CLINICAL DIAGNOSIS BY WHOLE GENOME SEQUENCING IN JUST ONE DAY

A new speed record for the time between arrival of the blood sample in the lab and the identification of the pathogenic variant by whole genome sequencing (WGS) has been entered into the Guinness Book of Records by a team from Stanford University School of Medicine. In a study published by Gorzynski et al.[1] in the February 17th issue of the New England Journal of Medicine, ultrafast WGS was performed for 12 critically ill patients. The shortest time between arrival of the blood sample to the initial diagnosis was 7 hours and 18 minutes. A diagnosis was found in 5 patients and had immediate clinical consequences, such as changes in medication. The speed record was possible by the application of the PromethION 48 sequencer from Oxford Nanopore that produces reads with a length of up to 1 Mb, but with higher error rates compared to the conventional short-read (up to 250 bp) sequencing-by-synthesis approaches. This was corrected by the use of the artificial intelligence-based PEPPER-Margin-DeepVariant software, developed by Google and the University of California Santa Cruz Genomics Institute, combined with NVIDIA Clara Cloud-based storage and real-time processing for base calling and alignment of the terabytes of raw data.

Is this giving us a glimpse of the future of clinical genetic diagnosis? Is this the way genome analysis will transform health care? A team led by Stephen Kingsmore of the Rady Children's Institute for Genomic Medicine in San Diego identified the cause of thiamine metabolism dysfunction syndrome 2 in a child with epileptic encephalopathy in 14 hours and 33 minutes. Thiamine and biotin medication were started, preventing permanent neurologic damage, and the child was discharged from hospital on the third day following admission (Owen et al.[2], New England Journal of Medicine June 3rd issue of 2021 for details).

1- https://www.nejm.org/doi/pdf/10.1056/NEJMc2112090?articleTools=true

2-https://www.nejm.org/doi/pdf/10.1056/NEJMc2100365?articleTools=true