



**THE HUMAN GENOME PROJECT AND ITS
ETHICAL, LEGAL AND SOCIAL IMPLICATIONS**

Tim Williams
Science and Technology Division

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INTRODUCTION

On 26 June 2000, the President of the United States, Bill Clinton, and the British Prime Minister, Tony Blair, announced the completion of the first stage of the sequencing of the human genome, the result of both private and public enterprises. The human genome has been described as the blueprint from which humans are derived. Knowledge of this blueprint is widely touted as the first step toward the prevention, diagnosis, and treatment of disease, as well as its cure.⁽¹⁾ While some have called the announcement “hype,”⁽²⁾ others suggest that knowledge of the human genome will have an unpredictable impact on medical science and that the full meaning of the Human Genome Project (HGP) has been underestimated.⁽³⁾ Still others have suggested that the most important impact will be on how we view others and ourselves.⁽⁴⁾

At this time, the outcome of the Human Genome Project is unknown. Where knowledge of the human genome takes us will be guided by how we choose to use the information. In making this choice it is essential that the possible ethical, legal and social outcomes be discussed as fully as possible, in order that lawmakers may reach a well-informed consensus.⁽⁵⁾ The following paper is a discussion of the Human Genome Project and some of the ethical, legal and social implications of knowledge of the human genome.

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- (1) White House Press Release, “President Clinton Announces the Completion of the First Survey of the Entire Human Genome: Hails Public and Private Efforts Leading to This Historic Achievement,” 25 June 2000.
 - (2) Gabor Mate, “The Human Genome: Decoding the Hype,” *Globe and Mail* (Toronto), 6 July 2000.
 - (3) Dr. Mike Schultz, as cited in Doug Beazely, “Gene Project’s Answers Come with Risks,” *Edmonton Sun*, 3 July 2000.
 - (4) Eric Landers and Robert Weinberg, “Genomics: Journey to the Center of Biology,” *Science*, Vol. 287, 10 March 2000.
 - (5) Stephen Scherer and Lap-Chee Tsui, “The Unwritten Story of the Human Genome Project,” *The Toronto Star*, 6 July 2000.

A. The Science of the Human Genome

1. Genes and Genomes

The genome is the complete set of molecular information that encodes the instructions for making an organism. In most organisms (except some viruses) the genome is made up of deoxyribonucleic acid (DNA). The properties of DNA allow for the encoding of the information necessary for producing a set of proteins that defines the physiology and structure of the cells and organs that make up an organism and provides the basis for passing on this information to the next generation. In humans, each cell, not including reproductive cells, has two copies of the complete genome, one inherited from each parent.

Four different kinds of smaller molecules, referred to as nucleotides and represented by the letters G, T, C and A,⁽⁶⁾ when joined together in a strand make up the larger DNA molecule. Most DNA occurs as two DNA strands that wrap around each other to resemble a twisted ladder, whose rungs are formed by the interaction of complementary nucleotides, A always matching with T and C with G. The human genome consists of approximately 3 billion of these nucleotide pairings, often referred to as base-pairs, in reference to the portion of the nucleotides that interact.

In forming proteins, the DNA molecule is decoded as a series of three letter words called codons. Each codon is associated with one of the amino acids, which are the building blocks of proteins. The four letters can make up 64 different three-letter words, while there are only about twenty amino acids; therefore, most amino acids have more than one codon. The series of nucleotides that contains the information associated with all the amino acids for a particular protein is called a gene; however, not all DNA encodes genes. In fact, only about 5% of the human genome is thought to encode information for proteins and the function of much of the remaining 95% remains unknown. The number of genes in the human genome is estimated at anywhere between 30,000 and 150,000.

The making of a protein involves two steps. In the first, the DNA ladder is “unzipped.” One side of the DNA molecule, known as the template strand, is then used for the formation of a messenger molecule consisting of ribonucleic acid (RNA) molecules that are

(6) A (adenosine), T (thymidine), C (cytidine), and G (guanosine).

strictly complementary to the DNA nucleotides. Amino acids then bind to this RNA message in the order dictated by the position of the respective three-letter codon. It is the order of amino acids in a protein that determines what the function of the protein will be; for example, a structural component of a cell, or an enzyme involved in metabolism. The gene does not strictly govern the final order of amino acids in a protein, as both the RNA messenger and the protein itself can be modified independently. Since each cell has the complete set of genes to make an organism, the specific nature of a cell is determined by the degree to which each gene is turned on and the degree to which the RNA and protein are subsequently modified.

The strictly complementary nature of the nucleotides of the DNA molecule also provides the means by which genetic information is passed from one generation to another. Before a new cell is formed, the DNA ladder is split and respective complementary nucleotides are added to form two molecules of DNA, identical to the first, yielding a cell with four copies of the complete genome. Shortly after this stage, the DNA is contained within the 23 pairs of microscopically visible structures known as chromosomes, after which it separates into two; the cell divides to yield two identical cells, each with two copies of the genome. In sexual reproduction an additional cell division occurs, without a DNA duplication step, so that the resulting cells, either egg or sperm, have only a single copy of the genome. The fusion of an egg and a sperm once again produces a cell with two copies of the genome, one from each parent.

2. Genes and Disease

Approximately 5,000 human diseases are currently thought to have some genetic component. Some of the fundamental causes are easy to identify. In the case of Down syndrome for instance, there is an extra copy of chromosome 21, which is visible under the light microscope. Other genetic diseases that are strongly under the control of a single gene have also been relatively easy to identify. In the case of sickle cell anaemia (SCA), a change in a single nucleotide of one gene alters a codon so that a different amino acid is incorporated into haemoglobin, the protein responsible for carrying oxygen in the blood. Such a change, which is called a single nucleotide polymorphism (SNP), may cause a change in an amino acid that can have a range of effects depending on where the amino acid is located in the protein and the change in amino acid. An SNP can also occur without changing the amino acid because many

amino acids have more than one codon. In Huntington's disease, another disease that is strongly determined by genetics, a single gene has a series of nucleotides repeated many times.

In the case of SCA the gene is known as "recessive" because it requires two copies of the gene, one from each parent, to produce the disease in the offspring. If one parent donates the gene for the disease and the other does not, the child will not get the disease.⁽⁷⁾ In the case of Huntington's, the gene is "dominant"; that is, if one parent has the gene, then half of his or her sperm eggs will carry the disease and a child who receives the gene will get the disease. Thus, a child whose parent has Huntington's has a 50% chance of getting the disease.

As a result of strong single gene control over some diseases, close to 1,000 genes for a variety of diseases have been identified and localized to a chromosome through inheritance patterns. The genes involved in other diseases with some genetic component, such as cancer, heart disease and mental illness, are more difficult to identify because they involve multiple genes that are also heavily influenced by environmental factors.⁽⁸⁾ Environment is only one of many factors that control the degree to which harmful changes in a gene, or combination of genes, may cause health problems. Potentially harmful changes in genes may not result in problems if:

- associated environmental factors do not turn these genes on;
- there is only a partial set of the combination of genes underlying a disease;
- the gene or genes are not expressed strongly;
- the change leads to only a mild form of the disease;
- the gene is recessive and only one copy is present;
- genetic damage does not result from environmental substances or ageing.⁽⁹⁾

The extent to which health problems result from potentially harmful changes to genes is therefore very difficult to predict. At one extreme, we know that diseases such as Huntington's and SCA are strongly determined by changes in a single gene. As more genes

(7) Such offspring have been associated with increased tolerance to malaria.

(8) Scherer and Tsui (6 July 2000).

(9) Catherine Baker, *Your Genes, Your Choices*, Chapter 3.

become involved and environmental factors come into play, the genetic disposition to a disease becomes less and less obvious, however. Diseases that are heavily influenced by environmental factors and interaction with other genes are likely to be far more common than diseases with very strong genetic components. Even strongly deterministic genes, such as those for Huntington's, have a range of effects; for example, some people with the Huntington's gene live much longer than others.⁽¹⁰⁾

B. The Human Genome Project

The Human Genome Project (HGP) is an international effort, coordinated by the United States Department of Energy and National Institutes of Health, that aims to determine the sequence of every nucleotide in the human genome and to identify all the genes contained within the genome. Formally started in 1990, the project was intended to complete the working reference genome by 2005 but technical advances have decreased the timeframe to 13 years.

The genome itself, at six billion nucleotides long, is far too big to sequence as a whole. The initial approach was to break it into pieces, determine the order of the pieces, and then to determine the nucleotide sequence for each piece. A private company split from the public project, however, and began sequencing DNA segments in order to patent them. This forced the HGP to change its approach to match that of the private company and to provide the nucleotide sequence of the pieces before knowing the order of the pieces.⁽¹¹⁾ The statement by President Clinton and Prime Minister Blair 26 June 2000 announced not only the virtual completion of the sequencing of the pieces, but also a truce between the private and public projects. To obtain a reference copy of the human genome that is 99.99% accurate, and with all the pieces in order, will take another three or so years. Various groups around the world have been working on individual chromosomes and the sequencing of these is at different stages of completion. Chromosome 21, with the exception of three gaps 30,000 nucleotides in length, has already been completed to the final standard.⁽¹²⁾ Because this chromosome is implicated in Down syndrome, some researchers had begun to sequence it before the start of the Human Genome Project.

(10) Mate (6 July 2000).

(11) Scherer and Tsui (6 July 2000).

(12) Hattori *et al*, "The DNA Sequence of Human Chromosome 21," *Nature* 405, 18 May 2000.

Unlike some other countries, such as Great Britain and Japan, Canada has had no formal national human genome program and for this reason was not included in the announcement as a partner. Despite this, Canadian scientists have contributed to the HGP, for example through the sequencing of genes and ethics studies.⁽¹³⁾ The Government of Canada has contributed to this research; in the year 2000 budget, Genome Canada was allotted \$160 million for five centres of genome science research in Canada.

One of the most significant aspects of the HGP is that it reverses the way in which science is normally done. Usually, researchers approach a specific problem and then try to find its causes, among which might be the DNA sequence of a gene or genes. The HGP will yield the order of the nucleotides in the human genome, and identify putative genes, but will not identify their functions. It will take many years, if not decades, before the gene products are identified and many more years to understand how they interact with each other and the environment in developmental, biochemical and physiological processes.

The HGP has also involved the determination of the nucleotide sequence for the genomes of other organisms, many of which have been used as laboratory models and so have many well understood biochemical pathways and physiologies. Since their genomes have many similarities to the human genome, knowing their sequences will help to identify genes and the function of genes in the human genome.

C. Related Projects

1. Protein Structure Initiative

One of the ways to understand the functions of genes is to understand the structure of the proteins they produce. This form of study, which is referred to as structural genomics, is a huge undertaking. Current technology requires weeks and can cost tens of thousands of dollars to determine a single structure. Moreover, only a limited number of proteins can be examined in this way; many proteins, such as those embedded in membranes, are very difficult if not impossible to crystallize, a process necessary for the protein analysis technique of x-ray crystallography. Consequently there will be important information gaps,

(13) Scherer and Tsui (6 July 2000).

since many membrane-bound proteins are those targeted by drugs. While there may be approximately 100,000 genes, there are likely several hundred thousand proteins, the result of messenger RNA and protein modification. Including plants and microorganisms, there are millions of different proteins. The National Institutes of Health is starting a Protein Structure Initiative that aims to understand protein structural families, structural folds, and the relation of structure and function. Various private concerns are attempting to do the same, concentrating on what they feel are medically useful proteins.⁽¹⁴⁾

2. Human Epigenome Consortium

In addition to knowing the genome products, it is also necessary to know when and in what tissues the genes are switched on. One of the ways hypothesized is through the addition of a methyl group to cytidine (the C nucleotide). A consortium consisting of the Sanger Centre in the U.K., the Max Plank Institute for Molecular Genetics in Berlin, Germany, and a company called Epigenomics, is initiating a study that aims to identify every methylation site within the human genome. This could prove to be a project as large as the HGP itself.⁽¹⁵⁾

3. The Human Genome Diversity Project

The Human Genome Diversity Project is still in its planning stages but its goal is to understand the diversity and unity of the entire human species. The information should be useful in understanding human biological history, the biological relationships among different human groups, and the causes and treatments of particular human diseases. Currently, individual scientists carry on such research but no samples of human tissue have yet been taken under the auspices of the North American Committee of the HGDP, and will not be until the program is more fully planned and ethical guarantees are in place.⁽¹⁶⁾

(14) Andrew Pollack, "The Next Chapter in the Book of Life: Structural Genomics," *The New York Times*, 4 July 2000.

(15) Michael Hagman, "Mapping a Subtext in our Genetic Book," *Science* 288, 12 May 2000.

(16) Human Genome Diversity Project, FAQ's, <http://www.stanford.edu/group/morrinst/HGDP.html>

D. Ethical, Legal and Social Implications of the Human Genome Project

From the beginning, it has been understood that the Human Genome Project will have profound ethical, legal and social (ELS) implications; thus, between 3 and 5% of its budget has been devoted to the study of ELS issues. Ethical issues are generally defined as those raising questions concerning what is moral or right. Legal issues are those concerning the protections that laws or regulations should provide. Social issues are concerned with how events may affect society as a whole and individuals in society.⁽¹⁷⁾ Clearly, these aspects of the HGP and its possible outcomes are not independent of each other.

Many of the ELS implications are not new. The gene for Huntington's disease was discovered in 1993, after a ten-year search following the localization of the gene to chromosome 4 in 1983. A test for the disease was developed soon after. Many of the questions currently being addressed by the ELS issues program of the HGP have, therefore, been familiar for many years to families afflicted with Huntington's. As a result of the HGP, however, society as a whole will have to deal much more frequently with issues arising from knowledge of the human genome. Moreover, the implications may be less clear in the case of genes identified for diseases that have strong environmental aspects and involve interaction with many other genes.

1. The Existence of Genetic Information

The existence of genetic information with respect to individuals and the human population as a whole will have a profound impact on our day-to-day lives and may well change how we regard ourselves and one another.

The knowledge of predisposition to a certain disease and the ability to design "tailor made" therapies may greatly help in the treatment of disease. Already a company in Great Britain has applied for a patent on a device that can apparently detect different forms of over 2,500 genes said to be associated with traits including behaviour and intelligence.⁽¹⁸⁾

It has been argued, however, that it is not proper, particularly at this juncture in history, to search for such knowledge. For example, some have pointed out that science has often been co-opted as a tool to accentuate racial differences and to defend racist practices.

(17) Catherine Baker, *Your Genes, Your Choices*, Glossary.

Given that humans are far from resolving issues of race, it is thought that information from the HGP, and such follow-up projects as the Human Genome Diversity Project, may have the potential to inflame racism in an already overly racist world.⁽¹⁹⁾

Equally, some feel that if the goal of the HGP is to prevent disability and disease, increase life spans, decrease infant mortality, and increase intelligence, the money would be far better spent elsewhere.⁽²⁰⁾ Given that we already know that environmental and social factors can influence such diseases as diabetes in aboriginal populations and drug addiction among the socially marginalized, some consider it unconscionable to dispense limited resources looking for genetic causes for these diseases.⁽²¹⁾

The legal aspects of knowledge of the human genome are enormous. Already DNA evidence is being used as a powerful legal tool, particularly in exonerating wrongly accused individuals. Does this mean that the criminal system should be able to keep a bank of DNA information on anyone accused and/or convicted of a crime? Could the database be used for other purposes than simply identifying and eliminating suspects? A DNA database could contain much more information on individuals, both guilty and innocent, than does the current system of taking fingerprints.

On a more hypothetical note, should genes leading to a propensity for criminal activity be found, could they be used as prosecution or defence evidence in a trial? For instance, is a suspect who knows that he or she has a genetic disposition toward criminal behaviour and does nothing to avoid provoking such behaviour, guilty of a more serious crime than a suspect who is ignorant of having such a propensity? On the other hand, could genetic disposition be used as a defence on the grounds that the crime was really the fault of the gene, not the person?

When a patient tests positive for a gene linked to risk of disease, does the physician (or the patient) have a legal responsibility to inform the patients' relatives of their own risks? Suppose a patient finds out that she has a genetic propensity for breast cancer, but neither

(18) Andy Coghlan, "Nowhere to Hide," *New Scientist*, 11 March 2000.

(19) Barabara Katz Rothman, "Genetic Maps and Human Imaginations: The Limits of Science in Understanding Who We Are," as cited in Gail Vines, "Why Map a Human?" *New Scientist*, 29 January 2000.

(20) Barabara Katz Rothman (29 January 2000).

(21) Mate (6 July 2000).

she nor her doctor informs her relatives; would a relative who later developed that form of cancer be able to sue, on the grounds that the genetic information had not been disclosed?

Ensuring that the judge and jury in a trial are sufficiently educated to deal with these issues is yet another problem with which the legal system will have to deal.

On a larger social scale, knowledge of the human genome could be used to emphasize the similarities among all humans. The genetic differences between people within an identified group have already been shown to be greater than the differences between groups. In other words, people within an “ethnic” population are more different from each other than the group as a whole is different from other “ethnic” groups.⁽²²⁾ This fact is unlikely, however, to deter those who wish to emphasize any ethnic differences that may be found.

On a more individual level, the results of the HGP might encourage people to view themselves as being wholly under the control of their genes. What has traditionally been viewed as the human spirit might in future be seen as limited by pre-programming at birth. Thus, though we cannot predict exactly how knowledge of the human genome will affect society, it could clearly have important consequences.⁽²³⁾

Individual decisions, such as choices with respect to mates and reproduction, could also be influenced by knowledge of genetic makeup. Awareness of personal genetic differences from a perceived norm might lead to confusion and uncertainty about the potential for disease, particularly in the absence of adequate professional consultation. Genetic analysis might reveal a myriad of genetic flaws that may or may not lead to disease, depending on what they are and how they interact with the environment. How will individuals select from a debilitating array of lifestyle choices, none of which has a certain outcome? Again, analysis of one’s own genetic makeup could reveal the genetic makeup of parents and siblings, including, for example, unsuspected information about paternity. How willing would people be to share this knowledge and, if they decided to withhold it, how would they be affected by living with the secret?

(22) Human Genome Diversity Project, North American Committee, FAQ’s, <http://www.stanford.edu/group/morrinst/hgdp/faq.html#Q6>.

(23) Lander and Weinberg (10 March 2000).

2. Ownership and Commercialization

On 11 November 1997, UNESCO passed its Universal Declaration on the Human Genome and Human Rights. Article 4 of the Declaration states that “The human genome in its natural state shall not give rise to financial gains.” In most countries, however, DNA, when isolated from an individual, is not considered to be in its natural state and therefore can give rise to financial gain. One of the benefits of the HGP and genomics research in general is expected to be a thriving biotechnology industry with the potential, in the United States, to be worth \$45 billion (U.S) by 2009. In most technological industries, innovation has been encouraged through the granting of patents on inventions.

Researchers who devise an invention that is useful, new, and unobvious are given approximately 20-year proprietary rights over its use. To be patentable, discoveries must involve some human intervention and inventiveness.⁽²⁴⁾ In return for these rights, the inventor must make the invention public so that others may, at a price, use it to further their research.

For approximately 20 years, sequences of DNA that correspond to human genes have been claimed in patents. Conceptually, the string of DNA molecules is considered no different from other chemicals isolated from living organisms, such as penicillin, as long as it passes the tests for patentability (being new, useful, and unobvious).

For a number of reasons, some believe that human gene sequences should never be patentable. A fundamental, philosophical reason is the belief that the human genome, as an intrinsic part of every person, is a common heritage that all humans should share. This line of reasoning has led the Parliamentary Assembly of the Council of Europe to recommend that European Union countries renegotiate the agreed Directive that allows the patenting of human genes that are isolated from the body and applicable to industry, and specifically prohibit the patenting of human genes.⁽²⁵⁾

The World Trade Organization’s Trade Related Aspects of Intellectual Property Agreement includes some discussion on what member countries can exclude from patentability. Article 27(2) states that anything that is necessary to protect the “*ordre public* or morality” can

(24) *Nadon J. President and Fellows of Harvard College v. Canada* (Commissioner of Patents) (T.D.), 21 April 1998.

(25) “Human Genes Cannot Be Patented, Says Assembly,” 29 June 2000, http://stars.coe.fr/index_e.htm.

be excluded, as long as the exemption is not made simply because it is prohibited by law. Section 27(3)(a) states that member countries may also exclude diagnostic, therapeutic and surgical methods for humans and animals. No specific clause would seem to prevent a member country from excluding the patentability of human genes. Canada's *Patent Act* does not have an "ordre public" clause.

Some offer logistical reasons to explain why patents should not be extended to DNA sequences. They suggest that such patents, particularly on partial gene sequences, would inhibit innovation rather than encourage it, as the patent system is supposed to do. This could arise in a scenario, dubbed the "tragedy of the anticommons," in which numerous people and organizations held patents on different DNA sequences governing an overall biochemical pathway that could be the target for a medical treatment. To research that treatment, someone would have to negotiate for the rights to all the DNA sequences from all the respective owners; this might be so costly and onerous as to make further research unlikely. Pure researchers, who would not have the money, the time or the expertise for a complex series of transactions, would be the most severely affected. Others, however, refute this argument, citing the case of the computer industry. Patents on the various parts of computers certainly do not seem to have impeded the growth of that industry, though some might say that it has impeded innovation. Others point out that in the computer industry, the free flow of information has been a driving force behind such innovations as the GNU-Linux operating system.⁽²⁶⁾

It has also been suggested that DNA does not pass the tests for patentability on the ground that, since DNA exists in nature, knowledge of it is simply a discovery, not an invention. Therefore, while drugs should be patentable, the DNA sequence upstream from the target of the drug should not be.⁽²⁷⁾ Moreover, it is said that many of the techniques used to isolate and manipulate DNA are now routine, and therefore the inventions are too obvious to be patentable.

In North America, the focus is more on what level of utility must be shown in order for genes to be patented, rather than on whether they are patentable at all. The Canadian

(26) Andreas Russ *et al.*, "Open-Source Work Even More Vital to Genome Project Than to Software," *Nature*, 404, 20 April 2000.

(27) John Sulston, "Forever Free," *New Scientist*, 1 April 2000.

Patent Act, as it is written, has for a long time been interpreted as meaning that genes are patentable material. A problem has arisen because many private companies have concentrated on sequencing genes in the hope of obtaining patents on a gene that may one day prove to be useful. Most of the genes sequenced by the HGP and private enterprises have as yet unknown functions; thus, applications are being made for DNA sequences that have no genuine utility. Since the sequences do encode a protein, some companies have gone so far as to claim that, at a minimum, the protein could be used for animal feed or in a molecular biological technique as a DNA probe. In one well known case in the United States, the company Human Genome Sciences obtained a patent on a gene that was subsequently discovered by a different researcher to be an entry portal through which the AIDS virus infects cells. Any future treatment of these cells that alters this entry portal will require royalties to be paid to Human Genome Sciences.⁽²⁸⁾ While the Canadian *Patent Act* is similar to its U.S. equivalent, Canadian patenting procedures are generally more stringent with respect to the utility of the invention than are those in the United States, the country where the controversy is greatest. The U.S. Patent Office has recently announced that it will increase the stringency of the utility requirement for patenting DNA sequences.

Searching for medically useful, and therefore potentially profitable, genes also raises many ethical questions. Heritable disease patterns sometimes emerge in populations that have not mixed extensively with other populations; as a result, private companies are doing genetic exploration in such relatively isolated areas as Newfoundland, Iceland and certain tropical islands. In Iceland, a company called deCODE has been given the rights to produce a health sector database that will include genealogical, environmental, and molecular genetic information, along with the combined anonymized patient records of the country. In Newfoundland, political leaders are apparently coming to the conclusion that Newfoundlanders should maintain control over their unique genome.⁽²⁹⁾ How to regulate the gene hunters without scaring off investment is a familiar problem to governments that already have experience with

(28) Andrew Pollack, "U.S. Hopes to Stem Rush toward Patenting of Genes," *The New York Times*, 28 June 2000.

(29) John Greenwood, "The Business of Genes: Newfoundland Hopes to Reap the Benefits after Its Genetic Heritage Has Helped Decode the Human Genome," *The Globe and Mail* (Toronto), 24 June 2000.

charging royalties and regulating natural resource operations. Gene “mining” companies, however, present a much more complex and emotional set of ethical issues than does the natural resources sector.

3. Genetic Treatment of Disease

From the outset, one of the defining goals of the HGP has been its potential for molecular medicine. The concept is that, once the functions of genes are known and we understand the effects of malfunctioning genes, we will be able to correct the problem either through the use of designer drugs or by replacing the faulty gene. It is the latter option that has created the most controversy.

There are two routes to replacing a faulty gene. The first route, germ line therapy, has the goal of replacing a harmful gene in a fertilized human egg with a properly functioning gene that would be passed on to future generations. The other route, somatic gene therapy, aims to replace the gene in target organs or tissues of an adult, so as to fix the symptoms in that individual but not in the next generation. Germ line therapy has the more profound ethical, legal and social implications.

As yet germ-line therapy in humans is not possible and some have argued that it will continue to be so for the foreseeable future. While this kind of therapy may be a long way off, it would bring, on the one hand, the hope of eradicating some genetic diseases but, on the other hand, the spectre of eugenics.

The eradication of disease through germ-line therapy might not seem, by itself, to raise many ethical questions. After all, humans have eradicated the smallpox virus from the world, why not diseases with genetic components? Do doctors not have the moral obligation to provide the very best treatment to their patients and would not the eradication of the disease be more cost effective in the long run than continually treating adults with somatic gene therapy? The main ethical problem arises in defining a “treatable” disease.

Some might say that eradication of a genetic disease for which there is no treatment and which is always fatal, should be pursued with all means possible. Others say that this would be the start of a slippery slope moving on toward the treatment of less obvious diseases and then to genetic enhancement. Some argue that if the technology is advanced in

order to eradicate some diseases, it will inevitably be used by parents wishing to “enhance” their children, giving them the genes for raven black hair and blue eyes or athletic prowess. It was serious ethical concerns about genetic enhancement that prompted the Council of Europe to adopt the Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine. Article 13 of the Convention states that “an intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants.” Article 11 of the UNESCO Universal Declaration on the Human Genome and Human Rights states that “practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted.” It is left to individual states, however, to define exactly what they believe these practices to be. Thus, while some countries, such as the signatories to the European Convention, may prohibit germ-line therapy, others may not. It is the existence of national differences in regulation of research on human embryos that has allowed controversial research to be performed, for example, in Singapore. Regulation has thus slowed down the progress of research but not prevented it.⁽³⁰⁾

Another ethical consideration with respect to germ-line therapy is defining what is normal, what is a disability, and what is a disease. Which of the genetic variations within a population ought to be eradicated, if any? In trying to eradicate a certain variation, are we demeaning those in the population who currently carry the gene?

Somatic gene therapy has its own, less controversial, set of ELS implications. These may be less ominous than eugenics but are of perhaps more immediate concern, given the more advanced state of the technology. Effectively, gene therapy involves the introduction of a properly functioning gene into target tissues in the hopes that it will be translated into a properly functioning protein, which will mask the malfunctioning protein. Often the new gene is placed into a modified virus, which is then introduced into a patient in the hope that the gene will be introduced into a tissue and properly expressed.

Such types of therapy, after much research on laboratory animals, have now reached the clinical trial stage. Unfortunately, what works for a mouse does not always work for

(30) Rachel Nowak, “Decision Time,” *New Scientist*, 8 April 2000.

a human being. In one highly publicized case, a patient, Jesse Gelsinger, was given an injection of a virus in the hope of introducing a protein into the liver. Mouse studies showed good absorption of the gene into the liver; however, the mouse has a much higher concentration of viral receptors on its liver cells than do humans. The virus did not absorb well into the human patient and, for still unknown reasons, created a massive immune response, causing the patient to die.⁽³¹⁾ The original plan for the trials had been to use the virus only on children in a coma caused by the lack of the particular liver enzyme; however, ethical and safety reviews caused the researchers to change the trial direction and use adults only. Many questions are now being asked regarding the ethics and scientific judgment of those performing such clinical trials. How well are “volunteer” patients informed of the possible risks and benefits? How objective are investigators who have equity in the companies that are funding the trials?⁽³²⁾ One of the risks at this stage of gene therapy is the excessive public anticipation, created in part by some researchers, with respect to future benefits. This anticipation may turn to public distrust of science, if the benefits fail to be realized and problems such as that in the Gelsinger case continue to occur. Some clinical trials have shown positive results,⁽³³⁾ and so there is still hope that somatic gene therapy will become a powerful medical tool.

4. Discrimination

One of the problems some fear might result from knowledge of the human genome is the emergence of a whole population of socially marginalized individuals, unable to obtain a job, a family, insurance, or health care and stigmatized by the rest of society. Insurance companies already insist that those identified at risk of Huntington’s disease must take a genetic test. If the results are positive, insurance is frequently refused. Insurance companies are on record as saying that if genetic information was available, they would use it in their risk assessment.⁽³⁴⁾ In Canada, the refusal to insure a Huntington’s patient does not have dire

(31) Eliot Marshall, “Gene Therapy on Trial,” *Science*, 288, 12 May 2000.

(32) Leon Rosenburg and Alan Schecter, “Gene Therapist Heal Thyself,” *Science* 287, 10 March 2000.

(33) Marina Cavazzana-Calvo *et al.*, “Gene Therapy of Human Severe Combined Immunodeficiency (SCID)-X1 Disease,” *Science* 288, 28 April 2000.

(34) Laura Landon, “Insurance Giant Wants Your Gene Map: ‘If the Information Is There, We Would Like to Be Able to Use It.’ ” *The Ottawa Citizen*, 6 July 2000.

consequences; in general, public insurance covers many aspects of care, though the level of care varies across the country and the coverage for pharmaceuticals is less clear. In countries without a public health insurance system, however, the plight of such a non-insured person can be a nightmare.⁽³⁵⁾ Care may be available but finding it is very difficult. As more genetic tests become available, insurance is likely to be more and more expensive for those carrying what the insurance companies deem to be risky genes. The public insurance schemes may also start to feel the pressure for such genetic testing, and be forced to make policy decisions based on the funding available and the knowledge of genetic predisposition to disease within populations. Gene therapy is at the experimental stage at this point but will certainly be very expensive when it first comes into regular use. Who will pay for it? If not public insurance, will the therapy be available only to rich people, thus creating an ever widening gap between groups in society, based on both money and genetic inheritance?

Employers may also want access to genetic information. Some genes might reveal a susceptibility to environmental damage that was incompatible with a certain workplace environment. Employers might choose to screen out workers carrying that gene rather than trying to improve the environment. Individuals with genes associated with certain behavioural traits might also be excluded from the workplace.

Some action has already been taken to prevent the possibility of genetic discrimination. For example, President Bill Clinton has signed an executive order prohibiting federal departments and agencies from using genetic information in any hiring or promotion action. He has also endorsed an Act, introduced in 1999 by a Senator and a member of Congress, that would extend such protection to the private sector.⁽³⁶⁾

CONCLUSION

Many of the ethical, legal and social issues that are being discussed with respect to the Human Genome Project are not new. Genetic tests for a variety of diseases are currently

(35) Huntington's Society of Canada, interview, July 2000.

(36) The White House, Office of the Press Secretary, "President Clinton Takes Historic Action to Ban Genetic Discrimination in the Federal Workplace," 8 February 2000.

available and some people are already struggling with the ethical and practical implications. What will change over the next few years, as a result of the Human Genome Project, is the scale of the issues and how society will have to cope with the greyer areas of genetic disease and disability. Dealing with a single gene that causes death or chronic disability is one issue, dealing with whole sets of genes whose impacts vary depending on environmental interactions is another. The rate of scientific advancement has tended to outstrip the legislative capacity of governing bodies and there has been some media “overhype” with respect to genetic research and its potential for treatment of disease. It will be years before many of the genetic tests are available and before genetic diseases can be treated. Society as a whole must use this time to discuss and decide on how genetic information ought to be used, before the choices are made for them. It is a discussion that those with genetic dispositions to diseases such as Huntington’s have long wanted to make more public.