DAYZERO DIAGNOSTICS

Blood2Bac: species ID and AMR prediction of bacterial pathogens at low concentrations in blood using a rapid ultra-high enrichment process and nanopore sequencing

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Background

Each year in the United States there are over 1.7 million cases of sepsis that account for a third of hospital deaths. A key to reducing morbidity and mortality rates is early, appropriate antibiotic therapy. Most new diagnostic approaches still suffer from insufficient sensitivity to low bacterial loads in blood and limited sets of detection targets for bacterial species identification (ID) and antimicrobial resistance (AMR) determination. As such, blood culture remains the gold standard for diagnosing bacteremia despite limitations such as >2-day turnaround time (TAT), incompatibility with fastidious organisms, and frequent inability to recover causative pathogens.

Methods

50 clinically relevant bacterial pathogens, made up of 30 gram-positive and 20 gram-negative bacterial species, were spiked into 2 to 4 healthy donor blood samples at 1 to 10 CFU/mL. The samples were run through our proprietary Blood2Bac™ pipeline, sequenced on a nanopore platform, and data were passed through Keynome®, our proprietary machine learning algorithm to determine species ID and AMR.

Results

By assessing the efficiency of pathogen DNA enrichment and genome coverage post sequencing, we report high performance at 4 to 10 CFU/mL for 8 bacterial species and ≤ 3 CFU/mL for 39 species, which includes *S. aureus*, *E. coli*, and *Streptococcus* spp., three of the leading causes of sepsis.

For all 50 bacterial species tested, Keynome called species ID with 100% accuracy, with accurate identification of 43 species at ≤ 3 CFU/mL. In addition, Keynome also predicted the AMR profile of pathogens with 100% accuracy for 19 drug/species AMR combinations, including ciprofloxacin for *E. coli*, clindamycin for *S. aureus*, and aztreonam for *K. pneumoniae*.

Conclusion

Blood2Bac is able to enrich a wide range of bacterial pathogens directly from blood and enable bacterial whole genome sequencing with an estimated TAT of 12 hours. When coupled with Keynome, our process provides accurate species ID and AMR calls for key BSI pathogens even at single-digit CFU/mL concentrations. Our species-agnostic and culture-free process enables detection of a diverse range of bacterial species with high sensitivity, providing a robust and comprehensive diagnostic.

