INNOVATING CROSS-DOMAIN SOLUTIONS TO DETECT EMERGING BIOLOGICAL THREATS

Chip-scale Mass Spectrometry For Point-of-care Breath Diagnostics

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Background: The recent COVID-19 pandemic has underscored the urgency of swiftly identifying infected individuals to intervene early and prevent the progression to severe illness and to curb the transmission within communities. Exhaled breath diagnostics can provide such rapid screening approach while being non-invasive, cost-efficient, and potentially adaptable to detect various infectious agents. Traditional breath analysis methods often entail collecting breath samples using tubes or bags for transportation to labs where Gas Chromatography-Mass Spectrometry is employed for detecting trace-level organic compounds. While considered the gold standard, this method is both costly and logistically cumbersome. To address this, Detect-ION has leveraged its cutting-edge "Chip-Scale Mass Spectrometry" technology, enabling a compact 10-L Preconcentrator-Thermal Desorption-Gas Chromatograph-Mass Spectrometer (TD-GC-MS) system, called “CLARION”, for analyzing exhaled breath.

Objective: In CLARION, our goal is to identify the relevant VOC biomarkers in exhaled breath that distinguish between infected individuals and a healthy population. Our targets infection type include viral (Influenza and SARS-CoV-2) and bacterial pathogen (Streptococcus pneumoniae and Acinetobacter baumannii). If successful, a single CLARION device could require no more than a 1-minute breath sample per individual and conduct up to 160 breath analyses per day. Moreover, this approach could be more cost-effective than rapid PCR tests, enabling early detection of infections and facilitating high-throughput screening in large populations.

Methods: In CLARION project, we have established an institution review board (IRB) and plan to enroll asymptomatic and symptomatic human subjects across two sequential breath collection campaigns of cohort sizes of 100 (Campaign-1) and 500 (Campaign-2) respectively. Human subjects enrolled for the study will provide breath specimens, as well as nasal and throat swabs. Rapid antigen tests will evaluate the specimens for influenza, SARS-CoV-2, RSV, and group A streptococcus. In addition, RT-PCR will also be performed as a secondary diagnostic to validate antigen testing, with plans to perform BioFire® Respiratory 2.1 panel to accurately detect and identify the pathogens most associated with respiratory infections. Breath samples will be collected into the portable CLARION device for analysis, and into Tedlar bags and sorbent tubes for laboratory analysis on a commercial benchtop GC-MS. GC-MS data from the CLARION platform will be processed to generate a fingerprint pattern consisting of calibrated retention times and chemical identities for each VOC peak. These patterns along with the controls, which categorize each subject as uninfected or infected, will be provided as input to a Partial Least-Squares Discriminant Analysis (PLSDA) model building tool to develop detection algorithms.

Preliminary Results: The IRB has been accepted and we plan to begin enrollment for Campaign-1 in June 2024. A miniature breath collector with an embedded thermal desorption stage has been developed and successfully integrated into the CLARION platform. The MBC has smart collection technology to perform volumetric sampling of breath. Initial studies of vapor phase analytical standards have shown sensitivity of the system in the low parts-per-billion to high parts-per-trillion range.
Impact on DTRA JSTO Mission: Fieldable GC-MS system adapted to collect and analyze exhaled human breath can provide a versatile diagnostics capability for rapid screening of warfighters fitness and readiness in austere environments.

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