152. rapid Ultra-high Enrichment of Bacterial Pathogens at Low Concentration from Blood for Species ID and AMR Prediction Using Nanopore Sequencing

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Session: O-29. Innovations in Diagnostics

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: 31 clinically relevant bacterial pathogens, made up of 17 gram-positive and 14 gram-negative bacterial species, were spiked into 2 to 4 healthy donor blood samples. 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. For all 31 bacterial species tested, Keynome called species ID with 100% accuracy. 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 metronidazole for E. coli.

Conclusion: Blood2Bac™ is able to enrich a wide range of bacterial pathogens directly from blood and enable whole bacterial 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.

Disclosures: Chiahsao Tsui, n/a, Day Zero Diagnostics (Employee, Shareholder); Lisa S. Cunden, PhD, Day Zero Diagnostics (Shareholder) Nicole Billings, PhD, Day Zero Diagnostics (Employee) Imaly A. Nanayakkara, PhD, Day Zero Diagnostics (Employee, Shareholder) Ian Herrriott, BS, Day Zero Diagnostics (Employee, Shareholder) Rachel R. Martin, n/a, Day Zero Diagnostics (Employee, Shareholder) Miriam Huntley, PhD, Day Zero Diagnostics (Employee, Shareholder)

153. pilot Study of a Novel Whole-genome Sequencing Based Rapid Bacterial Identification Assay in Patients with Bacteremia

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Session: O-29. Innovations in Diagnostics

Background: Bloodstream infections (BSI) are among the leading cause of morbidity and mortality. Yet, gold standard culture-based diagnostics have limited ability to guide therapeutic intervention due to multi-day turnaround time and low sensitivity. Day Zero Diagnostics has developed Blood2Bac™, a culture-free, species specific assay to enrich bacteria direct from whole blood. Coupled with whole genome sequencing (WGS) and Day Zero Diagnostics Keynome algorithmic tools for species ID and antimicrobial resistance (AMR), we conducted the first proof-of-concept feasibility study in an inpatient clinical setting.

Methods: Study participants were enrolled and specimens collected from Boston Medical Center. Eligibility criteria included hospitalized adults with suspected or documented BSI, irrespective of empiric antibiotic therapy duration. Whole blood samples were processed with Blood2Bac, sequenced on a nanopore platform, and bacterial ID determined with Keynome ID. Keynome ID results were compared with blood culture results to measure concordance.

Results: From 21 participants were processed with Blood2Bac and nanopore sequencing. For 20/21 samples, Keynome ID calls were concordant with clinical blood culture, where 6 discordant positive and 14 were concordant negative. In 3 discordant samples, Keynome ID called positive while concurrent blood cultures were negative. However, all ID’s corresponded to positive blood culture duration. Whole blood samples were processed with Blood2Bac, sequenced on a nanopore platform, and bacterial ID determined with Keynome ID. Keynome ID results were compared with blood culture results to measure concordance.

Conclusion: These results highlight the sensitivity of a real-time blood WGS approach to identify BSI and its utility as a diagnostic to minimize unnecessary antibiotic exposure contributing to the antibiotic resistance crisis.

Disclosures: Archana Asundi, MD; Zachary Munro, n/a; Paul Knysh, PhD; Day Zero Diagnostics (Employee, Shareholder) Zachary Munro, n/a; Zachary Munro, n/a; Zachary Munro, n/a; Miriam Huntley, PhD; Day Zero Diagnostics (Employee, Shareholder)

154. comparative Genomics Reveals Extra-hospital Transmission Networks of Carbapenem-resistant Acinetobacter baumannii sustained over Multiple Years in a U.S Midwest City

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Session: O-30. MDRO Epidemiology and Transmission

Background: The transmission dynamics of Acinetobacter baumannii (Ab) outside of the setting of hospital outbreaks is underinvestigated. The BJHC Healthcare System in St. Louis, MO has not experienced an Ab hospital outbreak since 2012. Despite this, nearly 60% of all BC Ab isolates are carbapenem-resistant Ab (CrAb).

Methods: We acquired whole genome sequences (WGSs) of 110 Ab isolates identified in five BJHC hospitals from July 2017 to May 2019. We performed multilocus sequencing typing, core genome alignment and pairwise average nucleotide identity analysis to compare WGSs from BJHC isolates and GenBank-available WGSs of Ab isolates from other US hospitals. Further epidemiologic characterization was performed using BJHC electronic medical records and detailed chart review.

Results: Though the majority of CrAb isolates in other US studies belonged to globally prevalent sequence type 2 (ST2 [Pasteur scheme]), 62% and 26% of BJCr Ab isolates belonged to ST499 and ST406, respectively. BJCr ST499 and ST406 isolates were phylogenetically distinct compared to corresponding isolates from other US hospitals. Under the assumption that Ab transmission occurs primarily through nosocomial spread, we expected BJCr isolates from the same hospital and time span to share the highest degree of homogeneity. However, geographic proximity between ST499 and ST406 BJCr isolates was a poor predictor of their genetic relatedness, according to multiple comparative methods. Review of patient metadata did not identify epidemiological links between BJC CrAb isolates within phylogenetic subgroups.

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155. Public Health Action-based System for Tracking and Responding to U.S. can- dida Drug Resistance: AR Lab Network, 2016–2019

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Session: O-30. MDRO Epidemiology and Transmission

Background: Many U.S. clinical laboratories lack capacity to definitively identify fungi or perform antifungal susceptibility testing (AFST). To expand testing access, CDC’s Antibiotic Resistance Laboratory Network (AR Lab Network) provides Candida species identification and AFST to U.S. facilities for clinical and public health purposes. We describe the first three years of Candida AR Lab Network resistance data.

Methods: Isolates from any body site with species identification and AFST performed July 2016–June 2019 are included. Submissions were based on clinical

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