DAYZERO DIAGNOSTICS

IDWeek 2024
Submission Summary

Pathogen Whole Genome Sequencing for Rapid ID & AST Directly from Multiple Clinical Sample Types

Novel Diagnostics Pipelines Session

Clinical application of technology:

Day Zero Diagnostics is developing an IVD device to perform rapid diagnosis of bacterial and fungal infections using whole genome sequencing direct from clinical samples. The platform will be broadly applicable across multiple sample types including bloodstream, urinary tract, and respiratory infections. The IVD will report ID and AST in <8 hours with a fully automated end-to-end solution.

What is novel about this technology?

Sequencing pathogen genomes from clinical samples is challenging due to the inherent low signal to noise. In clinical samples with low pathogen loads, human DNA massively outnumbers pathogen DNA, for example in whole blood at 1 CFU/mL loads, there is a billion times more human DNA than microbial DNA. Sequencing such samples, e.g. by cell free DNA or metagenomic sequencing, recovers only a small portion of the pathogen genome, creating a difficulty in distinguishing true pathogen presence from sources of noise such as reagent contamination or transient pathogen DNA presence.

We developed Pathovate, an ultra-high enrichment technology which enriches intact pathogen cells from clinical samples while massively depleting host DNA (8-10 logs of enrichment), thereby enabling recovery of the full pathogen genome. Genomes are sequenced with ONT in under 90 minutes and processed by our Keynome analytical platform to determine pathogen ID and AST, using novel AI algorithms. The Pathovate technology was first developed for application to whole blood, and has since been shown to be applicable to other sample types, including urine, BAL, and positive blood culture.

Performance data:

In whole blood, extensive contrived-sample testing was performed across 35 different species that were spiked into whole blood at <6 CFU/mL. Samples were processed with Pathovate and sequenced with ONT. Close to 100% of the pathogen genome was recovered across most species / replicates (panel A). Early clinical testing on patient whole blood showed 88.2% Categorical Agreement to AST phenotype using an AI predictive AST algorithm. In urine samples, contrived-sample testing performed across 7 species confirmed whole genome recovery via Pathovate. In addition, Keynome genomic AST determination had high accuracy relative to phenotypic AST (panel B). In BAL samples, preliminary testing has demonstrated the ability to recover whole genomes. A secondary module has been developed for respiratory samples to measure pathogen abundance from the sequencing data; preliminary results indicate that a metric (Keynome Value) correlates well with CFU input concentration (panel C).

Potential Clinical Impact:

The platform will deliver ID and AST directly from clinical samples in hours rather than days, enabling earlier targeted antibiotic therapy and reducing mortality, morbidity, and length of stay.