



THE HUMAN GENOME PROJECT

In June 2000, scientists gathered in Washington to announce they had completed the first survey of the entire human genome and had roughly established the sequence of approximately three billion genetic letters that make up the code of our genes. This achievement has profound implications that will take us a long time to understand. This discovery, at least for me, is deepening the mystery of what it means to be human, not simplifying it.

But what is the nature of this Human Genome Project milestone? What are the near-term, mid-term, and long-term implications? Most importantly, how will Catholic health care address these potential ethical dilemmas?

NEAR-TERM IMPLICATIONS

Cancer Treatment In the next five years, we will see major advances in identifying persons at risk for certain cancers. These advances have already begun with both breast and colon cancer. Cancer, in many respects, is a genetic disease. Cancer is created by a series of genetic errors in the somatic cells of our body. Researchers at Johns Hopkins have shown that colon cancer is the result of five to seven different genetic errors that shut down certain protective mechanisms; when they've all failed over 50 to 60 years as cells divide, the result can be a form of cancer. Cancer happens because of changes in the DNA



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Dr. Reilly is CEO of Interleukin Genetics, Inc., Waltham, MA. This article is adapted from a talk given at the 85th annual Catholic Health Assembly, June 11-14, 2000, San Francisco. Videotapes of this presentation CHA; call 314-253-3458.

*Recent
Genetic
Advances
Will Have
Far-Reaching
Implications
for Catholic
Health Care*

BY PHILIP R.
REILLY, MD, JD

molecule, although environmental agents cause many of those changes.

Heart Disease Even though the major risk factors for heart disease are high cholesterol, high blood pressure, a sedentary lifestyle, diabetes, and family history, half the people in the United States who die of heart disease this year will have normal cholesterol and normal blood pressure, exercise regularly, and not have diabetes. Obviously other things need to be learned about heart disease, and many of the risk factors will likely turn out to be genetic. One risk factor won't explain 10 percent or 20 percent of this risk—the answer will be several smaller risk factors. We will need very powerful tools, which are being developed, in the area of bioinformatics to crunch all these risk numbers and create a profile. Many problems will be associated with assessing those risks. In a way, the genetic physician of the near future will be somewhat like a meteorologist—right most of the time, but not completely certain about the risks and outcomes.

MID-TERM IMPLICATIONS

DNA-Based Newborn Screening Virtually every child in the United States, by compulsory state law, is currently screened for a number of genetic disorders that can be treated by intervention, such as phenylketonuria and hypothyroidism. However, in the next 10 years, we are poised to greatly expand the number of screenable disorders, which raises fundamental questions. For example, what constitutes a disease? What should we be screening for? Why? What criteria do we need to know to treat the disease? How are we going to share the information?

Personalized Pharmaceuticals The pharmaceutical industry has made a multi-billion-dollar bet on an entirely new approach to drug development in which pharmaceuticals will be tailor-made to



individual DNA differences. Not one drug for a single person—although that may be possible 100 years from now—but different drugs geared toward different groups of patients. For example, for a given disease, 10 percent of patients might react negatively to a drug that would help the other 90 percent. If we could isolate that 10 percent and not give them that drug, a drug that might have been kept off the market because of a bad risk profile would be an excellent treatment for the other 90 percent.

Expanded Premarital Screening

Many genetic tests are offered to people before they marry, such as for sickle cell anemia among African-Americans, Tay-Sachs disease among Ashkenazi Jews, and cystic fibrosis among people of northern European extraction. More of these tests lie in our future. This type of screening raises profound questions about the role of science and medicine in human reproduction that must be confronted squarely—and soon.

Somatic Cell Gene Therapy Gene therapy, despite its current riskiness, is inevitable in the next 10 years. Hurdles will appear and mistakes will be made, but both will eventually be overcome.

Xenotransplantation Xenotransplantation refers to the genetic manipulation of animals, such as the pig, to develop organs that our bodies would recognize as human. Xenotransplantation has the potential to overcome the chronic lack of organ donors, such as for people with end-stage kidney disease. Xenotransplantation is likely to occur in the next 10 years and will be a two-edged sword.

LONG-TERM IMPLICATIONS

I hesitate to peer much more deeply into the future than 20 years, considering how far we've come in the last 20 years. In this time frame, I see a set of profoundly challenging ethical and social dilemmas.

Universal DNA Banking Universal DNA banking is a very realistic possibility for the next generation. This term refers to collecting DNA samples of every individual at birth, storing the data, analyzing the data, and using it to guide that person's health.

Here, room for nefarious misuse exists: What kinds of controls do we need to move ahead in this arena in a reasonable way?

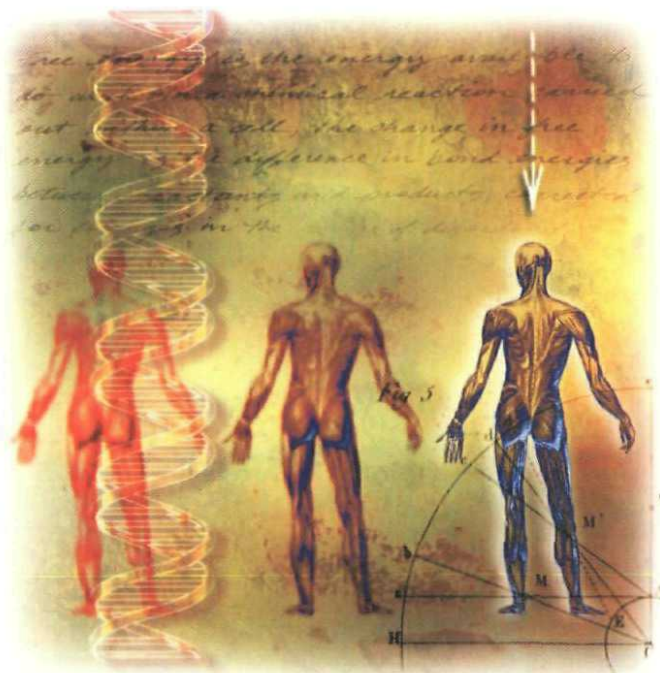
Childhood Intervention One potential reality of the genetic revolution is deeply troubling to me because of the lack of discussion about it in the scientific and clinical communities. As we come to understand the role of genetic variation in human disease, and as we understand how people are born with risks, interventions may be among healthy people, young people, and children. Imagine that if one in 100 women is born with a very high genetic risk for breast cancer, intervention may include therapy before the breast develops to change the milieu in which the breast tissue unfolds.

Psychotic Disorders What would we do if we could identify genetic variations

that predispose in a very substantial way to schizophrenia or bipolar disorder? Treatment of these diseases represents a huge percentage of the American health care dollar. How will we treat families with the burden of that disorder? Imagine a scenario such as the following. Tests show that a 10-year-old child, who is completely healthy, is at risk for schizophrenia because one parent has the disease. A new medicine may greatly reduce her chance of developing the disease, but the drug may cause serious side effects. Imagine the ethical dilemma faced by the family and the physician. No guarantee exists that the child will have the disease, but perhaps the drug wouldn't work as well once the condition manifests. These aren't even the hard questions.

Fetal Diagnoses In the next 20 years, we will have the technology to find out things about fetuses that we've never been able to discover before. Given the culture we live in, some conditions that today are considered normal could be considered to be imperfect by some groups in the future. What does this mean for our sense of what it means to be human?

Germ-Line Therapy Germ line gene therapy is the direct manipulation of either a two-cell or four-cell human being (a pre-embryo) to insert or alter a gene to avert disease. Many of us could accept





this manipulation as a way to encourage a life and to avert disease. But what about enhancement? For example, some time in the next few years scientists will be able to clone the gene for perfect pitch. This gene is dominant and is being mapped at the University of California-Berkeley. Evidence so far suggests that if you're not born with it, you can never acquire it. In light of this discovery, one wonders about the overall temptations of genetic enhancement that will undoubtedly arise.

Human Cloning I do not expect human cloning to be of much importance to the human family, but it will be technologically possible in 20 years. Dolly, the first cloned sheep, was created only three years ago. Hearing about the cloning of various mammals is now routine. The topic of whether cloning could actually increase the human life span is currently being broached; as studies have shown in cattle, we have the first hint that it will.

SHARING GENETIC INFORMATION

We must work together to analyze the implications of this powerful new technology for humanity. Who should have access to this information? For what purposes should it be used? A good way to organize your thinking is to ask what you would

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like to know about yourself. Right now, what would you like to know about yourself genetically? Why would you want to know it? For example, a certain percentage of the population has a genetically high risk for early-onset Alzheimer's disease. Would you like to know if you fall into this category? The answer to that question is attainable today through a low-cost test. But so far, the medical community has said, "Don't use the test for that purpose because it's a 'little uncertain.'"

How will we share genetic information, especially within families? If I fall and break my ankle, the injury won't matter much to my brother. But if I learn that I have the gene for colon cancer, that knowledge could be immensely important to him. We have no ethical or legal rules for sharing genetic information. How this information will be shared in extended families—in which not everyone cares for everyone else in exactly the same amount—is a troubling question.

In addition, no one shares information in exactly the same way. I once made the diagnosis of fragile X syndrome in a young boy. Because of its genetic nature, I knew that his aunts were at risk for bearing a child with the same problem. When I told the mother, she absolutely forbade me to share the information with her sisters—she was staunchly pro-life, and her sisters were pro-choice. She said to me, "I will not contribute in any way to the possibility of an abortion of a nephew." These are the issues that tear families and societies apart.

Should a doctor ever breach genetic confidentiality? Genetic information is different from other medical information in that such knowledge can be relevant to other family members. We don't have any rules on this. What if a physician found out that a patient had a genetic risk for sudden death from a rare form of heart disease that may be shared by other family members? Would a doctor ever be permitted to breach that wall of confidentiality?

LEGAL RAMIFICATIONS

A Nebraska Supreme Court case a few years ago provides a perfect example of an issue that makes me concerned. At the heart of the case was a woman who had a family history of ovarian cancer. She had completed her child bearing and wanted to have an ovariectomy to reduce the future risk of ovarian cancer. She had consulted with clinical endogeneticists who basically agreed with her. At the time, no DNA testing was available for ovarian cancer, as would be possible today. Her insurers refused to pay for the operation because they said she was healthy, had normal

IMPLICATIONS OF THE HUMAN GENOME PROJECT

NEAR-TERM IMPLICATIONS (FIVE YEARS)

- Major advances in identifying persons with a predisposition to certain cancers
- Advances in predicting the course of certain types of cancer and the response to therapy
- New insights into development of heart disease in persons without standard risk factors
- Wide use of stem cell therapy

MID-TERM IMPLICATIONS (10 YEARS)

- DNA-based newborn screening for scores of disorders
- Development of drugs based on genetic differences
- Expanded premarital screening options
- Somatic cell gene therapy
- Xenotransplantation

LONG-TERM IMPLICATIONS (20 YEARS)

- Universal DNA banking
- Interventions in children to avert adult-onset diseases
- Special considerations in treating psychiatric disorders
- Technology to avoid birth of children with severe genetic disorders
- Germ-line gene therapy possibilities
- Human cloning possibilities



ovaries as far as could be determined, and there was no certainty she would get the disease. To make a long story short, she had the operation and then sued to recover the costs against her insurer. The Nebraska Supreme Court justices, by a telling vote of four to three, had to interpret the insurance policy regarding whether she had a bodily disease or illness. If they determined that she did, she would be covered. They decided the case, I believe, with their hearts, not their minds, and said she *did* have a bodily disease or illness; therefore the insurance company had to pay.

The implication of that decision is that we are all ill because each one of us is genetically predisposed to several conditions—we just haven't determined which ones yet. Well, we're going to in the next 20 years.

The threat of misuse of genetic information by third parties has been called "genetic discrimination." This concept has been debated throughout the 1990s, almost since the inception of the Human Genome Project. Many responses have been given. In the United States today, 30 states have laws to prohibit the use of genetic information in group health care underwriting. The federal law known as the Health Insurance Portability and Accountability Act does essentially the same thing. The Equal Opportunity Employment Commission has issued a ruling interpreting the Americans With Disabilities Act (ADA) to say that genetic information cannot be used as a criteria in hiring or promotion. However, recent U.S. Supreme Court interpretation of several ADA cases puts this broad ruling in jeopardy.

One of the most important areas for discussion is the role of genetic information and life, health, and disability insurance. In general, legislative action has been taken to curb the use of genetic information in health care underwriting. Not so in life insurance. Americans think of life insurance in a somewhat different way. In survey after survey, when Americans are asked, "Do you think everybody should have access to affordable life insurance?" 80 percent say yes. But ask those same people, "Would you pay a few dollars more so everybody else could get access?" and 80 percent say no. Thus the dilemma of a democracy.

The Association of British Life Insurers has voluntarily agreed not to use genetic information in mortgage-backed life insurance in Great Britain, a noble act. What I see evolving in the United States is a two-tiered system in which for a minimum amount of life insurance, say \$100,000 or \$200,000, genetic information would not be a factor in obtaining coverage. But

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going to meet
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a large amount of coverage might give insurers the right to ask certain questions, as long as they treated all potential customers the same.

UNASKED QUESTIONS

Our society is not yet asking the toughest questions. If we have these powerful tools that will become even more powerful in the future, what does it mean for our school systems and the way we look at children? What if we can perform genetic tests at birth and identify children at risk for learning disabilities, attention deficit disorder, or autism? Society—personified as a kindergarten teacher—can either say, "I know this kid has a potential problem, so I'm going to do everything I can to help her," or "I know this kid has a genetic problem, so there's nothing I can do about it." What are we going to do? Which way are we going to go?

Genetics reaches into every corner of society. For example, from a privacy perspective, it is not well-known that—almost without any public debate—every state in the United States has enacted a mandatory DNA felon data banking law. At parole, a convicted felon must give his or her DNA information because of the high recidivism rate for repeat criminals, particularly rapists. If we have DNA on file, we can use it at crime scene testing to capture individuals without any eyewitness identification.

Of note, the Innocence Project run out of New York has shown that of people convicted of rape, a small percent are shown to be innocent of the crime when their DNA is analyzed. DNA evidence represents a tool, both for catching the criminal and for exonerating the innocent. But it also raises the specter of the government having DNA information about each one of us—which understandably scares many people.

I have saved the most troubling question of all for last. In the past 100 years, we have a dark history of misuse of information purported to be genetic. Not only in Nazi Germany, but also in the United States, where 60,000 people were sterilized in the name of genetics between 1907 and 1960—all institutionalized persons with mental retardation. In China today, the Maternal and Child Health Law that was enacted in 1995 has language very similar in tone to the laws that were enacted in the United States earlier in the last century and in Germany. How are we going to meet the challenge of taking these extraordinarily powerful and wonderful tools and harnessing them for the public good to serve ethical goals? This role is not for scientists. It is the role of communities, of thinking, caring people, who want to channel this wonderful gift in the right direction. It's really *your* challenge. □

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