AI/ML AND VIRTUAL HUMAN PLATFORMS FOR THREAT AGENT HAZARD ASSESSMENT AND MEDICAL COUNTERMEASURE DISCOVERY AND DRUG DEVELOPMENT

Intelligent Immunity – Modeling Innate Immune Responses For Agnostic Diagnostics, Therapeutics And Prediction Of Disease Severity

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The interaction of pathogens with the host results in an immediate and effective induction of innate immunity – a universal response that is capable of agnostic identification and response to all pathogens. We hypothesized that mimicking innate immunity in the laboratory can provide us with a universal approach for agnostic diagnostics and therapeutics. To accomplish this gargantuan task, our team has been working on an ambitious effort entitled Intelligent Immunity, which is comprised of four essential components – 1) developing reproducible and reliable physiologically relevant innate immune signaling data in vitro, 2) generation of data integration and mechanistic modeling pipelines, 3) machine learning algorithms to predict and resolve patterns of innate immune recognition and 4) iterative development using real-world clinical data.

One of the most significant roadblocks to development of machine learning models in biology is the availability of reliable and reproducible data. Previous work from our laboratory have unraveled complex interactions between host immune pathways, carriers and pathogen associated molecular patterns (PAMPs). These interactions have allowed us to develop a physiologically relevant, tunable experimental pipeline to generate innate immune data. Using this approach, we developed a model for gram-negative bacterial pathogens using Lipopolysaccharide-mediated induction of toll-like receptor 4 (TLR4) in year 1. Results of model development and ability to predict signature patterns will be demonstrated, as well as a comprehensive assessment of various machine learning approaches as applied to complex biological data – with pros and cons, will be demonstrated. In order to validate our experimental pipeline and theoretical models, we iterate the outcomes of our approach with real-world clinical data in order to refine and develop a robust pipeline. Previous work from our laboratory has shown that host lipid profiles dramatically impact the trafficking and presentation of pathogen signatures in the human host. This observation indicates why dyslipidemia, atherosclerosis, obesity, HIV and other co-morbidities may impact the severity of disease in a given individual. We will present our approach and preliminary data towards understanding disease severity in clinical samples.

For viral infections, we have chosen the ongoing COVID-19 pandemic as a model system and using clinical data of innate immune signatures measured from patients, demonstrate the tunability of our approach and extedability to diverse pathogens. However, these findings also demonstrate the challenge of only using clinical data - which is neither reproducible, nor reliable- for model development, and call to attention the need to establish sound biological foundations for effective machine learning models in biological sciences. Our ultimate goal is to develop a comprehensive “intelligent” model of innate immunity which can be capable of predicting early infection of all pathogens as a warning system for emerging infections.

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