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

Rapid Assessment Of Platform Technologies To Expedite Response (RAPTER)

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The COVID-19 pandemic has highlighted the need for rapid development of effective countermeasures targeting new and emerging pathogens. Safe and effective vaccines are a critical component to establishing a robust response to combat current, emerging, or future biological threats. However, vaccine design, testing, and manufacturing are time-consuming and expensive activities. The cost of developing a single vaccine to phase 2a clinical trials has been estimated at $68 million with failure rates as high as 94%, therefore vaccine development typically starts with multiple candidates following a lengthy linear workflow to mitigate these risks, increasing the cost proportionally. To streamline this process, we are developing a machine learning (ML) tool to predict the most suitable vaccine platform technologies for a given pathogen to increase the rate of success and reduce the number of initial vaccine candidates required. Vaccine platforms have inherent variabilities that limit their use against certain pathogens which can be quantified and used to predict their performance. The complicated nature of innate and adaptive immune responses and the large variability in existing data sets have limited a direct comparison between vaccine platform technologies. To address this, we applied computational modeling and broad literature mining techniques to normalize and draw conclusions from diverse data sources and identify an immunological profile for eight vaccine platforms and for three pathogens, two viral and one bacterial, as a proof-of-concept. Targeted experiments with standardized protocols were performed to fill data gaps for Ebola virus and Burkholderia pseudomallei, ensuring a direct comparison of each vaccine platform technology. The Rapid Assessment of Platform Technologies to Expedite Response (RAPTER) ML predicts to what degree each of eight vaccine platforms is compatible with each pathogen using (1) carefully curated data mining tools applied to all publicly available articles, vaccine databases, and clinical trials records; (2) mathematical models developed to compare pre-clinical datasets to known protective immune responses ranging from small animal models of disease to humans; and (3) molecular simulations quantifying structural features and limitations of how each vaccine platform presents a given antigen. In phase II, we are not expanding the ML tool by incorporating data and analysis for 12 additional pathogens, seven viral and five bacterial. The RAPTER ML tool developed, tested, and validated in this effort will revolutionize the future of vaccine development by rapidly down-selecting suitable vaccine platforms for any viral and bacterial pathogen.

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