CRISPR-SNP-Chip: Electronic Measurements of Single Nucleotide Polymorphisms without DNA Amplification

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This Nature Biomedical Engineering publication demonstrates that Cardea's new CRISPR-powered transistors, dubbed "SNP-Chip," has the power to enable a new generation of genetics testing that will democratize genetics by removing the need for a lab.

Cardea Bio, a Tech+Bio company integrating molecular biology with semiconductors electronics via graphene-based biology-gated Cardean Transistors, announced today that its Chief Science Officer, Dr. Kiana Aran, and collaborators published a paper entitled "Discrimination of single-point mutations in unamplified genomic DNA via Cas9 immobilized on a graphene field-effect transistor" in Nature Biomedical Engineering on April 5th 2021.

The paper reports a new version of the Cardean CRISPR-Chip called SNP-Chip that can rapidly detect and quantify single nucleotide polymorphisms (SNPs), or point mutations, in unamplified, genomic DNA, and it demonstrates the platform's potential to streamline genetic testing for diagnostic and research purposes.

The SNP-Chip is a CRISPR-powered system that runs on Cardean Transistors. It uses the natural search power of CRISPR via reprogrammable gRNAs and CAS enzyme orthologues to detect target SNPs and rapidly return results on a screen. In contrast with other genetic tests methods like PCR and sequencing, which require much more time and a well-equipped lab with highly trained technical staff to execute complex sample prep and measuring processes, the SNP-Chip needs only a minimally processed sample (e.g., from blood, saliva or plant material), to work. As such, SNP-Chip is the first SNP detection method that does not suffer from the problems and bottlenecks caused by DNA amplification, nor does it require expensive optical detection instruments.

In the paper, the authors validated SNP-Chip's utility for testing SNPs associated with two human genetic diseases: sickle cell disease and amyotrophic lateral sclerosis (ALS). In both clinical models, the SNP-Chip was able to discriminate between homozygous samples

containing two copies of the healthy SNP vs. the disease-associated SNP. It was also able to detect heterozygosity, which confers the often-silent potential to transmit a genetic disease.

“SNP-Chip’s digital, direct, rapid, and accurate SNP analysis will revolutionize the screening for genetic mutations,” said Irina Conboy, PhD, Professor of Bioengineering at UC Berkeley and co-author on the paper. “This new technology will inform the discovery of the processes underlying disease and aging and will enable faster, more effective clinical translation,” Professor Conboy concluded.

In fact, SNP-Chip stands to enable easy and point-of-care electronic screening for a wide range of genetically driven health issues, since SNPs make up 50 percent of mutations known to cause genetics disease. In the paper, reprogramming SNP-Chip to identify different disease markers is shown to be a straightforward process: the authors simply designed different guide RNAs to bind to SNPs specific to sickle cell disease and ALS.

They reported that virtually any genetic disease can be detected via SNP-Chip, as long as a guide-RNA can be designed to seek the target. In addition, SNP-chip is not just limited to human diagnostics, but can also be used for SNP detection in any genetic material of interest for a wide range of applications such as genotyping for agricultural and environmental monitoring.

“Merging a diversity of CRISPR-Cas biology with electronics via Cardean Transistors opens up a whole new range of possibilities for diagnostic and research applications,” said CRISPR pioneer Virginjus Siksnys, founder and chairman of CasZyme, professor at Vilnius University, member of Cardea’s Innovation Counsel, and co-author on the paper. “Using the Cas9 orthologue for SNP detection is just the tip of the iceberg of opportunities.”

SNP testing typically runs on large, immobile lab instruments using complex workflows that can take hours or days to return results. In contrast, Cardean Transistors™, such as those that SNP-Chip runs on, are the first example of diagnostic devices at the intersection of biology and nanomaterial-based electronics. They lay the groundwork for the next generation of highly accurate, near real-time sensing devices with practical attributes such as a small size, making it amenable to being incorporated into a handheld device; the capacity to linked directly up to the internet for analysis; and the ability to deliver near real-time point-of-care results.

“The ability to detect SNPs on a chip does not just get to the core of human health genetics, it also gives us valuable and actionable insight into areas like agriculture, industrial bioprocesses, and even evolutionary change, such as mutations conferring resistance to antibiotics or mutating viruses,” said Dr. Aran. “By eliminating the need for amplification and large optical instruments, SNP-Chip will make SNP genotyping for these purposes readily accessible. Our hope is that this paper will inspire scientists worldwide to explore SNP-Chip’s capacity for detecting genetic variation “

The publication was the result of a collaboration between Cardea Bio, Inc., the Keck Graduate Institute, the University of California Berkeley, and the University of California Irvine, as well as CasZyme and Vilnius University, Lithuania, both via Professor Virginjus Siksnys.

“We’re proud to have worked with such a talented group of innovators and scientists to create a technology that represents a major milestone in reshaping nucleic-acid-based detection methods,” said Dr. Aran.

The SNP-Chip is a product version of Cardea’s previously reported CRISPR-Chip™ technology, which is capable of detecting large nucleic acid insertion and deletions and was featured on the cover of Nature Biomedical Engineering in June 2019. The many layers of new technology used in the publication were developed by Cardea Bio.

Read the original article on Business Wire.