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The Human Genome Project and the Courts: Gene Therapy and Beyond

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The Human Genome Project and the courts

GENE THERAPY AND BEYOND

The courts will be called upon to settle an array of disputes involving genetic medicine among patients, health care professionals, insurers, and the government.

by Maxwell J. Mehlman

The impact of the Human Genome Project will be much broader than just making it possible to test people or to screen populations for genetic disorders. Gene therapies—both in the form of drugs manufactured with genetic technology and gene transfer involving the actual manipulation of cellular DNA—will usher in a new era of genetic medicine.

Gene therapy already is a reality. Hundreds of clinical trials are underway to test the safety and efficacy of gene therapy to treat disorders such as cystic fibrosis and Parkinson's disease.[1]

So far, these new technologies are limited to producing so-called "somatic" effects in patients—that is, effects that do not alter reproduc-

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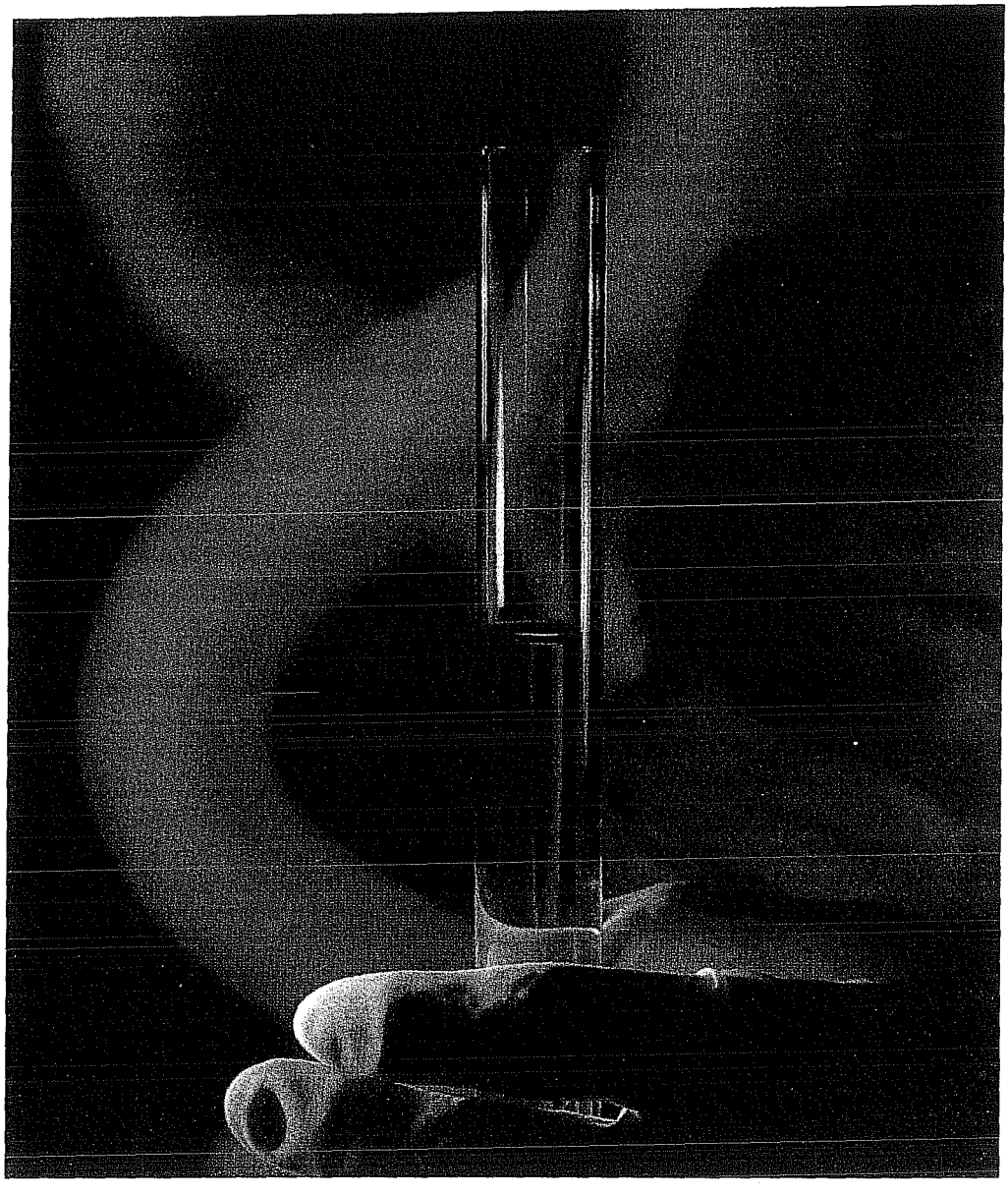
1. *See* McLachlan, Ho, Davidson-Smith, Samways, Davidson, Stevenson, Carothers, Alton, Middleton, Smith, Kallmeyer, Michaelis, Seeber, Naujoks, Greening, Innes, Dorin, and Porteou, *Laboratory and clinical studies in support of cystic fibrosis gene therapy using pCMV-CFTR-DOTAP*, 3 GENE THER. 1113-1123 (1996); Colledge, *Cystic fibrosis Gene Therapy*, 4 CUR. OPIN. GENET. DEV. 466-471 (1994); McElvaney, *Is gene therapy in cystic fibrosis a realistic-expectation?*, 2 CURR. OPIN. PULM. MED. 466-471 (1996).



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tive cells and therefore that would not be passed on to the patient's offspring. But studies have been proposed in which genetic manipulations would change the DNA inside eggs or sperm.[2] These so-called "germ line gene therapies" introduce the possibility of eliminating genetically-related diseases in succeeding generations.

The future holds the prospect of even more daring genetic manipulations. The Human Genome Project will provide scientists with the data and tools to identify and understand the basis of genetic diseases and disorders, as well as other genetically-related traits. This creates the possibility of genetic interventions to enhance non-disease traits, for example, to increase strength, stamina, and perhaps even intelligence. Nor are these enhancement technologies just in the realm of science fiction. Scientists have begun to use gene transfer technologies to enhance the immune systems of advanced cancer and HIV-infected patients, and they are experimentally transferring "foreign" genes (i.e., not one's own) into healthy subjects in search of new mechanisms to deliver gene therapies to patients.[3]

These new technologies will create a host of difficult, often unprecedented, ethical and legal controversies, many of which will find their way to the courts for resolution.

2. Cooke, *Pushing the Human Limit: Gene Therapy That Could Affect Future Generations Too*, NEWSDAY, August 30, 1990, at A6.

3. *See* Recombinant DNA Advisory Committee, Discussion Regarding the Use of Normal Subjects in Human Gene Transfer Clinical Trials, March 6-7, 1997, pg. 2 (in author's possession) (discussing protocol to characterize local, systemic and distant compartment immunity in normal individuals after intradermal administration of a replication deficient Ad5-based vector carrying gene coding for the E. coli enzyme, cytosine adenase).

patients at risk for genetic ailments about the benefits and risks of new genetic technologies. Not only will they have to inform and advise patients about the complex matrix of individual genetic risk factors revealed by an expanding array of genetic tests, and to help patients compare the medical benefits and risks of various gene therapies and alternative treatments; they also will be the primary source of patient information about the non-medical costs of accessing genetic technologies, including the risks of insurance and employment discrimination.

Beyond gene therapy

As mentioned at the outset of this article, the revolution in human genetics will extend beyond identifying and preventing or treating genetic ailments. The same techniques that respond to genetic disorders also will be applicable to non-disease traits. Currently much work is underway to identify the proteins that genes "code for" in order to correct protein imbalances that produce illness. The same process can be used to produce drugs that affect any other protein-dependent characteristic, not just those that are regarded as illnesses. Similarly, gene transfer technology that will be used to remove errant DNA or to install healthy DNA also will be able to manipulate DNA for other purposes.

At this point it is not known how many non-disease human characteristics are, at least in part, inherited. But research already has confirmed that certain traits that many would consider fundamental to personal well-being and social success—traits such as beauty, strength, and intelligence—are substantially influenced by a person's genetic endowment.[13] Many of these traits probably are "multifactorial"—that is, the result of the interaction of numerous individual genes and with environmental factors. Altering the function of one of these genes may have undesired effects on other physical or mental characteristics. Eventually, however, research is likely to reveal techniques for successfully "improving" or "enhancing" a person's non-disease genetic traits. This raises a host of problems that will begin to confront the judicial system in the next century. I want to discuss a few of the most challenging issues here.

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Parental authority

It is a truism that parents typically want to give their children the best chance in life that they can. Indeed, some parents seem to know no bounds, such as the mother who was sentenced to 10 years in jail for plotting to murder a popular junior high school cheerleader so that her daughter could fill the vacancy on the cheerleading squad.[14]

Parents not only put their children in private schools and pay for piano lessons; increasingly they turn to medical interventions to give their kids a perceived advantage over others. An endocrinologist reports being asked by parents to prescribe human growth hormone to their child so that she could gain the two inches in height needed to make her an irresistible candidate for college volleyball scholarships.[15] A recent report in the press says that a growing number of parents in California and other Sunbelt states are giving their daughters breast implants as high school graduation presents.[16]

The question that the courts will be forced to struggle with is whether there is a legal limit to the authority of parents to manipulate the genetic characteristics of their children. One way this issue will arise is when parents give their children drugs to improve performance in sports competitions or mental achievement tests. Even if these practices are not expressly forbidden by law or by the private legal rules governing the activity, the possible health risks may subject parents to charges of child endangerment. Similar doubts about parental fitness would arise if parents agreed to let their children participate in experiments to determine the safety and efficacy of enhancement prod-

13. *See, e.g.*, Bouchard, *Genes, Environment, and Personality*, 264 SCIENCE 1700 (1994) (stating that "two-thirds of the reliable variance in measured personality traits is due to genetic influence"). *See also* Finkel et. al., *Heritability of Cognitive Abilities in Adult Twins: Comparison of Minnesota and Swedish Data*, 25 BEHAVIOR GENETICS 421, 430 (1995) (estimating that cognition in early and middle adulthood has a heritability factor of approximately 81%); Petrill et. al., *The Genetic and Environmental Variance Underlying Elementary Cognitive Tasks*, 25 BEHAVIOR GENETICS 199 (1995) (demonstrating that elementary cognitive tasks display genetic effects).

14. *See, Cheerleader Case Sentence*, N.Y. Times, Sept. 10, 1996, at A23 ("[a] woman who offered her diamond earrings in a murder-for-hire plot aimed at getting her daughter on the junior high cheerleading squad was sentenced to 10 years in prison today").

15. Personal communication from Thomas H. Murray, President, The Hastings Center.

16. Cleveland Plain Dealer, April 23, 1999, at 19-A.

ucts. In none of these cases, moreover, would the parents be able to hide behind the shield of religious freedom, as they often can now in making questionable treatment decisions for their children.[17]

Yet parents are not likely to wait until a child is born in order to attempt to influence its genetic inheritance, including its inheritance of non-disease characteristics. The availability of genetic tests will open the door to several types of genetic enhancements that will take place much earlier. The first of these is *pre-conception enhancement*, in which decisions about whether or not and with whom to conceive a child would be made on the basis of pre-conception genetic testing. Just as some people now test themselves to avoid conceiving a child with another person who is a "carrier" for a recessive genetic disorder, prospective mates in the future could test themselves to ascertain if they were likely to produce offspring who were "superior" in terms of non-disease characteristics. Unsatisfactory results would lead to decisions not to marry or not to conceive, at least not without employing genetic manipulations to improve the genetic profile of the offspring.

Another form of genetic enhancement stemming from genetic testing would be *enhancement via selective abortion*. Fetuses would be tested in utero and those that did not match up to parents' expectations would be aborted, just as fetuses currently might be aborted if they tested positive for abnormalities or incurable diseases. An alternative to selective abortion would be *embryo selection for enhancement*, which combines genetic testing with in vitro fertilization so that embryos were tested before they were implanted in the womb, and only embryos with advantageous characteristics were implanted.

Finally, and most dramatically, an early-stage embryo might be genetically altered prior to implantation, with DNA inserted or deleted to produce desired traits in the resulting child. If performed at an early-enough stage of embryonic development, the alteration would affect all subsequent fetal cells, including germ cells—that is, those that became eggs or sperm. This would result in *germ-cell enhancement*, in which genetic changes would be passed on when the enhanced individual reproduced.

Those who can afford to purchase genetic enhancements will gain significant social advantages.

Some of these actions undoubtedly lie within the realm of constitutionally protected personal autonomy and reproductive freedom, for example, the decision about whom to marry based on genetic testing. Other activities may not be so clearly protected. Some scholars argue, for example, that the state has a legitimate interest in regulating selective abortion and embryo selection when performed for enhancement purposes, even though parents have a constitutional right to abort and perhaps even to select embryos for implantation when they do so for medical reasons, such as to avoid the birth of a child with a genetic illness.[18]

An interesting question is what the state's interest would be in regulating parental access to genetic enhancement for their children. The interest might be the need to prevent harm to the future child, similar to the justification offered for government actions to prohibit illegal drug use by pregnant women that threatens the health of the fetus. Yet assuming that genetic enhancement techniques are developed that do not physically harm the child, the state would have to rely on less tangible forms of harm. Some commentators have suggested that genetic enhancement interferes with the child's right to genetic autonomy—that children deserve a genetic endowment free from parental manipulation.[19] Yet parents invariably manipulate their children's futures once they are born. What is so different about doing so before the child is born, assuming that the manipulation is beneficial to the child?

A stronger basis for upholding governmental restrictions on parents' ability genetically to enhance their children might be the negative impact of genetic enhancement on our democratic political system. Genetic enhancement is likely to be accessible only to wealthier families, since it is not likely to be covered by public or private health insurance plans.[20]

Assuming that genetic enhancement is effective at improving personal traits that correlate with social success, those who can afford to purchase genetic enhancements will gain significant social advantages, and the ability to genetically enhance their children, particularly the use of germ line enhancements that are passed on to succeeding generations, could create a "genobility" with an unassailable lock on power and privi-

17. *See, e.g.*, Massie, *The Religion Clauses and Parental Health Care Decisionmaking for Children: Suggestions for a New Approach*, 21 HASTINGS CONSTL. L. Q. 725 (1994).

18. *See, e.g.*, Malinowski, *Coming Into Being: Law, Ethics, and the Practice of Prenatal Genetic Screening*, 45 HASTINGS L.J. 1435, 1450 (1994). *Cited in* Robertson, *Genetic Selection of Offspring Characteristics*, 76 B.U. L. REV. 421 (1996).

19. *See generally* Agar, *Designing Babies: Morally Permissible Ways to Modify the Human Genome*, 9 BIOETHICS 1-15 (1995); Elliot, *Identity and the Ethics of Gene Therapy*, 7 BIOETHICS 27-40 (1993); Kahn, *Genetic Harm: Bitten by the Body that Keeps You?*, 5 BIOETHICS 289-309 (1991); Persoson, *Genetic Therapy, Identity and the Person-Regarding Reasons*, 9 BIOETHICS 18-31 (1995); Zohar, *Prospects for "Gene Therapy"—Can a Person Benefit from Being Altered?*, 5 BIOETHICS 275-288 (1991); Dwyer, *Parents' Religion and Children's Welfare: Debunking the Doctrine of Parents' Rights*, 82 CAL. L. REV. 1371, 1446-1447 (1994), *Cited* in Robertson, *supra* n. 18.

20. For a fuller discussion of wealth-based access to genetic enhancement, see Mehlman and Botkin, ACCESS TO THE GENOME: THE CHALLENGE TO EQUALITY (Georgetown University Press, 1999).

lege. The threat that this poses is more than just a philosophical objection to social inequality; it is a threat to the fundamental belief in equality of opportunity that sustains our political system in the face of frank disparities of wealth, privilege, and power. If, as the result of wealth-based access to genetic enhancement, society becomes divided into genetic haves (the enhanced) and have nots (the unenhanced), the possibility of upward social mobility will be seen as illusory. In the face of such a hardened class structure, the underclass is likely to rebel, in turn provoking anti-democratic repression by the genetic upper class. Even if a stable political system eventually emerged, it would not resemble Western liberal democracy.

Avoiding such a fate is a sufficiently compelling state interest to justify a wide range of restrictions on parental enhancement of offspring, as well as substantial limitations on the freedom of adults to purchase enhancements for themselves. For example, the law might legitimately ban the use of germ line genetic enhancements, and it might allow persons to purchase somatic enhancements for themselves only on condition that they make an enforceable commitment to employ their advantages for social and not just personal benefit, in much the same way that we license professionals such as doctors and lawyers.[21]

Unfairness

No matter what approach society takes to genetic enhancements, some individuals undoubtedly will obtain them—whether by becoming licensed or by purchasing them in an unregulated free market or through black or gray markets in a highly restricted system of access. These individuals will gain significant advantages over unenhanced persons with whom they interact or compete. How should the law respond to the potential unfairness of these interactions?

The law is no stranger to imbalances between interacting parties. In certain situations, courts are called upon to enforce bans on such interactions, such as the private rules that prohibit the use of performance-enhancing drugs in the Olympics or other sports competitions, or the securities laws that ban trading on inside information. In other situations, the law requires the advantaged party to disgorge the advantage to the benefit of the other party, such as by requiring disclosure of information to correct a material mistake by the other party to a contract negotiation.[22] The doctrine of unconscionability allows courts to void a contract if the outcome, resulting from an imbalance of market power or information between the parties, seems too unfair.[23] In still other contexts, the law eliminates the arm's length nature of the transaction, making the advantaged party a fiduciary who must act in the other party's best interests.[24] Yet in some instances, the rules seem blind to the potential unfairness. SAT scores for college applicants are not weighted in terms of IQ, despite the obvious unfairness. Shorter basketball players are not allowed to shoot from stepladders.

These varying responses of the law make it difficult to predict how courts will respond to the unfairness created by genetic enhancements. Yet it seems certain that, at least in some cases, courts will feel compelled to level the playing field.

Negligence

A final illustration of the potential impact of genetic enhancement on the courts is its effect on the standard of care to which people are expected to adhere when they create risks of injury to one another. Should an enhanced person be held to the standard of care of an ordinary reasonable person, or to the standard of an enhanced person? An obvious answer might be that, if enhanced persons ought to be better at avoiding accidents than unenhanced persons, then the enhanced persons should be held to an enhanced person's standard of care. In other words, they should not escape liability by showing that they met a reasonable person's standard of care when, by virtue of their enhancements, they ought to have done better.

Automobile drivers with enhanced vision who run over children, for example, should not be heard to argue that, although they could have seen the child in enough time to stop, they were not negligent since an ordinary person would not have been able to stop in time. This seems to be the answer that the Restatement of Torts would give, since section 289 states that, at least in regard to appreciating the risk created by one's behavior, an actor must use "such superior attention, perception, memory, knowledge, intelligence, and judgment as the actor himself has."

A good argument can be made, however, that when it comes to reducing the costs of accidents, we indeed ought to hold an enhanced person to the lower standard of an ordinary "reasonable" person. The reason is that by not penalizing them with an enhanced person's standard, we will encourage more people to enhance themselves, thereby reducing accidents simply because, as a result of their better vision or reflexes or intelligence, enhanced people are better at avoiding them.

A different society

The broad scope of the issues mentioned in this article—from automobile accidents to altering the genes of future generations—demonstrates the breadth of the impact that gene therapy and related technologies will have on our society. They will challenge conventional notions of illness, insurance, personal worth, and desert, and the limits of governmental control over individual freedom and parental discretion. Ultimately the courts will decide how far the law can go in response to these challenges. One thing is certain: the society that emerges will look very different from our own.

21. For a more complete discussion of these societal responses, see Mehlman, *The Law of Above Averages: Leveling the New Genetic Enhancement Playing Field*, IOWA L. REV. (forthcoming).

22. *See* RESTATEMENT (SECOND) OF CONTRACTS §161(d) (1981).

23. *See* RESTATEMENT (SECOND) OF CONTRACTS §153 (1981).

24. *See* RESTATEMENT (SECOND) OF TRUSTS §170 (1957).