Genome advances promise personalized medical treatment

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A whirlwind of activity is under way to apply the findings of the $3 billion Human Genome Project to improve health care in the United States and around the world.

Six years after scientists finished decoding the human genome -- the genetic instruction book for life -- they're starting to take their new knowledge from the research laboratory to the doctor's office and the patient's bedside.

"We hope all this knowledge of the genome will lead to more kinds of therapies," said Francis Collins, who ran the federal government's Human Genome Project from 1993 to 2008.

Researchers are seeking ways to tailor treatments to individuals -- they call it "personalized medicine" -- in order to improve patient outcomes and to lower costs in the overburdened U.S. health care system.

The goal is to deliver the right drug at the right time in the right dose to the right person, and eliminate treatments that don't work.

"Already some of these personalized treatments are finding their way into practice," Collins told a recent seminar in Washington. "We want to optimize the way we practice medicine, diagnosis and risk prediction."

For example, instead of a standard therapy to treat breast cancer, personalized medicine allows doctors to employ a treatment precisely

designed to fit one woman's specific needs. If a gene test shows that her tumor overproduces a substance called HER-2, she's considered to be a good candidate for the drug Herceptin, which cuts her chance of a recurrence nearly in half. If the test is negative, using the drug could be wasteful.

Advocates say that personalized medicine also can reduce unnecessary suffering and expense by minimizing the chance of adverse drug reactions. According to the Food and Drug Administration, there were 319,741 serious illnesses and 49,958 deaths due to unexpected reactions to drugs last year in the United States alone. A British study estimated the cost of such reactions at $847 million per year in the United Kingdom.

For instance, heart patients who have two tiny mutations in their genomes have an increased risk of serious problems, even death, if they take the popular anti-clotting drug Plavix, according to Rick Hockett, the chief medical officer of Affymetrix, a genetics firm in Santa Clara, Calif.

Experts caution, however, that it's premature to say that an era of individually customized medicine has arrived. Major scientific and policy hurdles remain before patients can benefit widely from the promises of personalized medicine. Issues of insurance coverage, medical training, privacy and safety remain to be resolved.

"It is not ready for moving into the clinic. It is not ready for prime time," Pamela Sankar, a medical ethicist at the University of Pennsylvania, told the seminar.

Nevertheless, advances in genomic medicine are accelerating, thanks to new, high-speed sequencing machines. Unlike the slow, painstaking methods used to decode the first sample genome, second-generation

robotic machines can analyze hundreds of thousands of units of DNA in minutes.

Collins said the improvement in speed of sequencing had been "breathtaking." Costs have come down proportionately.

In 2003, it cost an estimated $300 million to decode the first genome of an individual human. By 2007, the cost per person had come down to $100 million, and by 2008, it was $60,000. The current cost is about $20,000, according to Clifford Reid, the chief executive of Complete Genomics Inc., a gene-processing company in Mountain View, Calif.

Radoje Drmanac, the chief scientist at Complete Genomics, predicted that it soon will be possible to sequence a person's genome in one day. "For the first time, this will enable large numbers of patients to be sequenced to get to the bottom of thousands of genetically controlled diseases," Drmanac said.

Collins said the goal was to be able to sequence a complete human genome for $1,000 by five years from now, making it a staple of medical practice. People routinely will have their genomes sequenced to predict their individual risks of disease and responses to drugs, he predicted.

So far, fewer than two dozen complete human genomes have been published in scientific journals, but more are being sequenced rapidly. Larger efforts are also under way.

Last year, an international consortium launched a "1000 Genomes Project" to sequence the genomes of at least a thousand people from around the world by 2012. The goal is to produce a catalog of all the genetic variations that exist in at least 1 percent of the human population. The cost is estimated to be $30 million to $50 million.

"This will change the way we carry out studies of genetic disease," Collins said.

Already, studies of variant genes have provided clues to hundreds of diseases, he said.

Scientists are beginning to apply a new idea to cut the cost dramatically and speed the process of reading a person's genome. It's based on the fact that only about 1 percent of the 3 billion units of DNA in a person's genome contain the genetic code to produce proteins, the chemical building blocks of an organism. The rest used to be called "junk DNA," but some of it's now known to perform important functions, such as turning genes on or off.

So, instead of sifting through a "vast ocean of stuff," as one researcher called the complete genome, only the coding bits, known as the "exome," need to be read. The faster, simpler, cheaper exome process is sometimes called the "One Percent Solution."

Scientists at the University of Washington in Seattle reported in the journal Nature last week that they've sequenced 12 human exomes and have identified the cause of Miller syndrome, a rare disease that causes terrible facial and limb abnormalities in children.

ON THE WEB

National Human Genome Research Institute: www.genome.gov

1000 Genomes project: www.1000genomes.org

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