LOCALIZING CHEMICAL AND BIOLOGICAL THREAT DETECTION

Host-response Biomarkers In Interstitial Fluid: Individual Baselines, Marker Kinetics, And Implications For Wearable Devices And Continuous Monitoring.

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The PatchDx Bacterial/Viral (PDx-BV) diagnostic test is intended to measure host-response biomarkers in interstitial fluid (ISF) to differentiate bacterial from viral infections. The test is built upon similar principles and biomarkers as the existing tests from MeMed and Lumos Diagnostics but moves the test from blood or serum into a less invasive interstitial fluid sample extracted with a microneedle collector based on designs published by Sandia National Labs. The test is being designed with a lateral flow assay (LFA) analyzer-based measurement and quantitation against a statistical algorithm. PDx-BV itself is similar in use to the blood- or serum-based tests but provides an important first step toward the use of interstitial fluid as a primary sample matrix, especially for wearable devices that may provide continuous monitoring.

The SRI-led PDx-BV program has developed devices capable of collecting 5-10 µL of ISF in 5 minutes with minimal discomfort for use in both ELISA microplate studies and the point-of-care (POC) LFA being designed for the final device. Rapid collection of ISF in usable volumes is a critical step toward adapting any blood-based diagnostic for use in ISF as a POC test or for continuous monitoring. While most biomarkers present in blood can also be detected in ISF, their relative abundance, kinetics and concordance to blood-based data is target-dependent and must be verified experimentally for any ISF diagnostics to be approved by the FDA.

Data collected by SRI in this program shows long-term baseline stability in ISF measurements among a cohort of healthy subjects recruited at SRI across a period of 4-12 months. Perturbations in individual baselines can be seen consistently among the cohort after immunizations for COVID and influenza; data shows ISF biomarkers correlating closely with serum levels after immunization events. In cases where subjects had contracted an illness where physical symptoms had already resolved, the tail-end of the blood and serum biomarker response that has been reported in the literature is also observed in ISF. Additionally, in several cases where samples were coincidentally collected 24-48 hours before the donor developed physical symptoms of illness (e.g., fever or sore throat), biomarker elevation above the established individual baseline was observed, suggesting that ISF biomarkers may provide a predictive diagnosis before a subject is aware of an infection if personalized biomarker levels are monitored continuously. We plan to conduct a pilot ISF/blood comparison study of asymptomatic and symptomatic patients at the Naval Health Research Center (NHRC) in San Diego to provide proof-of-concept ISF data in cohorts of patients with confirmed viral or bacterial infections for the first time.

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