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# 2008 Inamori Ethics Prize Speech: The Promise and Peril of the Genomic Revolution

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# The Promise and Peril of the Genomic Revolution

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Edited Transcript of the 2008 Inamori Ethics Prize Speech

On this occasion, I thought it would be appropriate to talk about the science of the human genome and some of the ethical challenges it has placed in front of us. Many of these challenges are in the process of being addressed, but we are far from done. Because science keeps changing, the ethical challenges that demand our attention are constantly evolving as well.

The title of my lecture may sound dramatic, but we are living in dramatic times. The reading of our own DNA instruction book, the human genome, is leading to unprecedented revelations about human biology that promise to transform medicine in a way that has not happened since the introduction of antibiotics. However, this transformation will not happen overnight. So far, studies of the human genome have had a direct impact on the medical care of only a few people. For most of us, the moment of genomic information shaping our own medical future has not quite arrived. Still, I envision it coming pretty quickly, and, in fact, that is where I see both the promise and peril of genomics residing.

Before we look to the future, let us briefly consider the past. We went from having the structure of DNA deduced in April 1953 to just fifty years later, in April 2003, the successful completion of the Human Genome Project, ahead of schedule and under budget. The United States had the privilege of taking the lead in this historic endeavor, but it was very much an international project that included a substantial contribution from our friends and colleagues in Japan, as well as in China, United Kingdom, France, and Germany. We shared goals that were well articulated, we stood up for immediate data release, and we maintained data quality standards of the highest possible level. All of these folks selflessly worked together to make this happen because they believed in the promise of this project: to transform our understanding of human biology and medicine.

It was great that the Human Genome Project built us a reference sequence of the human genome, a foundation for understanding the part of the genome

that we all share. But what about that small fraction of the genome—about 0.5%—that varies from individual to individual? We needed more tools to explore that variable part and how those genetic variants interact with the environment to influence our risk of heart disease, diabetes, cancer, and other common diseases.

So, we pulled together another international consortium involving nearly two thousand scientists to produce a catalog of human variation, dubbed the Haplotype Map (HapMap). This effort has enabled investigators who are trying to identify genetic risk factors for common diseases to conduct systematic, genome-wide association studies (GWAS), a far more efficient process than the previous approach (known as the candidate gene strategy). The first among many GWAS successes came in 2005 with the identification of a gene, called complement factor H, for age-related macular degeneration, a common cause of blindness in the elderly. The discovery was a complete surprise because complement factor H was not on anybody's list of candidate genes. However, it has led to a revolution of our understanding of that disease and a host of ideas about prevention and treatment.

Another project that builds upon the foundation laid by the Human Genome Project is the Cancer Genome Atlas. This project aims to look at the genetic mutations involved in many common types of cancer and to do so in a very systematic, comprehensive way. This is the leading edge of what is going to be an outpouring of new genomic information about cancer in the next few years.

What impact will all of this have on medicine? One opportunity will be to use genomic information to predict who is at risk for what disease, even while they are still healthy. But if I could give you the opportunity to find out your risk factors for a dozen common diseases over the next few decades at a reasonably accurate level, would you really want that information? I think many people would say, "Is there something I could do about it? If there isn't, please spare me." This means we need to think about how we can pair genome-based diagnostics with preventive medicine strategies. In some instances, such as inherited forms of colon cancer that can be prevented by regular colonoscopy and polyp removal in high risk individuals, we are already there. In others, such as people at high risk for inherited forms of Alzheimer's disease, we still have a long way to go.

Another clinical area that is quite exciting is called pharmacogenomics. When you are given a drug for a particular condition, sometimes it works pretty well. Sometimes you do not seem to get the benefit. Sometimes

maybe you get a side effect. What is that all about? We are all different, and our responses to drugs are different. So, if you give a group of patients with the same diagnosis the same drug, a lot of them will do well, but some will get no response or a toxic effect. We should be able to predict that ahead of time for a lot of drugs as we get smarter about what is in the genome.

Ultimately, though, I think the main promise of understanding the genome is that it will allow us to identify the targets for therapy that are much closer to the action than what we currently know about. You cannot expect these kinds of promises to come true without very strong support for biomedical research in the coming years, but the promise has never been greater than it is today.

Those are just a few of the things that those of us working in this field are excited about in terms of genomics' transforming capabilities for medicine. But what about the possible ethical, legal, and social implications (ELSI) of such newfound knowledge and abilities? One of the things that makes me the most proud about the Human Genome Project is that it took ELSI concerns seriously from the very beginning. In fact, it has been estimated that the research support for ELSI in the genome arena is the largest amount of money that has ever been spent on bioethics research. We have created an environment in which bioethics is not shoved off in a corner, or considered something to think about later; it is part and parcel of this genomics revolution.

Let me mention a few of the many complex ELSI issues facing the field of genomics. To begin with, we cannot discount the fact that the field of human genetics got off to a very bad start in the early twentieth century with its focus on eugenics. We must not forget the lessons of the past, and be constantly on guard for the kind of misunderstanding and misapplication of genetics that can have horrendous consequences. We also need to be cognizant of how our expanding knowledge of human genetic variation may play into issues of race and ethnicity. Historian Evelyn Brooks Higginbotham once said that everyone talks about race as if they know what it is, but if you ask someone to define what they mean by race, they will arrive almost immediately at confusion. Yes, race is connected in some way with ancestral geographic origins, but it may also carry with it history, cultural practices, socioeconomic status, environmental exposures, and even stress. So, when you see that a particular disorder seems to be more frequent in one racial group than another, for example, diabetes in Pima Indians, you should not rush to the conclusion that the answer is genetic. In most cases, when the dust settles, I think we will learn that health disparities are enormously complex.

Another very complex, but quite different, ELSI concern is intellectual property. I am very proud of the fact that in 1996, when the international sequencing leaders met for the first time as a group, we had a frank discussion about this issue. On the whiteboard during that meeting, we set forth this bold goal: "Aim to have all sequence freely available and in the public domain for both research and development in order to maximize its benefit to society." Now, that was a moment, a moment where a group of scientific leaders, without necessarily having the approval of all the authorities in their respective countries, but in the spirit of doing the right thing, made a decision to change the ethics of data release in a profound way, not waiting for publication, not waiting for anything, releasing the data every twenty-four hours. That attitude of immediate data release has now extended well beyond that decision twelve years ago into many other areas of biomedical research, providing great benefit to the public because of the way it accelerates the discoveries that need to happen and levels the playing field, giving anybody with a good idea the chance to start working right away.

Genetic discrimination was another ELSI issue identified right from the beginning as particularly important. We knew that if we did not fix this, people were going to be afraid to find out about their own DNA because they would be discriminated against by losing their health insurance or their jobs. Should that be used to take away your access to health care, or to a job for which you are otherwise well-qualified? No, that is unjust, and, frankly, puts all of us at risk. If you came here thinking you were the perfect genetic specimen, I have really bad news for you. There are not any—each of us has a few dozen genetic glitches that increase our risks for particular diseases.

Clearly, we needed to do something about the genetic discrimination issue. In 1990, the Americans with Disabilities Act was passed and that had some potential of being helpful. States began to take action on this issue in the 1990s, and in 1995, Louise Slaughter, a Democratic representative from New York, introduced the first federal legislation about genetic discrimination, HR 2748. In 1996, Congress passed the Health Insurance Portability and Accountability Act, which included genetic information on the list of things that cannot be used to take away your health insurance if you are in a group plan. But that act did not say anything about individual health plans, and, obviously, none of us know if we might need an individual plan at some future point. Time went on, with bills being introduced in Congress every other year and going nowhere. In 2000, President Clinton issued an executive order that protected federal employees from genetic discrimination,

but more was still needed. Happily, this story has a good ending. On May 1, 2008, the bill, now called the Genetic Information Nondiscrimination Act (GINA), cleared Congress and President George W. Bush signed the bill into law twenty days later.

We now finally are in a circumstance in this country where one need not fear that the genetic information will be used for discriminatory purposes in health insurance or in the workplace. But that most certainly does not solve all our problems. What about genetic testing? Is it subject to sufficient oversight? Can you be sure, if somebody is trying to get you to take a genetic test, that the results are trustworthy? And, of course, that becomes of particular interest right now because there are companies out there marketing genome-wide analysis directly to the public. The science behind these efforts is pretty good, but the problem is we do not know very much about the interventions that someone might want to consider if found to be at high risk. We can guess at them, but it would be nice if we actually knew what would be beneficial. Are we jumping the gun here? Also, if health care providers were involved in these kinds of interchanges, would your doctor or your nurse be able to tell you what this information meant? Not necessarily. Most health care professionals have had no training in genetics; they are also struggling to make sense of this.

And what about using genomics as a tool to enhance human traits? Many people are particularly worried about that. They are fine with using genomics to cure cancer, but do not approve of genomic tinkering aimed at making the next generation smarter or more athletic. Currently, most of the scenarios for enhancement are totally unrealistic. Researchers will not be in a circumstance to modify the DNA that gets passed from parent to child in humans anytime in the foreseeable future. Even if they could, it would be unethical because we really would not know the consequences for generations to come—and that will not pass muster with any ethicists that I know.

Finally, we need to ask ourselves whether, in our enthusiasm for scientific progress, we may be ascribing to DNA properties that it does not really deserve. Are we increasingly thinking of ourselves as hardwired by our DNA and, as such, beginning to neglect many other vital aspects of what it means to be human, such as parenting, education, and spirituality? That would be a profound misunderstanding of the science. Even when we have completely understood the human genome, we will not understand free will. May it always be that, as we venture deeper into science, we hold even firmer to our humanity.