A Microscopy-Based Platform For Rapid, At-will Antimicrobial Resistance Testing

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Antibiotic resistance is compromising our ability to treat bacterial infections. Clinical microbiology laboratories guide appropriate treatment through antimicrobial susceptibility testing (AST) of patient isolates. However, increasingly, pathogens are developing resistance to a broad range of antimicrobials, requiring AST of less commonly used or recently introduced agents for which no commercially available or FDA-cleared testing methods exist. Agar or broth dilution are gold standard methods for AST that can be used to test any antimicrobial; however, labor and technical complexity precludes their use in hospital-based clinical laboratories. Therefore, bacterial isolates often must be sent to a reference laboratory with a 4-6 day delay in results. Further, even standard methods require overnight incubation prior to readout. Therefore, there exists a significant AST testing gap in which current methodologies cannot adequately address the need for rapid results in the face of unpredictable susceptibility profiles. Our laboratory has recently verified inkjet, digital dispensing technology as a novel platform to facilely perform reference AST for any antimicrobial at will. In this proposal, we aim to harness technical assets and expertise at HCBI/IDAC to leapfrog current technology through: (1) development of a method for microscopic imaging of bacterial replication in solid-phase 384-well microplate AST format, thereby determining susceptibility for any drug in <4 hours and (2) verification of the clinical performance of the new assay using well-characterized clinical solates. We anticipate establishing a prototype method that will address the AST testing gap and thereby help our health system more effectively address the antimicrobial resistance threat.