World Record-Setting DNA Sequencing Technique Helps Clinicians Rapidly Diagnose Critical Care Patients

Initiative led by the Stanford University School of Medicine identifies genetic diseases in as little as 7.5 hours using NVIDIA Clara, Google DeepVariant and Oxford Nanopore Technologies sequencing.

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Cutting down the time needed to sequence and analyze a patient's whole genome from days to hours isn't just about clinical efficiency — it can save lives.

By accelerating every step of this process — from collecting a blood sample to sequencing the whole genome to identifying variants linked to diseases — a research team led by Stanford University took just hours to find a pathogenic variant and make a definitive diagnosis in a three-month-old infant with a rare seizure-causing genetic disorder. A traditional gene panel analysis ordered at the same time took two weeks to return results.

This ultra-rapid sequencing method, detailed today in the New England Journal of Medicine , helped clinicians manage the epilepsy case by providing insight about the infant's seizure types and treatment response to anti-seizure medications.

The method set the first Guinness World Record for fastest DNA sequencing technique: five hours and 2 minutes. It was developed by researchers from Stanford University, NVIDIA, Oxford Nanopore Technologies, Google, Baylor College of Medicine and the University of California at Santa Cruz.

The researchers accelerated both base calling and variant calling using NVIDIA GPUs on Google Cloud . Variant calling, the process of identifying the millions of variants in a genome, was also sped up with NVIDIA Clara Parabricks , a computational genomics application framework.

Euan Ashley, MB ChB, DPhil, the paper's corresponding author and a professor of medicine, of genetics and of biomedical data science at Stanford University School of Medicine, will be speaking at NVIDIA GTC , which runs online March 21-24.

Identifying genetic variants associated with a specific disease is a classic needle-in-the-haystack problem, often requiring researchers to comb through a person's genome of 3 billion base pairs to find a single change that causes the disease.

It's a lengthy process: A typical whole human genome sequencing diagnostic test takes six to eight weeks. Even rapid turnaround tests take two or three days. In many cases, this can be too slow to make a difference in treatment of a critically ill patient.

By optimizing the diagnosis pipeline to take only 7-10 hours, clinicians can more quickly identify genetic clues that inform patient care plans. In this pilot project, genomes were sequenced for a dozen patients, most of them children, at Stanford Health Care and Lucile Packard Children's Hospital Stanford.

In five of the cases, the team found diagnostic variants that were reviewed by physicians and used to inform clinical decisions including heart transplant and drug prescription.

"Genomic information can provide rich insights and enable a clearer picture to be built," said Gordon Sanghera, CEO of Oxford Nanopore Technologies. "A workflow which could deliver this information in near real time has the potential to provide meaningful benefits in a variety of settings in which rapid access to information is critical."

The researchers found ways to optimize every step of the pipeline, including speeding up sample preparation and using nanopore sequencing on Oxford Nanopore's PromethION Flow Cells to generate more than 100 gigabases of data per hour.

This sequencing data was sent to NVIDIA Tensor Core GPUs in a Google Cloud computing environment for base calling — the process of turning raw signals from the device into a string of A, T, G and C nucleotides — and alignment in near real time. Distributing the data across cloud GPU instances helped minimize latency.

Next, the scientists had to find tiny variations within the DNA sequence that could cause a genetic disorder. Known as variant calling, this stage was sped up with Clara Parabricks using a GPU-accelerated version of PEPPER-Margin-DeepVariant , a pipeline developed in a collaboration between Google and UC Santa Cruz's Computational Genomics Laboratory.

DeepVariant uses convolutional neural networks for highly accurate variant calling. The GPU-accelerated DeepVariant Germline Pipeline software in Clara Parabricks provides results at 10x the speed of native DeepVariant instances, decreasing the time to identify disease-causing variants.

"Together with our collaborators and some of the world's leaders in genomics, we were able to develop a rapid sequencing analysis workflow that has already shown tangible clinical benefits," said NVIDIA's Mehrzad Samadi, who co-led the creation of Parabricks and co-authored the New England Journal of Medicine article. "These are the kinds of high-impact problems we live to solve."

Read the full publication in the New England Journal of Medicine and get started with a 90-day trial of NVIDIA Clara Parabricks , which can help analyze a whole human genome in under 30 minutes.

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