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The Genetics of Mice and Men: Can—and Should—We Intervene?

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The telephone, the airplane, the nuclear bomb, humanity's first journey to the moon, and the Internet: such major generational achievements shape how generations are perceived in history. Most scholars agree that more good than bad has resulted from each innovation or endeavor listed above. For example, the "Manhattan Project" was initiated to develop the nuclear bomb to end a long, brutal war. Historical accounts of World War II tell us that the "right side" won and that oppression and evil were crushed. However, the remnants of nuclear technology continue to haunt us today.

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In June of 2000, Dr. Francis Collins and Dr. Craig Venter announced that a draft sequence of the human genetic code had been completed. This accomplishment was actually more astounding than most scientific breakthroughs. Not only had the order of over 3 billion bits of genetic information nearly been determined, but the sequencing portion of the project was finished ahead of schedule and under budget. The April 2003 announcement that a 99.99% accurate assembly of the human genetic code had been completed was anti-climactic compared to the 2000 announcement. However, it was additional affirmation that our generation had finished a genetic "Manhattan Project," a venture that would offer tremendous future benefits to humanity.

As a molecular geneticist, I am responsible for operating a lab dedicated to "DNA sequencing," which is the methodology of reading the genetic code. After the 2000 announcement, a newspaper reporter asked me, "Now that the genome is finished, what will you do for a job?" How naive, I thought! I responded that completing the genome project was just the start. I explained that prior to this achievement, our knowledge of genetics was analogous to having an unabridged dictionary that was bound with straps. For years, all we could read was the word "Dictionary." Now, however, the straps had been removed, permitting us to read all the words and meanings inside.

Deciphering the Dictionary of Life

One thing we discovered when the genetic dictionary was opened is that many of the words and meanings are incomprehensible. Approximately 5% of the human genome contains genes. The purpose of the remaining 95% is anybody's guess. We know that God put this mystery DNA there for a reason. But like Adam and Eve in their quest for the fruit of knowledge, molecular geneticists seek to

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have their eyes opened so that the remaining 95% is not so mysterious.

If we view the human genome as a set of blueprints, we can regard it specifically as God's plan for building and maintaining life. Such a plan is in place for all organisms, as each organism has its own individualized set of blueprints. If we compare blueprints of different organisms, we start to see similar patterns of function. A gene in a mouse creates a protein used in muscles. Humans have the same gene, which produces a nearly identical protein with the same function. By parsing through genomes from different species, we can identify genomic landmarks of similarity that indicate what a particular gene might do. Likewise, we can identify genetic regions of dissimilarity that make the different species unique.

We call this methodology of comparing genomes of different species "comparative DNA sequencing." This methodology has revealed enormous amounts of information about the human genome that may have remained unknown had genomes of other species been unavailable for comparison. For instance, researchers seeking to uncover the cause of multiple sclerosis rely upon a number of "mouse models." In some of these mice, the gene for myelin basic protein (MBP) does not function correctly. Therefore, MBP is under intense scrutiny to determine if defects in this protein are related to multiple sclerosis in humans. By comparing the mouse MBP gene to the human MBP gene and studying the similarities and differences in how the mouse and human genes work, geneticists may be able to determine what causes multiple sclerosis.

The differences in genetic blueprints between species have tremendous implications for medical applications. I was recently asked why, if the genomes of apes are more than 99% identical to the human genome, ape organs can't be transplanted into humans. The reason this is not a viable option is rooted in the remaining 1% difference between the genomes. As a rough analogy, try placing an oil filter for a Ford truck engine onto a Dodge truck engine. The Ford filter may work fine for awhile, but there is a good chance that the Dodge engine may be irreparably damaged. The Ford filter was not made to the specifications of the Dodge engine, just like an ape's organs are not made to the specifications of human beings. Tragically, this principle was borne out in the recent case of Jésica Santillán, the young patient at Duke University Hospital who received organs from a human donor who was not a perfect genetic match. Although the genetic blueprints of Jésica and her donor differed by as little as 0.00003%, Jésica's body rejected the organs, causing her death.

Applications and Ethics

Now that we have uncovered the genetic blueprint of human life, what should we do with this information? Obviously, investigation of the human genetic code will intensify and comparative genetic studies between different species will continue. But when will we use the genetic information to manipulate and change an organism's genetic code? Or can we do this at all? Or, should we if we could?

The answers to the first and second questions are that we have already started to manipulate the genetic code of organisms. Changing the genetic code in bacteria is an everyday occurrence in molecular biology labs and is almost as easy as baking a cake. Geneticists can also "knock out" and "knock in" genes in mice to see what will happen if a gene is removed or added to mouse cells. Some of the "knock out" experiments are landmark studies, providing information about genetic diseases that can't be acquired by other means. Gene therapy has also been tested in humans and unfortunately has resulted in several people's deaths, prompting a call to ban gene therapy until more is known about its possible side effects.

The answer to the third question is more controversial. As with politics, bioethics has many complex layers. Some scientists are conservatives. Others are liberals. Some really don't care one way or the other about ethical issues and just adopt their colleagues' opinions. People's answers to this question can also depend on the institution or the country where the research in question is being performed. Thus, there is no easy consensus. I do believe, however, that everyone should be willing to approach the science of genetics with more foresight. The "right now" and "me first" attitudes prevailing at many institutions do not consider the future effects of genetic "breakthroughs." Had humanity given more thoughtful consideration to the risks of nuclear energy, better safeguards—both moral and legislative—could have been put in place. The genetic "Manhattan Project" has even greater social and ethical implications than what should have been considered when developing the atomic bomb.

One of the greatest ethical challenges will center on the dissemination of genetic information and privacy issues. We are accumulating genetic information more rapidly than we can use it. For example, the gene BRCA1 (breast cancer 1) is highly associated with an increased risk for breast cancer. Hundreds of mutations have been identified in BRCA1, and screening all high-risk females for BRCA1 mutations is not practical. First, it is expensive and insurance companies balk at covering the costs. Second, should we screen for specific mutations or all mutations? Finally, what do we tell a patient when a mutation is found? This last question leads to a greater dilemma. What are a patient's choices when a mutation is identified? In the case of BRCA1, a physician can recommend a prophylactic radical mastectomy as a possible course of action. But what about a patient with a mutation that increases the risk for developing brain cancer? Obviously, brain removal is not an option! Though we can tell people that they are at risk of getting sick, unfortunately we can't always offer them a method of prevention or cure for their disease. This last fact introduces a further dilemma, and that is how much genetic privacy someone should have, especially when insurance companies want to weigh the risks of insuring people with known genetic defects. This dilemma is a major ethical concern in which we all have a stake.

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The Human Genome Project has indeed opened a Pandora's Box of questions about how genetic data will be used. There is increasing demand for geneticists to pledge to and maintain high ethical standards. However, we must recognize that many of these standards are usually set by secular criteria. As Christians, we should first align our ethical standards with God's, and then seek to determine when, where, and how we will use our new-found knowledge. ■