

Ethical Issues Arising from the Study of the Human Genome

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“To know the mighty works of God, comprehend His wisdom and majesty and power, to appreciate in degree the wonderful working of His laws, surely all this must be a pleasing and acceptable mode of worship to the Most High to whom ignorance can not be more grateful than knowledge.” With this quote from Copernicus, Francis Collins, Director of the National Institutes of Health’s Human Genome Research Institute, characterized his motivation for the scientific enterprise. He was speaking at the March 7th lecture on “Ethical Issues Arising from the Study of the Human Genome.” Also speaking was Cynthia Cohen, lawyer, ethicist and Fellow of the Kennedy Center for Bioethics at Georgetown University.

Collins said that there were two general principles that emerge from the study of genetics: genes are involved in almost all diseases and there is no perfect genetic specimen. In light of these principles he called attention to three things discovered in the initial sequencing of the human genome. First, the genome is only about a third as large as was anticipated, with 30-40,000 genes. He noted that yeast has a genome of about 6,000 genes, the fruit fly 13,000 genes, and the round worm 18,000 genes. This suggests that the complexity of the human organism is the result not so much of the number of genes but their interaction.

Second, Collins pointed out that the sequencing the human genome has made it possible to calculate the relative mutation rates of males and females. It turns out that rate is about twice as great for males as for females. This means both that males account for about 2/3 of gene-related diseases and also about 2/3 of evolutionary change related to mutations.

Third has been the discovery that so-called “junk” DNA, DNA that does not code for proteins, has all of the signs of having a function, as shown by its evolutionary preservation in the genome. Although we do not know yet what that function is, Collins suggested that it is clear that this DNA should not be labeled as “junk.”

Collins went on to point out that the profound impact this growing genetic knowledge will have for medicine. Obviously, being able to identify genes related to diseases will enable early interventions that can eliminate or significantly reduce the likelihood of the disease. Collins noted that such genetic diagnostics are already being used in relation to such diseases as colon cancer.

Another important impact will be in the growing field of pharmacogenetics in at least two ways. Genetic knowledge can help predict which individuals might have a toxic reaction to the normal dosage of a particular drug. This would allow the drug to be used for therapeutic benefit but at a lower dosage. A more powerful application is the use of increased genetic understanding of the molecular processes that cause disease to design drugs that intervene in very targeted ways. Gleevec, a drug used to treat chronic myeloid leukemia, has provided a dramatic example of this possibility.

But every new scientific discovery, Collins cautioned, is like “Pandora’s Box.” This is one reason that NIH’s human genome research effort from its very beginning has had funds set aside to study the ethical, social and legal implications of the research and its potential applications.

Collins closed his remarks by identifying a number of ethical issues that, in his judgment, most need answers. The first of these has to do with protection against genetic discrimination in either employment or access to healthcare. He noted that several states have passed anti-genetic discrimination legislation but these state laws are variable in their quality and at best provide a “patchwork” of protection. What is required is federal legislation, and Collins was optimistic that such legislation could be passed and signed by the president this year.

There is a more general issue of access to these new forms of therapy. Collins noted that 40 million Americans do not have health insurance. Care must be taken that the benefits of genetic medicine are not limited to the wealthy.

There is the question of the relationship of new genetic knowledge to racism and prejudice. Collins declared, “Science provides a real opportunity to point out that many of our concepts on which prejudice is based are social and cultural, not biological and scientific.” He noted that in any heterogeneous mix of people, any selected pair will be 99.9% genetically identical. In addition, 90% of observed genetic variation is generally distributed across the human population and was already present in the founder community of *Homo sapiens*. This means that if we consider the genetic similarities and generally distributed variations, then we are 99.99% the same.

Genetic enhancement is another Collins called attention to the film *Gattaca*, which portrays a society in which parents are able to select the genetic make-up of their offspring including such traits as physical robustness, intelligence, and creativity. But he cautioned that such traits are not only very complex genetically but are also traits greatly dependent on environmental factors. Collins indicated that there is no consensus on what boundaries should be in place as genetic intervention moves beyond treatment of disease to the selection of traits. He emphasized that this issue is exacerbated because of the inequitable way that health care is currently available.

Collin’s final caution was with respect to the growing public acceptance of genetic determinism. Such an attitude, he warned, can make us neglect the role of the environment. It can also lead us to undervalue all those features of life that are not easily explained on the basis of biology: love, free will, and the need for God.

In her discussion, Cynthia Cohen spoke about the convergence of the new knowledge being developed through the human genome project and new reproductive technologies used to conceive children outside of the body such as *in vitro* fertilization (*IVF*) and intracytoplasmic sperm injection (*ICSI*). Merging these new reproductive technologies with gene testing will allow us to try to produce children without certain genetic disorders. This technique, preimplantation genetic diagnosis and selection, is controversial because it involves discarding embryos. This technique can also be used to choose embryos with genetic features that allow the children who are born to donate bodily materials to family members who suffer from serious

conditions. This second use is even more controversial because it involves producing children for their utility.

She mentioned that we may also develop the ability to alter the genes in the embryos rather than selecting embryos that have desirable genes. This will be a form of germline intervention. Such an intervention that will influence a child at all stages of development and will be inherited by the child's descendants.

Cohen pointed out that these growing possibilities for genetic intervention in human reproduction raise a number of ethical and theological issues, and she identified three sets of questions. The first set has to do with questions of safety. At present, techniques for the insertion of genetic material into the genome have the character of an "unguided missile." The insertion is not well targeted and so can cause irrevocable harm as well as benefit. To the extent that such interventions also rely on *IVF* and *ICSI*, the safety of these reproductive technologies is also a factor. Cohen called attention to a recent article in the *New England Journal of Medicine* that reported that children conceived using such technologies have double the rate of birth defects and lower birth weight than children conceived normally. The safety issues related to germline interventions are especially difficult because they are intergenerational and deleterious effects may be cumulative long after the initial intervention has been carried out.

A second set of issues is concerned with human evolution. Cohen cautioned that germline interventions run the risk of eliminating from the gene pool certain genes that, while associated with disease (e.g., sickle cell anemia), are also linked to benefits (e.g., malaria resistance). She noted that some think that human beings and their genes should be untouchable as a matter of moral and theological principle and that altering the human genome risks changing the very meaning of what it is to be human. But others note that we have been interfering with evolutionary process for a long time by, for example, saving infants from death who were born with serious disease and by treating people with diseases like diabetes thereby increasing the frequency of that genetic propensity in the population.

The final set of questions Cohen identified were those dealing with genetic enhancement. She noted that safe techniques that allow us to eliminate disease and serious disability may also give us the power to try to design human life. Like Collins she acknowledged that in some cases it is not easy to distinguish between therapy and enhancement. Cohen also noted that some argue that we already engage in enhancement from our choice of marriage partner to the efforts of parents help children reach a higher levels of performance in school, sports or artistic endeavors. But, Cohen proposed that there is a difference between giving children opportunities and biologically changing them irrevocably.

Cohen suggested that a move toward genetic enhancement involves a subtle shift in what we mean by having children and being parents. "What difference will it make," Cohen asked, "if we move from cherishing our children as they are born to selecting them. Children will no longer be gifts who surprise us, but projects that we manufacture." She concluded, "In such a situation traditional religious language of children as 'gifts of God' can only seem quaint. This can result in a lack of respect for the otherness of our children."