

## Brigham and Women's Hospital

### *Breath Volatile Metabolites for the Rapid Identification of Pneumonia Etiology*

Community acquired pneumonia (CAP) is the fourth leading cause of death worldwide, with 430---450 million cases and 3---4 million deaths per year. In the United States alone, there are 4---5 million CAP cases, 1.1 million hospitalizations, and over 52,000 deaths annually, accounting for over \$34 billion in direct health expenditures. Despite the high incidence of CAP, existing diagnostic tests for CAP are inadequate, identifying an underlying microbial pathogen in only 7---38% of cases. Even when a specific causal pathogen is identified, results often return long after it is necessary to make a clinical treatment decision. Because of the difficulty of identifying the microbial cause of pneumonia and the potentially severe consequences of not treating bacterial pneumonia promptly, clinicians often treat CAP empirically with antibiotics, even though a large proportion of these cases are viral in etiology. Unnecessary broad-- spectrum antibiotic prescriptions per year, in turn, fuel the emergence and spread of resistant bacteria, including most of the urgent and serious threat level pathogens on the Center for Disease Control and Prevention's list of urgent and antibiotic---resistant threats, on a population level. We propose a novel approach to CAP diagnosis based on distinct differences in the breath volatile metabolite profiles of patients with bacterial vs. viral pneumonia, using a rapid, portable gas chromatography--- differential mobility spectrometry (GC---DMS) Microanalyzer device at the point of care with parallel gold standard thermal desorption gas chromatography---tandem mass spectrometry (GC---MS/MS) in the laboratory to detect specific volatile metabolite signatures that (a) differentiate bacterial vs. viral CAP, and (b) identify certain common, specific causes of CAP, including *Streptococcus pneumoniae*. This rapid breath test for CAP would guide antimicrobial treatment decisions at the point of care, reducing antibiotic prescribing in patients who do not have bacterial pneumonia and slowing emergence of antimicrobial resistance on a population level.