Clinical application of technology:
Antibiotic susceptibility profiling direct from clinical samples without the need for culture for inpatient use. First application focus is bacterial and fungal species in sepsis, future applications in urinary tract infections, cerebrospinal fluid, respiratory, and joint/wound.

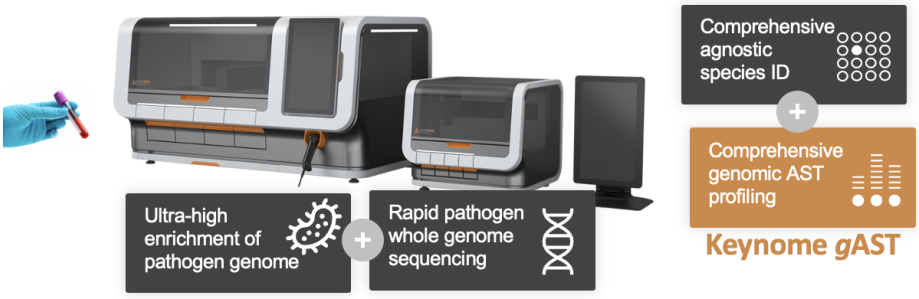
What is novel
Traditional antimicrobial susceptibility testing (AST) provides a direct observation of a pathogen's antimicrobial resistance/susceptibility phenotype. Unfortunately, these tests rely on culturing the bacteria from a clinical sample, which can take days to complete – time which a critically ill patient may not have. Recent advances in molecular diagnostics offer a quicker turn-around based on targeted amplification of known resistance markers in the pathogen DNA. But such techniques are limited to detecting only the most well-characterized resistance markers in the most widely-studied pathogens, thus severely limiting the negative predictive value of such tests. Here we present Keynome *g*AST (genomic AST) – a machine learning system for predicting antimicrobial resistance from pathogen whole-genome sequencing data derived directly from a clinical sample via an ultra-high pathogen DNA enrichment process. The technology presents an exciting prospect for a rapid and comprehensive diagnosis of bacterial infections, performing antibiotic susceptibility determination directly from blood within an 8 hour window.

Performance data
We demonstrate accuracy of Keynome gAST across a dataset of isolate strain genomic sequencing data, showing high accuracy across 68 species-drug combinations. Additionally, we show Keynome *g*AST accuracy on 100 contrived direct-from-blood (bacterial spike-in) samples, achieving >90% agreement with phenotypic AST across a panel of >40 pathogen-drug combinations. Finally, we demonstrate high accuracy on a limited dataset demonstrating Keynome gAST accuracy on polymicrobial contrived samples with 2 bacterial strains spiked into whole blood at low concentrations.

Clinical impact
With today's standard of care, the delay in diagnosing bacterial infections can be deadly for patients, whose risk of mortality in a severe infection (septic shock) can increase by 8% per hour if they are not treated with an effective antibiotic. Rather than waiting for the diagnosis, physicians treat using empiric therapy, an approach that is expensive, exposes patients to significant toxicity, encourages the spread of antibiotic resistance, and increasingly ineffective due to the rise of multidrug resistant pathogens. DZD is developing a culture free diagnostic for inpatient use that enables a physician to treat using a targeted antibiotic on the first day a patient is admitted to the hospital. By using DZD's diagnostic, hospitals will dramatically reduce hospital length of stay, overuse of expensive and often ineffective antibiotics that contribute to antibiotic resistance, and mortality rates.

Figure

DZD Technology: DZD is developing a technology to deliver a complete (ID + AST) diagnosis directly from a clinical liquid sample in less than 8 hours. Keynome *g*AST determines antimicrobial susceptibility profile directly from genomic sequencing data.



Keynome *g*AST Performance Data: Keynome *g*AST achieved high accuracy predicting antimicrobial susceptibility profiles of 100 bacterial strains across 10 species, spiked into whole blood at low concentrations and processed with our ultra-high enrichment technology.

Categorical Agreement between Phenotypic AST and Keynome *g*AST