not the kinds of risks that physicians normally view as the consequences of medical interventions, but they

could well be much more important to patients than a minute risk of a negative medical effect of, for example, a spinal tap.

Beyond the legal and ethical questions about the existence and scope of any informed consent obligation in the clinical use of genetic tests lies the question of *whose* informed consent. Should informed consent be required from the patient or the entire family that might be affected by the information? Knowledge of the genetic status of one relative provides powerful, sometimes conclusive, information about the genetic status of parents, siblings, and children. It could be argued that the obligation of clinical informed consent should be expanded to encompass all those strongly affected by the resulting information. Such an expansion might give other family members a veto over the patient's decision or merely give them information about the test and an opportunity to discuss the decision with the patient.

For research, US law generally requires informed consent from human subjects participating in research at institutions receiving federal funding or in research that will be used in a submission to the Food and Drug Administration (FDA). These rules, and similar rules in other countries, raise at least four important legal and ethical issues.

One currently heated battle involves the use of previously collected human biological materials for genetic research. Hospitals, universities, blood banks, states, and others have vast collections of human tissue samples, some with associated clinical information. These kinds of samples are potentially invaluable resources, particularly when tied to clinical data. On the other hand, the patients involved did not give informed consent for this kind of research use, and where their identities could be linked to the sample, the analysis could harm them—for example, by identifying them as at high risk for a disease (Clayton et al 1995). The US National Bioethics Advisory Commission is currently studying this issue; it is expected to report on it during 1998.

A second concern deals with the scope of uses that may permissibly be requested through informed consent. Some argue that research subjects can give consent only to research on specific and narrowly defined topics. Subjects could not be fully informed of the risks and benefits of research with their samples unless the research plan has been formulated. This position would arguably make it impossible for subjects to agree to allow their samples to be used as general resources for genetic studies, as the HGDP contemplates, or even, perhaps, to be part of the sequencing of the entire genome planned by the HGP. The research that might be conducted with that information, and the possible consequences for the subject, cannot be specified in advance.

A third issue focuses on the use of informed consent to restrict, in a binding way, the uses made of a research subject's samples. Research subjects, as part of informed consent, might be able to authorize use of their samples for research into diabetes but forbid their use for research into alcoholism. They

might require the destruction or return of their samples within a specified period or might put conditions, including financial conditions, on any subsequent use of their samples for commercial purposes.

It is not clear under existing law whether the informed consent process, as currently constituted, leads to a binding contractual agreement between the researcher and the subject. There seems no reason, however, to think that binding contracts could not be achieved in connection with informed consent. Such contracts could provide research subjects with potentially valuable ways to control the use of their samples, as long as the subjects had the ability, as well as the legal right, to enforce such contracts (Greely 1997a,b; North Am. Reg. Comm., Hum. Genome Divers. Proj. 1997).

Finally, for some kinds of research, as for some kinds of clinical genetic tests, one might ask whose informed consent should be required. This is particularly true for population genetics, where the object of the study is primarily the population as a whole and not the individual participants, but it could also apply to research with individuals or families affected with genetic diseases. When a group is the actual subject of the research, it might be appropriate to require the informed consent of the entire group, acting through whatever authorities it recognizes. A study of the genetic constitution of Icelanders, for example, affects all people from Iceland, whether they are among the individual research subjects or not.

If there are entities that the group recognizes as having authority over them as a group, such as a national or tribal government or an important religious or cultural body, such group consent might be demanded. This consent would have the beneficial effect of allowing the group, as a whole, to determine whether to run the risks of genetic research to their history, political standing, insurability, and so on. It would also, of course, be difficult to implement: What are the boundaries of a group, and what are the culturally appropriate authorities that speak for them? It could also be viewed as infringing on individual liberty by preventing willing group members from participating in research that they found worthwhile (North Am. Reg. Comm., Hum. Genome Divers. Proj. 1997).

SOCIAL REGULATION Apart from rules of property, privacy, and informed consent, other forms of regulation could be imposed on genetic technologies through, among other possibilities, professional organizations, governments, or international organizations. These regulations could cover many kinds of human genetic research or its applications. For example, many of those groups have already attempted to ban human cloning. Perhaps the most interesting case, at least in the United States, is the commercial availability of genetic testing.

In the United States, neither drugs nor biologicals can legally be sold or used without FDA permission, which is based on strong proof of their safety

and efficacy as well as close monitoring of the conditions under which they are produced. The FDA also limits the advertising, marketing, and labeling of drugs. Medical devices are subject to similar, though somewhat less stringent, regulation. The practice of medicine, however, is subject to no such limitations. While a new drug, vaccine, or device can be used commercially only after government permission, a physician can use a new medical procedure at any time, with fear largely of only possible malpractice litigation.

Depending on how they are offered, genetic tests may be treated like medical procedures and not like drugs or medical devices. If the test is being offered as a service, by a clinical laboratory, the FDA has not asserted jurisdiction over it as a medical device. If, however, the test is packaged for resale to clinical laboratories, physicians, or individuals, it is a medical device and must be shown to be safe and effective before it can be sold. Not surprisingly, firms marketing genetic tests have chosen to market them as services and not as test kits, thus avoiding the stringent FDA approval process or real review of the value of test. The Clinical Laboratory Improvement Act Amendments of 1988 regulate the credentials and working conditions of the technicians who perform clinical laboratory analyses and provides for regular tests of laboratory competence, but it does not limit what tests can be performed. Some states have imposed more stringent limitations on clinical laboratories, but they have not required rigorous proof of the safety and efficacy of genetic tests. The extent to which the state or federal governments should, or will, impose such regulation remains in doubt.

Genes, Souls, and Destiny

The most important social implications of human genetic research may lie in its possible deep cultural effects. Two consequences seem particularly plausible: the "sacralization" of human DNA and an increasing belief in determinism. Both derive from attaching a seemingly exaggerated importance to a set of very long molecules.

It has been argued that, for some people, a human's genome has taken on attributes of the traditional Christian soul. It is uniquely individual (except in identical twins), it is a person's essence, and it is, at least in the form of information, potentially immortal. Nelkin & Lindée even note an effort to sell bits of celebrity DNA, which, they point out, parallels medieval practices with Christian relics (Nelkin & Lindée 1995).

In some cultures, the sacred nature of human biological materials already imposes some constraints on genetic research; for example, when DNA samples may be taken from cheek swabs or other tissues but not from blood. A broadening sense that human DNA is somehow sacred has implications for research, for genetic manipulation, and for privacy. At the same time, the de-

monstrably close connections between human genes and non-human genes could diffuse some of this sense of sacredness to other life.

The second possible consequence is a greater belief that individuals' abilities, and fates, are determined by their DNA. Reports of "gay" genes or "risk-seeking" genes, like phrenology, astrology, and other variants of fortune-telling, attempt both to predict and to provide explanations for human behavior and human outcomes (Hamer & Copeland 1998). The war between free will and determinism has been played out in different contexts during different eras in Western culture (and probably many other cultures as well), but the tension remains (Degler 1991). Increasing associations of genetic variations with particular traits may well increase the appeal—and the perceived "scientific truth"—of determinism.

In fact, much human genetic research does not support such a deterministic view (Lewontin et al 1984, Lewontin 1992, Hubbard & Wald 1993). Only a few, usually rare genetic conditions are solely and completely determined by a known gene or genes. Variation in the severity of the phenotype exists for many major genetic disorders, such as cystic fibrosis and sickle-cell anemia. Variation in the penetrance of other disease-related genotypes, the percentage of people with the genotype who will get the disease phenotype, is common, with examples from Alzheimer's disease to breast cancer to colon cancer. Many conditions with strong genetic components, such as phenylketonuria, and weaker ones, such as myopia, can be treated successfully. And most human traits, disease-related or otherwise, seem to be a result of a complex interaction of many genes and many environments, including perhaps prenatal environment. For some unfortunate humans, such as children born with Tay-Sachs disease, genes are destiny. For most of us, they are only one more influence in the contingent histories of our lives.

I believe that the paragraph above is correct. I also want to live in a society that believes it is correct. The possible serious undercutting of such a belief by research in human genetics would be, to me, its most negative consequence.

ETHICAL, LEGAL, AND SOCIAL ISSUES: COMMON STRANDS

Three common strands run through most of the issues discussed above. First, much human genetic research simultaneously raises many quite different issues. Second, the social consequences of human genetic research are similar to those of many other kinds of research. Third, the *perception* that genetic research is different is powerful. These latter two themes are important in themselves and combine to create a policy dilemma.

This chapter has carefully assigned different concerns arising from human genetics research to one of six categories, yet any given research project is

likely to raise many issues from different categories. For example, research on genetic links to some forms of intelligence would spark concerns about, among other things, discrimination, prenatal testing and abortion, eugenics, germ line genetic manipulation, genetics, property, and determinism.

The proposed HGDP, whose North American ethics subcommittee I chair, provides another example. This proposal for collection, storage, and analysis of DNA samples from a broad spectrum of human populations has been attacked as "biopiracy," as reinforcing racism, as violating informed consent principles, as breaking down culturally important myths, and as leading to discrimination against ethnic groups (if not biological warfare), among other things (Mead 1996; Rural Advancement Found. Intl. 1993, 1995, 1997; Cultural Survival Q. 1996). The breadth of the issues involved both confuses the analysis and guarantees that there will be something for almost anyone to worry about. The resulting debates have led to some working out of ethical principles (Human Genome Diversity Project 1994, UNESCO Intl. Bioethics Comm., Subcomm. on Bioethics and Population Genetics 1995, Human Genome Organisation 1996, Knoppers et al 1996b, North Am. Reg. Comm., Hum. Genome Divers. Proj. 1997, Natl. Res. Council, Comm. Hum. Genome Divers. 1997) and, perhaps, to some improved understanding between, and among, the researchers, activists, and populations involved. But the very breadth of the issues involved has made those understandings more difficult to reach, as well as underlining the necessity of some continuing ethical oversight of this and other such endeavors. The issues are too complex, the individual contexts are too important, and the participants are too human to create "the" solution to the issues this kind of effort raises; only a continuing and vigilant process can minimize negative consequences from such research.

The second common strand is that the issues discussed above do not arise uniquely from genetic research. They are consequences of information about people or peoples; in some respects, human genetic research just makes possible another kind of information.

Thus, the forensic use of DNA raises issues largely identical to the earlier introduction of fingerprints or blood group tests. Genetic tests merely extend the reach of discrimination in employment and individually underwritten health insurance from, for example, people with a history of breast cancer to people with a genetically high risk of getting breast cancer in the future. Any advantages wealthy parents could confer on their children from genetic selection are probably dwarfed by the educational and cultural advantages money buys during their lives. The historical use of population genetics just adds one more line of evidence to findings that may undermine common beliefs about ethnic, national, or human origins. Privacy is threatened whenever information people care about has value to others, whether it is genetic information, medical information, or credit information. Many clinical tests and not just genetic

tests should probably have expanded informed consent, as a "mere" test is not necessarily an entirely benign procedure.

The consistent thread is a new sort of information of value. Even some of the wilder issues, such as part-human chimeras, have parallels outside genetics, as in speculation about the legal and moral status of truly intelligent computers.

The third strand is that genetic information is often different from other kinds of information in its scientific origins and is always different in its perceived "essential" nature. Genetic information comes from examining invisible molecules. It is the result of the work of high-status scientists, laboring in clean laboratories in major universities. It is threatening (Rifkin & Howard 1981, Rifkin 1998), and it comes from one's "blueprint," the "Code of Codes," the stuff that "makes us what we are." And, perhaps as a result of those facts, research in human genetics, whether speculative or confirmed, is often on the front page of newspapers and the cover of news magazines (Nelkin & Lindée 1995).

This elevated status for the human genome is not only deeply inappropriate but also dangerous. At the same time, as a social phenomenon, it is very real. This sets up a serious dilemma that runs through many policy issues in genetics. Greater public knowledge of, interest in, and concern about genetic research gives this kind of research unusual power. Whether genetic information gives insurers anything more than medical information may be unclear, but if insurers believe it is powerful, it will have a greater effect on people's lives. And if people believe that, their anxiety concerning the uses of genetics will rise.

Thus, the mere perception of a peculiar power in human genetics may cause heightened risks that could justify special intervention for genetic information. Or, alternatively, the heightened concern might provide enough political support to ban, for example, medical underwriting for genetic susceptibilities even though sufficient support does not exist to ban medical underwriting for current or past health conditions.

But, on the other hand, providing special legislation or regulation may just feed the cultural belief that genetics truly *is* special. If that is the case, one might win a small tactical victory against the misuse of genetics in ways that harm people while reinforcing dangerous misperceptions of the power of genetics (Wolf 1995). This deep dilemma is perhaps the greatest ethical, legal, and social challenge posed by human genetic research.

CONCLUSION

This article is an attempt to forecast the major ethical, legal, and social implications of ongoing research into human genetics. It is, necessarily, a somewhat

idiosyncratic vision of those implications. Only two conclusions seem certain. The first is that the implications will be important, leading to changes in day-to-day matters like medicine and in concepts of our world and our humanity. This revolutionary expansion in our knowledge of the molecular biology of life, especially human life, will have major effects on all cultures that partake of it. The second conclusion is that this article's discussion will prove to be, in some important parts, wrong. Issues will not play out as expected, unforeseen problems will arise, and time and chance will have their effects. Most of the effects of DNA on human society will prove to be no more predetermined than most of its effects on individual humans.

Literature Cited

Alper JS, Natowicz MR. 1993. Genetic discrimination and the public entities and public accommodations titles of the Americans with Disabilities Act. *Am. J. Hum. Genet.* 53:26–32

Am. Soc. Hum. Genet., Ad Hoc Comm. DNA Technol. 1988. DNA banking and DNA analysis: points to consider. *Am. J. Hum. Genet.* 42:781–83

Andrews LB. 1987. *Medical Genetics: A Legal Frontier.* Chicago: Am. Bar Found.

Andrews LB. 1997. Gen-etiquette: genetic information, family relationships, and adoption. In *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era,* ed. MA Rothstein, pp. 255–80. New Haven: Yale Univ. Press

Andrews LB, Jaeger AS. 1991. Confidentiality of genetic information in the workplace. *Am. J. Law Med.* 17:75–108

Annas GJ, ed. 1992. *Gene Mapping: Using Law and Ethics as Guides.* New York: Oxford Univ. Press

Annas GJ, Glantz LH, Roche PA. 1995a. Drafting the genetic privacy act: science, policy and practical considerations. *J. Law Med. Ethics* 23:360–66

Annas GJ, Glantz LH, Roche PA. 1995b. *The Genetic Privacy Act and Commentary.* Boston: Boston Univ. Sch. Health

Billings PR, ed. 1992. *DNA on Trial: Genetic Identification and Criminal Justice.* Plainview, NY: Cold Spring Harbor Lab.

Billings PR, Kohn MA, Decuevas M, Beckwith J, Alper JS, Natowicz MR. 1992. Discrimination as a consequence of genetic testing. *Am. J. Hum. Genet.* 50:476–82

Bosk C. 1992. *All God's Mistakes: Genetic Counseling in a Pediatric Hospital.* Chicago: Chicago Univ. Press

Brock DW. 1992. The human genome project and human identity. *Houston Law Rev.* 29: 7–22

Buck v. Bell. 1927. 274 U.S. 200, 47 S.Ct. 584, 71 L.Ed. 1000

Caplan AL, Bartels DM, LeRoy BS, eds. 1993. *Prescribing Our Futures: Ethical Challenges in Genetic Counseling.* New York: Aldine de Gruyter

Capron AM. 1990. Which ills to bear? Re-evaluating the "threat" of modern genetics. *Emory Law J.* 39:665–96

Capron AM, Lappé M, eds. 1979. *Genetic Counseling: Facts, Values and Norms.* New York: Liss

Cavalli-Sforza LL, Menozzi P, Piazza A. 1994. *The History and Geography of Human Genes.* Princeton: Princeton Univ. Press

Cavalli-Sforza LL, Wilson AC, Cantor CR, Cook-Deegan RM, King MC. 1991. Call for a worldwide survey of human genetic diversity: A vanishing opportunity for the human genome project. *Genomics* 11: 490–91

Clayton EW, Steinberg KK, Khoury MJ, Thomson E, Andrews L, et al. 1995. Informed consent for research on stored tissue samples. *JAMA* 274:1786–92

Cook-Deegan R. 1994. *The Gene Wars: Sci-*

ence, Politics, and the Human Genome. New York: Norton
Cranor CF, ed. 1994. *Are Genes Us? The Social Consequences of the New Genetics.* New Brunswick, NJ: Rutgers Univ. Press
Degler CN. 1991. *In Search of Human Nature: The Decline and Revival of Darwinism in American Social Thought.* New York: Oxford Univ. Press
Duster T. 1989. *Backdoor to Eugenics.* New York: Routledge
Eisenberg RS. 1990. Patenting the human genome. *Emory Law J.* 39:721–45
Equal Employ. Oppor. Comm. 1995. *Order 915.002, Definition of the Term "Disability."* Reprinted in *Daily Labor Report.*, March 16, 1995, pp. E1, E23
Fletcher JC. 1988. *The Ethics of Genetic Control: Ending Reproductive Roulette.* Buffalo, NY: Prometheus
Frankel MS, Teich AH. 1993. *The Genetic Frontier: Ethics, Law, and Policy.* Washington, DC: Am. Assoc. Adv. Sci.
Gewirtz DS. 1994. Toward a quality population: China's eugenic sterilization of the mentally retarded. *NY Law Sch. J. Int. Comp. Law* 15:147–62
Gold ER. 1996. *Body Parts: Property Rights and the Ownership of Human Biological Materials.* Washington, DC: Georgetown Univ. Press
Gostin LO. 1991. Genetic discrimination: the use of genetically based diagnostic and prognostic tests by employers and insurers. *Am. J. Law Med.* 17:109–44
Gostin LO. 1993a. Genetic privacy. *J. Law Med. Ethics* 23:320–30
Gostin LO. 1993b. Privacy and security of personal information in a new health care system. *JAMA* 270:2487–93
Gostin LO. 1995. Health information privacy. *Cornell Law Rev.* 80:451–527
Greely HT. 1992. Health insurance, employment discrimination, and the genetics revolution. In *The Code of Codes: Scientific and Social Issues in the Human Genome Project,* ed. DJ Kevles, L Hood, pp. 264–80. Cambridge, MA: Harvard Univ. Press
Greely HT. 1995. Conflicts in the biotechnology industry. *J. Law Med. Ethics* 23: 354–59
Greely HT. 1997a. The control of genetic research: involving "the groups between." *Houston Law Rev.* 33:1397–430
Greely HT. 1997b. The ethics of the Human Genome Diversity Project: the North American Regional Committee's proposed model ethical protocol. See Knoppers 1997, pp. 239–56
Greely HT. 1998a. Informed consent, stored tissue samples, and the Human Genome Diversity Project: protecting the rights of research participants. In *Ethical Issues in Stored Tissue Samples,* ed. RF Weir. Iowa City: Univ. Iowa Press. In press
Greely HT. 1998b. Problems in protecting "genetic privacy." *Chicago-Kent Law Rev.* In press
Hamer D, Copeland P. 1998. *Living with Our Genes: Why They Matter More Than You Think.* New York: Doubleday
Holtzman NA. 1989. *Proceed with Caution: Predicting Genetic Risks in the Recombinant DNA Era.* Baltimore, MD: Johns Hopkins Univ. Press
Holtzman NA. 1995. The attempt to pass the Genetic Privacy Act in Maryland. *J. Law Med. Ethics* 23:367–70
Hubbard R, Wald E. 1993. *Exploding the Gene Myth.* Boston: Beacon
Hudson KL, Rothenberg KH, Andrews LB, Kahn MJE, Collins FS. 1995. Genetic discrimination and health insurance: an urgent need for reform. *Science* 278:391–93
Human Genome Diversity Project. 1994. *Summary Document.* Available at http://www.stanford.edu/group/morrinst/HGDP.html.
Human Genome Organisation. 1996. HUGO statement on the principled conduct of genetics research. *Genome Digest* 2 (May 1996). Also available at http://hugo.gdb.org:90/conduct.htm.
Inst. Med., Natl. Acad. Sci. 1993. *Assessing Genetic Risks: Implications for Health and Social Policy.* Washington, DC: Natl. Acad. Press
Judson HF. 1979. *The Eighth Day of Creation: The Makers of the Revolution in Biology.* New York: Simon & Schuster
Kevles DJ. 1986. *In the Name of Eugenics: Genetics and the Uses of Human Heredity.* Berkeley: Univ. Calif. Press
Kevles DJ, Hood L, eds. 1992. *The Code of Codes: Scientific and Social Issues in the Human Genome Project.* Cambridge, MA: Harvard Univ. Press
King M-C, Rowell S, Love SM. 1993. Inherited breast and ovarian cancer: what are the risks? What are the choices? *JAMA* 269:1975–80
Kitcher P. 1996. *Lives to Come: The Genetic Revolution and Human Possibilities.* New York: Simon & Schuster
Knoppers BM, ed. 1997. *Human DNA Sampling: Law and Policy—International and Comparative Perspectives.* The Hague: Kluwer Law Int.
Knoppers BM, Caulfield T, Kinsell TD, eds. 1996a. *Legal Rights and Human Genetic Material.* Toronto: Montgomery Publ.

Knoppers BM, Hirtle M, Lormeau S. 1996b. Ethical issues in international collaborative research on the human genome: the HGP and the HGDP. *Genomics* 34: 272–93

Kolata G. 1998. *Clone: The Road to Dolly and the Path Ahead.* New York: Morrow

Lander ES. 1989. DNA fingerprinting on trial. *Nature* 339:501–5

Lewontin RC. 1992. *Biology and Ideology: The Doctrine of DNA.* New York: Harper Collins

Lewontin RC, Rose S, Kamin LJ. 1984. *Not in Our Genes.* New York: Pantheon Books

Lyon J, Gorner P. 1996. *Altered Fates: Gene Therapy and the Retooling of Human Life.* New York: Norton

McEwen JE. 1997. DNA data banks. See Rothstein 1997, pp. 321–51

Mead A. 1996. Genealogy, sacredness, and the commodities market. *Cult. Surviv. Q.* 20(Summer):46–52

Milunsky A, Annas GJ, eds. 1975. *Genetics and the Law.* New York: Plenum

Milunsky A, Annas GJ, eds. 1980. *Genetics and the Law II.* New York: Plenum

Milunsky A, Annas GJ, eds. 1985. *Genetics and the Law III.* New York: Plenum

Moore v. Regents of the Univ. Calif. 1990. S. Cal. 3d, 120,793, p. 2d 479. 271 Cal. Rptr. 146

Müller-Hill B. 1988. *Murderous Science: Elimination by Scientific Selection of Jews, Gypsies, and Others 1933–1945.* Oxford: Oxford Univ. Press

Murray TH, Lappé M, eds. 1994. *Justice and the Human Genome Project.* Berkeley: Univ. Calif. Press

Murray TH, Rothstein MA, Murray RF, eds. 1996. *The Human Genome Project and the Future of Health Care.* Bloomington: Ind. Univ. Press

Natl. Res. Counc. 1992. *DNA Technology in Forensic Science.* Washington, DC: Natl. Acad. Press

Natl. Res. Counc. 1996. *DNA Technology in Forensic Science: An Update.* Washington, DC: Natl. Acad. Press

Natl. Res. Counc., Comm. Hum. Genome Divers. 1997. *Evaluating Human Genetic Diversity.* Washington, DC: Natl. Acad. Press

Natl. Res. Counc., Comm. Mapp. Seq. Hum. Genome. 1988. *Mapping and Sequencing the Human Genome.* Washington, DC: Natl. Acad. Press

Natl. Soc. Genet. Couns. 1997. Predisposition genetic testing for late-onset disorders in adults. *JAMA* 278:1217–20

Nelkin D, Lindée MS. 1995. *The DNA Mystique: The Gene as a Cultural Icon.* New York: Freeman

Nelkin D, Tancredi L. 1994. *Dangerous Diagnostics: The Social Power of Biological Information.* Chicago: Univ. Chicago Press. 2nd ed.

Norman-Bloodsaw v. Lawrence Berkeley Lab. 1998. 135 F.3d 1260 (9th Circuit)

North Am. Reg. Comm., Hum. Genome Divers. Proj. 1997. Proposed model ethical protocol for collecting DNA samples. *Houston Law Rev.* 33:1431–73

Paul D. 1992. Eugenic anxieties, social realities, and political choices. *Soc. Res.* 59: 663–83

Pence GE. 1998. *Who's Afraid of Human Cloning?* Lanham, MD: Rowman & Littlefield

Pollock R. 1994. *Signs of Life: The Language and Meanings of DNA.* Boston: Houghton Mifflin

President's Comm. Study Ethical Probl. Med. Biomed. Res. 1982. *Splicing Life: A Report on the Social and Ethical Issues of Genetic Engineering with Human Beings.* Washington, DC: The Commission

President's Comm. Study Ethical Probl. Med. Biomed. Res. 1983. *Screening and Counseling for Genetic Conditions: A Report on the Ethical, Social, and Legal Implications of Genetic Screening, Counseling and Education Programs.* Washington, DC: The Commission

Proctor R. 1988. *Racial Hygiene: Medicine Under the Nazis.* Cambridge, MA: Harvard Univ. Press

Rabinow P. 1996. *Making PCR: A Story of Biotechnology.* Chicago: Univ. Chicago Press

Rapp R. 1988. Chromosomes and communication: the discourse of genetic counseling. *Med. Anthropol. Q.* 2:143–57

Reilly PR. 1995. The impact of the genetic privacy act on medicine. *J. Law Med. Ethics* 23:378–81

Reilly PR. 1977. *Genetics, Law, and Social Policy.* Cambridge, MA: Harvard Univ. Press

Rifkin J. 1998. *The Biotech Century: Harnessing the Gene and Remaking the World.* New York: Tarcher/Putnam

Rifkin J, Howard T. 1981. *Who Should Play God? The Artificial Creation of Life and What It Means for the Human Race.* New York: Dell

Robertson JA. 1990. Procreative liberty and human genetics. *Emory Law J.* 39: 697–719

Robertson JA. 1994. *Children of Choice: Freedom and the New Reproductive Technologies.* Princeton, NJ: Princeton Univ. Press

Rothenberg KH. 1995. Genetic information

and health insurance: state legislative approaches. *J. Law Med. Ethics* 23:312–19

Rothenberg KH, Thomson EJ, eds. 1994. *Women and Prenatal Testing: Facing the Challenges of Genetic Technology.* Columbus: Ohio State Univ. Press

Rothman BK. 1986. *The Tentative Pregnancy: Prenatal Diagnosis and the Future of Motherhood.* New York: Viking

Rothstein MA. 1993. Genetic discrimination in employment and the Americans with Disabilities Act. *Houston Law Rev.* 29: 23–84

Rothstein MA, ed. 1997. *Genetic Secrets: Protecting Privacy and Confidentiality in the Genetic Era.* New Haven, CT: Yale Univ. Press

Rural Advancement Found. Intnatl. 1993. *Communiqué: Patents, Indigenous People, and Human Genetic Diversity* (May 1993). Also available at http://www.rafi.ca

Rural Advancement Found. Intnatl. 1997. *Communiqué: The Human Tissue Trade* (Jan../Feb 1997). Also available at http://www.rafi.ca

Rural Advancement Found. Int. 1995. *Indigenous Person from Papua New Guinea Claimed in US Government Patent* (Oct. 4, 1995). Available at http://bioc09.uthscsa.edu/natnet/archive/nl/hgdp.html.

Silver LM. 1997. *Remaking Eden: Cloning and Beyond in a Brave New World.* New York: Avon Books

Skinner v. Oklahoma ex rel. Williamson. 1942. 316 US 535, 62 S. Circuit. 1110, 86 L. Ed. 1655

Task Force Genet. Inf. Ins., Natl. Inst. Health/Dep. Energy Work. Group Ethical, Legal, Soc. Implic. Hum. Genome Res. 1994. *Genetic Information and Health Insurance.* Bethesda, MD: Natl. Inst. Health

UNESCO Intnatl. Bioethics Comm., Subcomm. on Bioethics and Population Genetics. 1995. *Bioethics and Human Population Genetics Research.* Available at http://www.biol.tsukuba.ac.jp/~macer/PG.html

US Congr., Off. Technol. Assess. 1987. *New Developments in Biotechnology: Ownership of Human Tissues and Cells.* Washington, DC: US Gov. Print. Off.

US Congr., Off. Technol. Assess. 1988a. *Mapping Our Genes—The Human Genome Project: How Big, How Fast?* Washington, DC: US Gov. Print. Off.

US Congr., Off. Technol. Assess. 1988b. *Medical Testing in the Workplace.* Washington, DC: US Gov. Print. Off.

US Congr., Off. Technol. Assess. 1990a. *Genetic Witness: Forensic Uses of DNA Tests.* Washington, DC: US Gov. Print. Off.

US Congr., Off. Technol. Assess. 1990b. *Genetic Screening in the Workplace.* Washington, DC: US Gov. Print. Off.

US Congr., Off. Technol. Assess. 1992. *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening.* Washington, DC: US Gov. Print. Off.

US Congr., Off. Technol. Assess. 1993. *Protecting Privacy in Computerized Medical Information.* Washington, DC: US Gov. Print. Off.

US Dep. Justice. 1996. *Convicted by Juries: Exonerated by Science: Case Studies in the Use of DNA Evidence to Establish Innocence After Trial.* Washington, DC: Natl. Inst. Justice

Watson JD, Crick FHC. 1953. A structure of deoxyribose nucleic acid. *Nature* 171: 737–38

Weir RF, Lawrence SC, eds. 1994. *Genes and Human Self-Knowledge.* Iowa City: Univ. Iowa Press

Weiss KM. 1998. Coming to terms with human variation. *Annu. Rev. Anthropol.* 27: 273–300

Wertz DC, Fanos JH, Reilly PR. 1994. Genetic testing for children and adolescents: who decides? *JAMA* 272:875–81

Wertz DC, Fletcher JC, eds. 1989. *Ethics and Human Genetics: A Cross-Cultural Perspective.* New York: Springer-Verlag

Wolf SM. 1995. Beyond "genetic discrimination": toward a broader harm of geneticism. *J. Law Med. Ethics* 23:345–53