AI-POWERED DIAGNOSTICS

Identification Of Bacterial Infection By Innate Immune Signature

Daniel Jacobsen Los Alamos National Laboratory **Makaela Montoya** Los Alamos National Laboratory **Kaitlyn Martinez** Los Alamos National Laboratory **Kristen Wilding** Los Alamos National Laboratory **Apoorv Shanker** Los Alamos National Laboratory **Kiersten Lenz** Los Alamos National Laboratory **Carrie Manore** Los Alamos National Laboratory **Jessica Kubicek-Sutherland** Los Alamos National Laboratory **Harshini Mukundan** Lawrence Berkeley National Laboratory

Successful treatment of disease in humans often relies on early identification of pathogens causing infection. Universal and early recognition of pathogens occurs through recognition of evolutionarily conserved pathogen associated molecular patterns (PAMPs) by innate immune receptors and the consequent secretion of cytokines and chemokines. The intrinsic complexity of innate immune signaling and associated signal transduction challenges our ability to translate innate immune signals to actionable identification of pathogens. Machine learning methods can be leveraged to identify patterns of innate immune data. For machine learning methods to be successful, large amounts of high-quality data must be generated. To methodically generate high quality innate immune data, we measured cytokine and chemokine levels following exposure of human cells to PAMPs representing major sources of bacterial infection: lipopolysaccharide (LPS) from Pseudomonas aeruginosa representing Gram-negative pathogen infection and lipoteichoic acid (LTA) from Staphylococcus aureus representing Gram-positive infection. Expression of 84 messenger RNA (mRNA) transcripts were measured in human lung epithelial cells in response to the listed PAMPs. We evaluated over 32 biological replicates of each condition to determine reproducibility of outcomes. This data was then leveraged to develop machine learning models distinguishing Gram-negative, Gram-positive, and healthy states. The machine learning models identified alternate markers and patterns distinguishing disease states different from standard analysis. We show early steps towards developing machine learning-based methods of early pathogen identification using innate immune profiling. These host-based methods can potentially be used to identify biological threats in a pathogen-agnostic manner faster than current pathogen-based sensing.