Electronic DNA Sequencer

By Julia Karow, a GenomeWeb News reporter

NEW YORK, May 15 (GenomeWeb News) - A researcher at the University of Washington and a tech incubator have received $1.6 million from a foundation to develop a portable electronic DNA sequencer, *GenomeWeb News* has learned.

The Gordon and Betty Moore Foundation made the award to the researcher, who will share a portion of it with the firm, to develop a portable device to identify samples of animals and plants in the field by sequencing short stretches of DNA, so-called DNA barcodes. But the instrument, which will be the size of a grapefruit and cost less then $25,000, might have wider applications, including those in biodefense and forensics, according to its inventors.

"A lot of funding is going into DNA sequencing but none of it seems likely to lead to a portable DNA barcode reader," said a spokesman for the Moore Foundation, which plans to announce the award in a few weeks on its website.

The foundation has funded several other projects in genome-based taxonomy to develop DNA barcodes. This one is intended to give scientists an instrument to read the barcodes quickly: "One of the most difficult issues for field biologists is making accurate species identifications in the field, and we are trying to help address that problem," said the Foundation spokesman.

The technology will be developed by grant recipient Babak Parviz, a professor in the department of electrical engineering at the University of Washington, and Reveo, a technology incubator based in Elmsford, NY, which will also build and commercialize the finished product.

When developed, the device will read DNA bases electronically using a quantum mechanic effect called electron tunneling, and has the potential to sequence DNA within seconds without amplification, according to its inventors. It could reach beta testing in as little as two years, they said.

The foundation decided to fund Parviz's research because "the ideas in this grant are different from anything we have seen and have the best potential to lead to a portable device," the spokesman said.

The Moore Foundation brought Parviz and Reveo together because they said that pairing the two would "fit the goal of developing a portable instrument."

Reveo, founded by CEO Sadeg Faris, an inventor and IBM alumn with a PhD in electrical engineering, has already developed and spun out a number of technologies, including stereoscopic imaging, fuel cells, cholesteric liquid crystals, and optical communication components. The company has been independently working on the concept of a portable DNA sequencer, which will be its first life sciences product, for some time before its collaboration with Parviz, according to Faris, and is currently seeking additional funding from private investors for the project.

The device will use a technique called inelastic tunneling spectroscopy to read DNA electronically from a single molecule in a solid state environment. It will measure the energy spectrum of electrons passing through the DNA. Parviz, who is an expert in electronic molecular signatures, including electron tunneling, will develop this part of the technology.

While inelastic tunneling spectroscopy is not new - according to Parviz, it has been used in the automotive industry for many years to identify different oils - "it has never been used in the

context of what we want to use it for, because the tools that we have today were not available a few decades ago," he said. These tools include, for example, devices to position and move objects with sub-angstrom level precision and to record extremely small signals, on the order of femto amps, he added. Both were developed by the semiconductor industry in the last few years, he said.

Parviz said others have been able to identify organic molecules by applying voltage to them, measure the energy spectrum of tunneling electrons, and tell what functional group is present in the molecule. "But we have to show that we can do this on bases, and do this reliably," Parviz said. He said it will definitely be possible for relatively short DNA strands.

One challenge to overcome will be to reach single-base resolution, he said. Initially, his team will work on identifying a base when there are several bases of the same type in a row, and then eventually try to get down to single-base resolution.

Once Parviz has successfully demonstrated the ability to read DNA, Reveo will build the instrument, which will include several components. One is a scanning probe that moves along the DNA, which is stretched out on a solid support in a stepwise fashion, each step requiring just a few nanoseconds.

According to Faris, the nanoprobes, which he invented, are blade-shaped, are 10-20 micrometers wide, and have a sharpness of less than half a nanometer. The significance of the width, he said, is that even if the DNA is displaced by a couple of micrometers, the nanoblade will still land on it correctly.

Four of the nanoblades - one for each nucleotide - contact the DNA simultaneously. Each is functionalized with one of the four bases and forms a hydrogen bond when it hits a complementary base on the DNA, although Parviz said, using another option, it may not be necessary to functionalize them. After applying a voltage, the researchers should be able to measure electron tunneling and identify the DNA base.

The set of four nanoprobes, which is mounted on a piezoelectric stepper, then moves by a fraction of a nanometer to the next DNA base and repeats the process until the entire DNA molecule is read.

Faris said he hopes within a year to have a proof-of-concept, which would mean the ability to sequence between 10 and 100 bases. At the moment, eight of Reveo's 100-plus employees are devoted to the project. As soon as some experimental results are in - which could be in as little as six months - Reveo plans to spin out the sequencing technology into its own subsidiary, Faris said. Reveo has already spun out other technologies into four separate firms: VRex, eVionyx, Chelix Technologies, and PetaComm.

The first DNA sequencing product, which Faris said he plans to start beta-testing in approximately two years, will likely be able to sequence 1,000 to 10,000 base pairs and cost "well below" $25,000.

That product will not only be interesting for field biologists --- the application stipulated by the Moore Foundation --- but for anyone who needs to sequence DNA on the spot, Faris said. For example, it could be used to identify biothreats, such as pathogens or strains of viruses, he pointed out. Another application could be forensics, which requires DNA sequencing in some instances.

But Parviz and Reveo are not the only ones pursuing portable DNA analyzers. In March 2005, Integrated Nano-Technologies won a two-year, $500,000 Small Business Innovation Research

grant from the National Science Foundation to further develop its DNA detection technology for biological agents.

Two years ago, HandyLab received a $2 million grant from the National Institute of Standards and Technology to develop its portable DNA-analysis device, which uses microfluidics and electrochemical detection for biodefense applications and for clinical diagnostics in hospital settings.

Also, Parviz and Reveo's instrument will not be the first single-molecule DNA sequencer with an electronic readout: The National Human Genome Institute, for example, has funded 10 projects focusing on nanopore technology in which DNA is threaded through a molecular pore. But Faris pointed out that nanopores are fraught with challenges, including the fact that long DNA molecules get stuck inside them.

At least one group funded by NHGRI - James Lee at Oak Ridge National Laboratory - is also developing a method to detect DNA bases by tunneling conductance measurements.

Julia Karow covers *the next-generation genome-sequencing market for GenomeWeb News. E-mail her at jkarow@genomeweb.com.*