Genomic Medicine: The Trek Toward the Clinic

Significant advances will occur in applications to medicine over the next few years, predicts Eric D. Green, MD, PhD, director of the National Human Genome Research Institute (NHGRI).

After 2020, those advances will have an impact on improving the effectiveness of health care, but it will be a "long, hard process," Green said.

“We have a long way to go to fully understand the human genome,” Green said. “The Human Genome Project was the starting line and by no means the end.”

Unraveling the genetic risk factors for common complex diseases like diabetes, heart disease, and cancer will continue to be a priority because these diseases represent a major health care burden.

“Until the human genome is understood, it will remain a mystery what makes us different,” Green said.


The scientific community currently has only a Cliff Notes view of the functional landscape of the human genome. To change the view from Cliff Notes to encyclopedia, NHGRI sponsors the ENCODE (Encyclopedia Of DNA Elements) project to compile a comprehensive catalog of functional elements that control the expression of genetic information in a cell.

ENCODE was launched just a few months after the 2003 completion of the Human Genome Project. During the post-Human Genome Project era, scientists have learned that the “whole story” cannot be told by the primary DNA sequence alone, Green said. Epigenetic factors that “decorate the DNA sequence,” to modify the expression, or activity, of specific genes are another major player in the genome.

Less than 2 percent of the human genome contains the 20,000 genes that encode proteins. The remaining 98 percent encode transcription factors and other elements, not all of which are known.

The “non-protein parts” are not as well understood as the protein-coding genes, Green said. But they will continue to attract more attention because mutations in the non-protein parts, not the protein-coding genes, are the main DNA contributors to risk for developing commonly occurring, non-Mendelian, multi-genetic diseases such as kidney disease, diabetes, hypertension, cardiovascular disorders, and cancer.

In contrast, the rare, single-gene Mendelian disorders such as cystic fibrosis are caused by mutations in the protein-coding genes, Green said.

To jumpstart the discovery of risk variants for commonly occurring diseases, NHGRI and private companies have created research programs, including the Genome Wide Association Study (GWAS), the HapMap Project, and the 1,000 Genomes Project.

Yet scientists’ ability to store, analyze, and interpret data has not advanced as quickly as the sequencing technologies that can decipher exomes, the protein-coding genes, and whole genomes.

“The numerous DNA sequences that have been deciphered since 2003 combined with new information about the genetic contribution of disease is the ‘rent bottleneck’ in genomic medicine,” Green said, and “is the largest current bottleneck in genomic medicine.

“We have a big data problem,” he said. “We’ve victimized our own success.”

Less than a decade ago it took 3 to 4 months and $10 million to $30 million to decipher the human genome.

Today an individual’s genome can be sequenced in three to four days for $4000 to $8000. Soon it will cost $1000, Green said, enabling the widespread application of DNA sequencing in the clinic as well as the lab.

A second bottleneck likely to be addressed in coming years is information dissemination. Including clinical genomics information systems in electronic health records systems may be one approach.

“Philosophically there is a long way from submitting their patients’ full genomes for sequencing, not because the price is high, but because the data are difficult to interpret,” wrote Nobel laureate Harold Varmus, MD, a former Director of NIH and now head of the National Cancer Institute in Genome Medicine.

[SIGNIFICANT ADDITIONS WILL OCCUR IN APPLICATIONS TO MEDICINE OVER THE NEXT FEW YEARS, PREDICTS ERIC D. GREEN, MD, PhD, DIRECTOR OF THE NATIONAL HUMAN GENOME RESEARCH INSTITUTE (NHGRI).]