Human Genome Project

Dr. Ray Bohlin takes a brief look at the accomplishment, purpose and consequence of the Human Genome Project.

 *This article is also available in Spanish.*

What's All the Fuss About the Human Genome Project?

In February of 2001, virtually every media outlet, whether TV news, newspapers, radio, Internet news services, or news magazines, was all worked up about the announcement of the completion of the Human Genome Project. In this article we will explore this monumental achievement and what it means for the future of medicine and our understanding of ourselves.

To appreciate this important accomplishment, we need to review a little basic genetics. It may actually astonish most adults just how much genetics the National Institutes of Health assumes we know about our genetic heritage. The educational video from the HGP includes a three-minute review of basic genetic processes like DNA packaging, transcription of DNA into message RNA, and the translation of message RNA into protein. It's no exaggeration to say that when I played this short piece during a lecture for high school students and their parents, mom and dad were left in the dust.

Honestly, I did that intentionally; because we are only in the beginning stages of a genetic revolution that will transform the way we diagnose and treat disease and how we may even alter our genetic structure. These new technologies bring with them numerous ethical and moral dilemmas we have only begun to address and for which there may not be simple answers. If we don't take the time to familiarize ourselves with genetic research and its implications, we risk responding out of fear and ignorance and potentially throwing away crucial medical

advances.

I have contended for a long time that we can no longer afford to remain ignorant of genetic technologies. They simply harbor far too great a power for both tremendous good and tremendous evil. We must work hard to take every thought captive to Christ and see what there is of benefit and what avenues of research and application we need to avoid to preserve human freedom and dignity.

Well let's talk about our genome, the sum total of all our genes. In most of the 100 trillion cells of our body are 46 chromosomes. These chromosomes are tightly coiled and packed strings of a remarkable molecule called DNA (Deoxyribonucleic Acid). DNA is a polymer, a repetitive sequence of four molecules, which I will only refer to by their one-letter abbreviations, A, G, C, and T. The human genome sequence is simply the sequence of these four molecules in DNA from all our chromosomes. If you laid out the DNA from all our chromosomes in each of our cells end to end, it would stretch six feet long.

A gene is a segment of DNA that contains the precise coding sequence for a protein. And proteins do all the real work in our cells. By looking at our completed sequence, it is predicted that our genome consists of 30,000 to 45,000 genes in each of our cells. So, now that we have the sequence, what does it mean? We'll begin answering that question in the next section.

What Does the Human Genome Project Hope to Accomplish?

The National Institutes of Health in cooperation with several international research organizations began the HGP in 1990 in the U.S. There were four primary objectives among the many goals of the HGP{1}.

The first and primary goal of the HGP was to map and sequence the entire human genome. There is a critical and significant difference between a map and the sequence. There are over three billion letters, or base pairs, in the human genome, spread out over 23 pairs of chromosomes. Trying to locate a sequence of say 1,000 letters, the code for a large protein, is a one in a million task. Therefore, researchers needed a refined roadmap to the genome. The map entails particular sequences that can be used like signs on a road map. If the trait a scientist is studying always seems to be present with this marker, the gene involved is probably nearby. In 1995, a detailed map was published with over 15,000 markers, one for every 200,000 base pairs. This will aid greatly in associating genes with particular diseases. And now with the sequence nearly complete, with over 99% accuracy, determining the precise effect of this gene on disease will be even easier.

A second critical goal was to map and sequence the genomes of several important model organisms: specifically, the bacterium E. coli, yeast, the roundworm, fruit fly, and mouse. This information is helpful, because each of these organisms have been used for laboratory studies for decades. Being able to coordinate knowledge of their genomes with cellular and biological processes will certainly inform our study of the human genome and its various functions.

The third important objective of the HGP was to systemize and distribute the information it gathered. Any sequence over 2,000 base pairs is released within 24 hours. The sequence and map data is contained in publicly accessible databases on the Internet. The HGP has also been creating software and other tools for large-scale DNA analysis.

The fourth and final primary goal of the HGP was to study the ethical, legal, and social implications of genetic research. A full 5% of all funds appropriated for the HGP have been earmarked for these kinds of considerations. There are many concerns revolving around the use of genetic sequence data.

Not the least of which are worries about ownership, patenting, access to personal sequence data by insurance companies, potential for job discrimination based on personal sequence data, and the prospects for genetic screening, therapy, and engineering. In the next section we'll begin investigating how the HGP thinks this information can be used.

What are the Long Term Hopes for the HGP?

The completion of the sequence was announced jointly in February 2001 in the journals *Nature*{2} and *Science*{3}. Both *Science* and *Nature* have made these landmark issues available, without subscription, on their websites.

The importance of recognizing the sequence of a particular gene has three important ramifications.{4} The first is diagnosis. Over the last few years, single genes have been found leading to deafness and epilepsy. Numerous genes, however, will influence most diseases in complex ways. Recently, genetic influences have been found in many forms of hypertension, diabetes, obesity, heart disease, and arteriosclerosis{5}. Genetic analysis of cancer tumors may someday help determine the most effective drug therapy with the fewest side effects. Genetic diagnosis has the potential to more precisely prescribe treatments for many medical conditions.

Second, diagnosing ailments with more precision with genetics will also lead to more reliable predictions about the course of a disease. Genetic information about an individual's cholesterol chemistry will aid in predicting the course of potential heart disease. Obtaining a genetic fingerprint of a cancerous tumor will provide information concerning its degree of malignancy. Third, more precise genetic information will also lead to the development of better strategies for prevention of disease.

Many more ailments in newborns can eventually be screened more

specifically to avoid disorders later in life. Currently, babies in the U.S. and other countries are routinely screened for PKU, a metabolic disorder that prevents the breakdown of a specific amino acid found in proteins. This condition becomes toxic to the nervous system, but can be prevented and managed with appropriate diet. Without dietary changes, affected babies face extreme mental retardation. Hopefully, the number of conditions this type of screening applies to can be expanded.

Screening can also be done for adults, to see if they may be carriers of potential genetic conditions. Certain Jewish and Canadian populations regularly obtain voluntary screening for Tay-Sachs disease, a known child-killer. This information has been used to help make decisions about future marriage partners.

Perhaps the greatest benefit will come from what is called gene-based therapy. Understanding the molecular workings of genes and the proteins they encode will lead to more precise drug treatments. The more precise the drug treatment, the fewer and milder will be the side effects.

Actual gene therapy, replacing a defective gene with its normal counterpart, is still very experimental. There are still many hurdles to overcome involving how to deliver the gene to the proper cells, controlling where that gene is inserted into a chromosome, and how it is activated.

Not surprisingly, some have seen the human genome sequence as a vindication of Darwin. We'll examine that contention next.

Did the Human Genome Sequence Vindicate Darwin?

Amid the controversy and exultation over the release of the near complete human genome sequence has been a not so quiet triumphal howling from evolutionary biologists. The similarity

of many genes across boundaries of species, the seemingly messy patchwork nature of the genome, and the presence of numerous apparently useless repetitive and copied sequences all have been laid out for us as clear validations of evolution. Really!

If Darwin were alive today, he would be astounded and humbled by what we now understand about the human genome and the genomes of other organisms.

Let's take a closer look at the claims of one bioethicist, Arthur Caplan{6}, who thought the major news story was missed. So let's just pick a few of the more glaring statements to help us understand that little in his comments should be trusted.

First, Caplan says, "Eric Lander of the Whitehead Institute in Cambridge, Mass., said that if you look at our genome it is clear that evolution must make new genes from old parts."

While it may be true that we can see some examples of shared sequences between genes, it is by no means true that we see wholesale evidence of gene duplication throughout the genome. According to one group of researchers,{7} less than 4,000 genes share even 30% of their sequences with other genes.

Over 25,000 genes, as much as 62% of the human genes mapped by the Human Genome Project, were unique, i.e., not likely the result of copying.

Second, Caplan says, "The core recipe of humanity carries clumps of genes that show we are descended from bacteria. There is no other way to explain the jerry-rigged nature of the genes that control key aspects of our development."

Not everyone agrees. The complexity of the genome does not mean, necessarily, that it has been jerry-rigged by evolution. There is still so much we do not know. Caplan is speaking more out of ignorance and assumption than data. Listen to this

comment from Gene Meyers, one of the principal geneticists from Celera Genomics, from a story in the *San Francisco Chronicle*:

> *'What really astounds me is the architecture of life,' he said. 'The system is extremely complex. It's like it was designed.'*
>
> *My ears perked up. 'Designed? Doesn't that imply a designer, an intelligence, something more than the fortuitous bumping together of chemicals in the primordial slime?'*
>
> *Myers thought before he replied. 'There's a huge intelligence there. I don't see that as being unscientific. Others may, but not me.'{8}*

Jerry-rigged? Hardly! Confusing at the moment? Certainly! But more likely to reveal hidden levels of complexity, rather than messy jerry-rigging.

It will take more than bluster to convince me that our genome is solely the result of evolution. The earmarks of design are clear, that is, if you have eyes to see.

What are the Challenges of the Human Genome Project?

In closing, I would like to address what are many people's concerns about the potential for abuse of this information. While there is great potential for numerous positive uses of the human genome, many fear unintended consequences for human freedom and dignity.

Some are justifiably worried about the rush to patent human genes. The public consortium, through the National Institutes of Health, has made all its information freely available and intends to patent nothing. However, there are several patent requests pending on human genes from the time before the HGP

was completed.

It is important to realize that these patents are not necessarily for the genes themselves. What the patent does protect is the holder's right to priority to any products derived from using the sequence in research. With the full sequence fully published, this difficult question becomes even more muddled. No one is anxious for the courts to try its hand at settling the issue. Somehow companies will need some level of protection to provide new therapies based on genetic information without hindering the public confidence and health.

Another concern is the availability of information about individual genetic conditions. There are legitimate worries about employers using genetic information to discriminate over whom they will hire or when current employees will be laid off or forced into retirement. Upwards of 80-90% of Americans believe their genetic information should be private and obtained or accessed only with their permission. The same fears arise as to the legality of insurance companies using private genetic information to assess coverage and rates. A recent bill (June 29,2000) before Congress to address these very concerns was amended to the Health and Human Services appropriations bill, but was removed in committee. The bill will be reintroduced this session.{9} I would be very surprised if some level of privacy protection is not firmly in place by 2002.

Moreover, many are apprehensive about the general speed of discovery and the very real possibilities of genetic engineering creating a new class, the genetically enhanced. Certainly, there is cause for vigilance and a watchful eye. I have said many times that we can no longer afford to be ignorant of genetic technologies. And while I agree that the pace of progress could afford to slow down a little, let's be careful not to throw the baby out with the bathwater.

After a series of lectures on genetic engineering and human cloning at a Christian high school, one student wrote me to say:

> *I am a senior, in an AP Biology class, and I find genetics absolutely fascinating. It's both fascinating and scary at the same time. . . . [You have inspired me] to not be afraid of the world and science in particular, but to take on its challenge and trust God.*

Amen to that!

Notes

1. "Genetics: The Future of Medicine," *NIH*, Publication No. 00-4873, 2.
2. *Nature*, 409 (15 February, 2001), www.nature.com.
3. *Science*, 291 (16 February, 2001), www.sciencemag.org.
4. Genetics: The Future of Medicine, 9-11.
5. Kevin Davies, "After the genome: DNA and human disease," *Cell*, 104 (Feb. 23, 2001), 465-467.
6. www.probe.org/did-the-human-genome-project-prove-that-darwin-was-right/.
7. Wen-Siung Li, Zhenglong Gu, Haidong Waing, and Anton Nekrutenko, "Evolutionary analyses of the human genome," *Nature*, 409 (15 Feb 2001):847-849.
8. Tom Abate, "Human Genome Map Has Scientists Talking About the Divine – Surprisingly low number of genes raises big questions," Monday, February 19, 2001, *San Francisco Chronicle*.
9. James M. Jeffords and Tom Daschle, "Political issues in the genomic era," *Science*, 291 (16 February, 2001), 1249-1251.

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