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

Nonnegative Matrix Factorization Approach To Identify Host-pathogen Interactions And Develop Medical Countermeasures To Stem Outbreaks

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Background: Infectious diseases caused by emerging pathogens, such as SARS-CoV-2, Ebola, Zika, Bacillus anthracis (anthrax), and Acinetobacter baumannii, present significant public health challenges and potential threats as biological weapons of mass destruction (WMD).

Purpose and Objective: This research aims to develop novel medical countermeasures (MCMs) by identifying critical host-pathogen interactions. By designing that target these interactions, we aim to effectively combat both current and emerging infectious threats, especially as the efficacy of existing drugs diminishes due to pathogen mutation, evolution, or deliberate modification by adversaries.

Rationale: Understanding host-pathogen interactions is crucial for developing effective MCMs. By dissecting the mechanisms through which pathogens invade, replicate, and spread within hosts, we can devise more targeted strategies for infection treatment and prevention.

Relationship to Other Areas of Study: This research intersects microbiology, immunology, and computational biology, incorporating advanced artificial intelligence and machine learning techniques to enhance our understanding of and response to infectious diseases.

Methods: We employed a deep learning-based matrix factorization model to integrate diverse genomic and proteomic data from both hosts and pathogens. This model is instrumental in predicting protein-protein interactions (PPIs) between host and pathogen proteins, pinpointing crucial interactions that could serve as drug targets. We also utilized high-throughput experimental techniques to identify and model numerous PPIs, paving the way for the prediction of new interactions.

Preliminary Results: The matrix factorization model exhibited over 90% accuracy, as measured by the area under the receiver operating characteristic curve, demonstrating its strong capability in modeling host-pathogen interactions.

Preliminary Conclusions: Our matrix factorization approach has been a powerful tool in unraveling the pathogenesis of emerging pathogens and in identifying potential drug targets among host and pathogen proteins. Future research will focus on prioritizing high-scoring host-pathogen PPI pairs and further exploring them through docking and molecular dynamics simulations for drug development.

Impact to the JSTO Mission and the Joint Force: The insights gained from this study into the pathogenesis of critical biothreats bolster the development of targeted MCMs, thereby directly enhancing the biological defense capabilities of the Joint Force and supporting the JSTO mission.