OVERCOMING LIMITATIONS OF ORGAN-ON-CHIP (OOC) TECHNOLOGIES TO ADVANCE THE CHARACTERIZATION AND MEDICAL MANAGEMENT OF CHEMICAL AND BIOLOGICAL (CB) THREATS

Microbiome Platforms For Prediction Of Human Health And Threat Resilience

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The human microbiome represents a target with tremendous potential for addressing national requirements in biological preparedness and precisely improving health and resilience in U.S. service members. To harness the power and intricacies of the human microbiome, predictive systems are needed to identify protective microbial features of resilience and novel methods for validation. We are addressing these needs by 1) establishing a high-performance computing pipeline for microbiome metagenomics, 2) constructing a data-driven machine learning platform for predictive microbiome analytics, and 3) developing an experimental system that facilitates rapid hypothesis evaluation, thereby improving the efficiency and success rate of future clinical testing efforts. To create cohesive microbiome datasets, we developed a pipeline for exploration and curation of microbiome data. Our data fusion process includes the combination of many diverse studies and maps common features across datasets to identify features specific for each study. To accommodate the complex and heterogenous characteristics of microbiomes, we employed multi-task machine learning (ML) to train models on internal and literature data. These models will improve predictive performance on individual datasets by training on them jointly. To alleviate the impact of high-dimensional data with limited sample size (large p, small n), we encourage the multi-task model to have sparse coefficients, that is, to induce a fraction of the model parameters to be zero. This automatically selects only the features relevant for the task at hand, e.g., disease risk prediction. We are further developing an experimental system to test the function of microbial consortia predicted to influence disease or resilience by creating a human intestinal microbiome-on-chip. This system includes an improved 3D biomimetic model of the human microbiome that provides critical advancements, including intestinal epithelial tissue architecture, barrier function, and environments capable of continuous monitoring. These capabilities will result in an end-to-end workflow for clinical data informed hypothesis generation and testing. Microbiome assessment and intervention represent a next frontier for precision medicine. Diagnosing and testing such interventions will enhance resilience against emerging threats for military and civilian populations, evaluating impacts of microbiomes on threat susceptibility. Our platform will also enable the testing and evaluation of solutions for deployment-associated disease. Such solutions will have far-reaching impacts for amplifying military operational readiness.