

Expectations Raised as DNA Analysis Costs Go Down

By Catherine Hollingsworth

Staff Writer

As companies move ever closer to the goal of low-cost technology for sequencing the human genome, personalized medicine seems inevitable.

But less clear is how drug research and, ultimately, patient care might change as a result of more affordable DNA sequencing technology.

The cost of those technologies has been falling steadily over the past several years, since Celera Genomics launched its \$300 million effort in 1998 to speed up the pace of a publicly funded 10-year project that cost \$3 billion in 2003.

Although the industry originally had set a goal of \$100,000 for next-generation DNA sequencing technologies, several companies are now in a race to cut the cost far below that mark. Applied Biosystems Inc. and Illumina Inc. both have said that their respective systems are designed to achieve DNA sequencing at a cost of \$10,000.

And, in June, Complete Genomics Inc. plans to begin offering DNA sequencing at a cost of \$5,000. That company is building the first, large-scale genome sequencing center with the capacity to sequence 1,000 genomes. It hopes to be able to sequence 20,000 human genomes next year.

The National Human Genome Research Institute, part of the National Institutes of Health (NIH), has provided grants to academic researchers and companies such as Menlo Park, Calif.-based Pacific Biosciences Inc. to develop sequencing technology at a cost of \$1,000.

Even though the International Human Genome Project has worked to sequence much of the human genome, the work continues as researchers seek to map and remap regions using more advanced technologies.

Impact of Genome Sequencing on R&D

The 1000 Genomes Project, an international effort to create a new map of the human genome, reported that the genetic blueprints, or genomes, of any two humans are more than 99 percent the same. However, the small fraction of genetic material that varies among people can hold clues to differences in individuals' susceptibility to disease, response to drugs and sensitivity to environmental factors.

"It takes out the guesswork about which part of the genome to look at," said Cliff Reid, CEO of Complete Genomics, adding that cancer research alone "is going to be dramatically affected by human genome sequencing at these low price points."

Already, Mountain View, Calif.-based Complete Genomics has started smaller-scale projects with academic institutions and pharmaceutical companies. It also is signing up customers for its planned large-scale genome sequencing center, which is still under construction.

Reid said the company's services could appeal to companies of all sizes, as well as to cancer research centers. But "price has been the key barrier," he said.

The company plans to publish its discount on large-scale discovery projects in June, when it launches its commercial services. It expects the price to be \$5,000 per genome for sequencing many hundreds of genomes.

But drug discovery is just one area in which DNA sequencing is relevant to drug development, said Adam Felsenfeld, program director of large-scale sequencing at the National Human Genome Research Institute.

"Knowing what genes are involved [in a disease] helps us identify drug targets," he told BioWorld Financial Watch. But finding new genetic mutations also can have implications for diagnosis and treatment.

An NIH-funded project, the Cancer Genome Atlas, has been sequencing the genome of tumors to understand genetic mutations in a tumor cell. While some of the genes involved in tumors were identified in previous sequencing studies, researchers now "have the ability to find them all," Felsenfeld said.

The first results from the brain tumor study were published last fall in the journal Nature.

Genome sequencing also could help drug firms better evaluate drug toxicity in ways that otherwise aren't available without genome sequencing, he said.

Patient Benefits Clear, but Some Urge Caution

The declining costs in DNA analysis could translate into more routine testing at birth, and could begin being used on a regular basis to provide greater predictability about a patient's condition, helping patients to decide whether to take action, Felsenfeld said.

At \$1,000, "the same cost as a routine medical test," he said, health care providers may seek to "sequence everyone's genome as a matter of course."

But the research firm Hayes Inc., which works with hospitals and payers to evaluate controversial and emerging technologies, has urged caution in interpreting the results of DNA sequencing.

The human genome is made of 3 billion base pairs from each parent, for a total of 6 billion. "What do you do with 6 billion pieces of information?" asked Diane Allingham-Hawkins, director of the genetic test evaluation service for Hayes.

Interpreting such huge amounts of data in a meaningful way will be a challenge, she said.

"These are great technologies because they do give us a lot of info, and it is bringing down the cost of research," she said. "And they will certainly help in the discovery of drugs, new technology, new devices."

But Allingham-Hawkins, a geneticist, said there may be a rush to push forward drug programs or gene-based diagnostic tests in the excitement over these technologies. She pointed to warfarin, a blood thinner associated with bleeding problems, as an example of where the case for genetic testing is "not really there."

Studies of warfarin have suggested that variants in two genes, CYP2C9 and VKORC1, can put patients at higher risk for bleeding. But the benefits are not yet clear on the advantages of the genetic test required for warfarin and "data are still coming in," she said.

Based on an internal report by Hayes, Allingham-Hawkins said there is insufficient or conflicting evidence about other gene variants and their effect on a drug's activity, such as the case of biomarkers being used to detect the EGFR or KRAS genes for treatment with third-line tyrosine kinase inhibitors in non-small lung cancer.

According to a March market analysis by Frost & Sullivan, the race toward the \$1,000 genome goal will allow more whole genome sequencing direct-to-consumer services to enter the market. Ideally, those DNA analysis services would be available directly to individuals, such as deCODEMe, a service launched in November 2007 by DeCode Genetics, of Reykjavik, Iceland, and a DNA analysis service introduced by Foster City, Calif.-based Navigenics Inc. in 2008.

The Next-Generation in Genome Sequencing

Applied Biosystems Inc. (ABI) said last year it lowered the cost of sequencing a genome to \$60,000, well below the industry's \$100,000 goal for next-generation DNA sequencing technologies. The \$60,000 cost is based on a project that company scientists were able to complete for less than \$60,000 using ABI's next-generation genetic analysis system.

The ABI team used the company's SOLiD system to sequence the genome of an anonymous African male of the Yoruba people of Ibadan, Nigeria, who participated in the International HapMap Project aimed at cataloging human genetic variation. Data from that project were made available to the academic community and commercial software developers to help further the development of analytical tools to interpret the data.

The data also were released to the National Center for Biotechnology Information, part of the National Institutes of Health's National Library of Medicine.

ABI, a division of Life Technologies Corp., said at the time that the project's cost of less than \$60,000 was the commercial price for all required reagents needed to complete the project. According to the company, that is a fraction of the cost of any previously released human genome data, including the roughly \$300 million spent on the Human Genome Project, an international research effort to map the human genome.

The cost is expected to drop even more with increasingly advanced systems on the horizon. Those larger-scale systems are expected to read longer stretches of bases, work faster and have higher output at a lower cost than current DNA sequencing systems.

Last month, Foster City, Calif.-based ABI began shipping a new SOLiD 3 system that is expected to enable scientists to sequence a human genome for less than \$10,000. San Diego-based Illumina Inc., which sells a DNA sequencing system known as the Genome Analyzer, recently announced advances in chemistry, hardware and algorithms that will improve its system and allow for sequencing at a cost of less than \$10,000.

As part of the 1000 Genomes Project, ABI, Illumina and 454 Life Sciences have agreed to sequence the equivalent of 75 billion DNA bases as part of the pilot phase of the project, which was announced in January 2008. Each company will contribute the equivalent of 25 human genomes over the first year, and additional sequence data over the project's expected three-year timeline.

The full-scale 1000 Genomes Project will involve sequencing the genomes of at least 1,000 people, drawn from several populations around the world. The project will use samples from donors who have given informed consent for their DNA to be analyzed and placed in public databases.

BioWorld Financial Watch March 23, 2009