MITIGATION - SCIENCE AND TECHNOLOGY ADVANCES FOR CHEMICAL AND BIOLOGICAL HAZARD MITIGATION

Innate Immunity As A Model System For Development Of Agnostic Diagnostics For Known And Emerging Threats

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Innate immunity is a pathogen agnostic evolutionarily conserved system that is capable of identifying new and emerging pathogens and mounting a response to them. It therefore follows that innate immunity can serve as an exceptional model system for the development of strategies to counter the next pandemic. This has been the driving thesis of our research for the past two decades; and has led to the development of strategies for deep understanding of innate immunity; and the associated development of diagnostics and countermeasures- significant aspects of it with support, in part, from the Defense Threat Aeduction Agency. In this abstract, we will integrate our findings from various studies over the past two decades in order to showcase a holistic understanding of innate immunity, and its application and validity for agnostic diagnostics in real-world samples.

Early work from our laboratory and others unraveled the association of pathogen associated molecular patterns with host lipoprotein carriers, resulting in the design of two agnostic strategies for diagnostics - membrane insertion and lipoprotein capture. Despite being agnostic, these assays were still limited in their need for ultra-sensitive sensing platforms, targeted ligands and reagents; and associated sample processing. All of these factors inhibit rapid application of innate immunity based diagnostics at the point of need. In order to overcome these limitations, we began to explore truly reagent-free and easily measurable ways of exploiting innate immune recognition via measurement of host cytokines and chemokines, instead of the pathogen signatures. However, being evolutionarily conserved, these signatures are shared among a variety of pathogens and the complexity of the signature patterns cannot be readily decoded manually. We postulated that machines can alleviate the challenge- resulting in the design of our effort - Intelligent immunity - to use artificial intelligence and machine learning to decode innate immune frameworks. Our previous work in evaluating diagnostics in real-world clinical samples resulted in further understanding of host-pathogen interactions in innate immunity, facilitating the design of physiologically-relevant in vitro models for the measurement of innate immune signatures (cytokines and chemokines). Using this, we developed a significant data inventory of physiologically relevant, reproducible bacterial and viral innate immune signatures, which were iteratively modeled against real world clinical data, in order to generate accurate machine learning models to predict immune signatures. This work, in addition to enabling reagent free diagnostics, has also uncovered key challenges associated with lack of standardization in the use of artificial intelligence and machine learning in biology. Finally, armed with this knowledge, we have begun to use hyperspectral sensing in order to measure these complex innate immune samples in clinical samples, and decode spectral patterns against our predicted patterns in order to obtain extremely rapid, reagent-free, agnostic diagnostics at the point of need. This has also led to further studies to uncover mechanistic underpinnings of contagiousness and disease severity, as associated with varying host parameters.

In this presentation, the system-level advantages of unraveling innate immunity in order to enable agnostic diagnostics and future precision medicine strategies - our past, present and future trajectories - will be discussed.

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