

## COMBATting FUTURE BIOLOGICAL THREATS – HOST-DIRECTED INTERVENTIONS TO EMERGING THREATS FOR RAPID RESPONSE

### Host-directed, Bioelectronic Immunomodulation For Protection Against Emerging Pathogens

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Acute care of hosts infected with biological threats such as emerging pathogens often relies on systemic administration of pharmaceuticals and monitoring of complex physiological symptoms to identify severity of illness or chance of mortality. The inherent delay in developing pathogen-specific treatments can lead to excess illnesses or deaths during this development period. Interestingly, a common cause of increased illness severity or mortality is often due to the host's immune system dysfunction, rather than the pathogen itself. To address this, we are developing a means to monitor and support the host's immune system via a closed-loop immunomodulation system capable of sensing immune system status in real time and modulating immune system response via vagus nerve stimulation (VNS). Current industrial products have shown the promise of utilizing vagus nerve stimulation to support the immune system, but thus far none have been used for acute infection, instead focusing on chronic autoimmune diseases. Additionally, VNS hardware is typically open loop, not taking into account real-time changes happening in the body to inform stimulation parameters. I will showcase two components in development: an electrochemical sensor to monitor cytokines (a biomarker for immune system status) in real-time and a stimulator capable of modulating immune system activity via VNS in animal models. Preliminary results show we are able to successfully fabricate a minimally invasive microneedle array to sense cytokine dynamics from interstitial fluid and measurably modulate cytokine dynamics in an animal model through VNS. Ultimately, we are working towards incorporating both elements into a single animal model which can then be used to monitor and respond to an applied inflammatory event. Potential impacts beyond this project include development of novel hardware capable of supporting the immune system, new wearable sensing platforms capable of detecting biomolecules beyond cytokines, and bioelectronic methods to treat infection that alter the paradigm in acute care beyond pharmaceuticals. Preemptive development of a precision immunomodulatory treatment that is agnostic to the causative pathogen will be a game-changer for pandemic preparedness, as we seek to cut the lag time to implementing targeted therapeutics from months to nearly zero.

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