Brigham Young University

Microbial Volatile Metabolites for the Rapid Diagnosis of Clostridium Difficile Infection

Treatment costs, increased length of hospitalization, and higher rates of morbidity and mortality. In particular for bloodstream infections, the need to rapidly identify both pathogen and resistance profile is crucial, as treatment with antibiotics to which the organism is sensitive is essential and time-critical. Indeed, sepsis is responsible for up to half of all deaths in hospitals, yet the current clinical identification process for suspected bacteremia typically requires >24 hours, as a sample must first be cultured before additional tests identify the infecting species and determine its antibiotic resistance profile. Additionally, although FDA approved PCR-based assays have promise for multiplexed species detection and antibiotic resistance profiling, blood is a complex matrix containing PCR inhibitors that interfere both with the DNA and enzymes, limiting reproducibility and reliability. Clearly, there remains a significant unmet medical need for rapid, sensitive, non-amplification and non-culture based diagnostic tests for bacterial species and antibiotic resistance typing in bloodstream infections. Thus, in this project, we will develop a novel rapid, amplification-free, optofluidic cartridge-based diagnostic test for blood sepsis. This goal will be accomplished by demonstrating and combining innovative approaches for sample preparation and analyte detection, in particular spectrally multiplexed analysis in optofluidic chips with demonstrated single nucleic acid molecule sensitivity. The system will be validated by simultaneous detection of 3 *Enterobacteriaceae* species and 4 common antibiotic resistance genes at levels as low as 10 CFU/mL from a 7 mL whole blood sample in <1 hr. The proposed system is designed for straightforward transfer into a commercial product that is marketed by our corporate partner, Great Basin Corporation, such that success in these studies will have an immediate and substantial human health impact in the diagnosis and treatment of sepsis.