Faster, low cost sequencing technologies needed to drive era of personalized medicine

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DNA testing is transforming health care and medicine, but current technologies only give a snapshot of an individual's genetic makeup. Any patient wanting a complete picture of their inherited DNA, or genome, would drop their jaw at the sight of the bill -- to the current tune of $10 million or more charged for every human or mammalian-sized genome sequenced.

Now, with a grant award from the National Human Genome Research Institute (NHGRI), scientists at the Biodesign Institute at Arizona State University are expanding efforts to dramatically lower the cost of DNA sequencing.

The NHGRI, part of the National Institutes of Health (NIH), has set an ambitious target of $1,000 or less - a cost 10,000 times lower than current technology - to make genome sequencing a routine diagnostic tool in medical care. The reduced cost may allow doctors to tailor medical treatments to an individual's genetic profile for diagnosing, treating, and ultimately preventing many common diseases such as cancer, heart disease, diabetes and obesity.

ASU chemist Peiming Zhang and his collaborator Jian Gu have been awarded a $897,000 grant under this program for an ambitious DNA sequencing project that combines physics, chemistry and nanotechnology with engineering. The researchers have been charged with the daunting task of shrinking down the 13 year, $2.7 billion Human Genome Project to days.

"If you want to develop a technology to sequence an individual genome for $1,000, you have to think about using nanotechnology," said Zhang, associate research professor in the Center for Single Molecule Biophysics at the Biodesign Institute. "The technology is available now to pioneer a new approach to sequencing."

Much like the computer industry, DNA sequencing technology is driven by the mantra of faster, cheaper and more reliable. In the past generation, sequencing costs have fallen 100-fold, from roughly a dollar a DNA base to a penny, but are still far out of reach for the public.

Zhang's technological vision would enable scientists to sequence billions of base pairs of DNA in a single day. This is the size of an average mammalian genome and is approximately 10,000 times more bases per day than can be sequenced using current technologies. By increasing the speed of sequencing and reducing its cost, genetic research may develop a more significant role in everyday medical practice.

In Zhang's sequencing project, billions of base pairs of genomic DNA could be sequenced on a single, cookie crumb-sized one centimeter by one centimeter chip. The technique uses hybridization, a process of joining two complementary strands of DNA, to sequence DNA by applying a sample to single stranded DNA probes attached to a chip.

An atomic force microscope (AFM), like a caffeinated speed reader, can then rapidly scan the surface of the chip to see where DNA from the sample has hybridized to the probes. Wherever sample DNA binds to the probes, the sequence is registered.

"Traditional approaches to sequencing by hybridization are limited by the number of probes that can be placed on a chip," said Jian Gu, a research staff member in the Center for Applied NanoBioscience at the Biodesign Institute and co-leader of the project.

By using nanoprinting techniques developed by Gu, the researchers hope to increase the number probes they can fit on a chip. "Right now, we have a mechanical printing technology that could put down billions of probes on a chip surface at very low cost," said Gu.

It is estimated that a single base pair can be sequenced for every DNA probe, which means that optimizing the nanoprinting process is critical to the goal of a $1,000 genome, according to Zhang.

The researchers' first goal is a proof of principal for their approach. They plan to synthesize a universal DNA nanoarray on a 100 micrometer by 100 micrometer chip, about the size of a dust mite, by 2009.

The award to Zhang and his team was one of nine grants given by the NIH to achieve the $1,000 genome goal. Zhang's effort also joins two other ASU research teams, led by Stuart Lindsay and Peter Williams, who have more than $2 million in other DNA sequencing projects funded at ASU.

"There are currently only 36 grants in the entire NHGRI sequencing program, so it's quite remarkable that ASU has three of them, which is almost 10 percent of the program," Williams said.

Williams, professor of chemistry and biochemistry, is working on a $100,000 genome project, part of the five-year goal of the NHGRI to drop the current price to a hundredth of the cost. His goal is to selectively sequence genes known to be involved in disease in a matter of hours, and for a few hundred dollars.

Lindsay, who is director of the Biodesign Institute's Center for Single Molecule Biophysics, is engaged in a different separately funded $1,000 genome project. Lindsay is threading DNA through a molecular ring, in this case a sugar called cyclodextrin, that can read the DNA sequence by

measuring the differences in friction as the molecule is pulled through the ring.

Source: Arizona State University