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 at 1 to 5 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 of 3 CFU/mL for 3 bacterial species and ≤ 2 CFU/mL for the 28 remaining species, which includes *S. aureus*, *E. coli*, and *Streptococcus* spp., three of the leading causes of sepsis.

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 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.

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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: Blood stream 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 agnostic process 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 and/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: Specimens 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 concordant positive and 14 were concordant negative. In 3 concordant samples, Keynome ID called positive while concurrent blood cultures were negative. However, all IDs corresponded with positive blood culture results from the day prior, suggesting potentially higher sensitivity for the Blood2Bac compared to blood culture. Two concordant positive IDs, resulted in >95% of the genome recovered and Keynome concomitantly resulted in AMR predictions with 100% accuracy compared to pathogen phenotype. In 1 discordant specimen, the Keynome ID result was negative while blood cultures 8 hours before were positive. In this case, the patient was on empiric therapy for 8 days prior to samples collection and cultures were negative 19-hours post specimen collection.

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**, **Gilead** (Scientific Research Study Investigator)**Merck** (Scientific Research Study Investigator)**ViiV** (Scientific Research Study Investigator) **Nicole Billings, PhD**, **Day Zero Diagnostics** (Employee) **Zoe H. Rogers, MPH**, **Day Zero Diagnostics** (Employee, Shareholder) **Lisa S. Cunden, PhD**, **Day Zero Diagnostics** (Shareholder) **Imaly A. Nanayakkara, PhD**, **Day Zero Diagnostics** (Employee, Shareholder) **Chiahao Tsui, n/a**, **Day Zero Diagnostics** (Employee, Shareholder) **Paul Knysh, PhD**, **Day Zero Diagnostics** (Employee) **Cabell Maddux, n/a**, **Day Zero Diagnostics** (Employee, Shareholder) **Zachary Munro, n/a**, **Day Zero Diagnostics Inc.** (Employee, Shareholder) **Ian Herriott, BS**, **Day Zero Diagnostics** (Employee, Shareholder) **Miriam Huntley, PhD**, **Day Zero Diagnostics** (Employee, Shareholder) **Nina H. Lin, MD**, **Gilead Sciences** (Scientific Research Study Investigator)**ViiV** (Scientific Research Study Investigator)

154. comparative Genomics Reveals Extra-hospital Transmission Networks of Carbapenem-resistant *acinetobacter Baumannii* sustained over Multiple Years in a US Midwest City

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Session: O-30. MDRO Epidemiology and Transmission

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

Methods: We acquired whole genome sequences (WGSs) of 110 *Ab* isolates identified in five BJC hospitals from July 2017 to May 2019. We performed multilocus sequence typing, core genome alignment and pairwise average nucleotide identity analysis to compare WGSs from BJC isolates and GenBank-available WGSs of *Ab* isolates from other US hospitals. Further epidemiologic characterization was performed using BJC 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 BJC CrAb index isolates belonged to the unrelated ST499 and ST406, respectively. BJC 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 BJC isolates from the same hospital and timespan to share the highest degree of homogeneity. However, geotemporal proximity between ST499 or ST406 BJC 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 isolates within phylogenetic subgroups.

Conclusion: We combined comparative genomics and detailed clinical chart review to characterize the transmission dynamics of two emerging US CrAb sequence types, ST499 and ST406. Though these highly homogeneous *Ab* isolates were identified over two years in multiple BJC hospitals, we found no evidence of robust intra-hospital transmission networks. Instead, it appears that these CrAb isolates independently emerged from yet-to-be-identified regional, extra-hospital *Ab* populations. To neutralize the threat of drug-resistant infections in the US, it is essential to identify, characterize and disrupt emergent CrAb transmission networks that exist outside of hospital environments.

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155. Public Health Action-based System for Tracking and Responding to U.S. candida 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