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

Modeling The Generation Of Vaccine-induced Antibodies From Multiple Vaccine Platforms

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The main clinical correlate of protection in most approved vaccines is the level of antibodies. However, the vaccine platform used for successful, licensed vaccines has varied among pathogens. Understanding the process of antibody generation and their dynamics over time, as well as the relationship between these processes and the type of vaccine, could inform decisions on the best vaccine platforms for a given infection. We have analyzed the dynamics of antibodies generated by different vaccine types against different pathogens, and developed a consensus in silico model that captures these dynamics across these different systems. This model includes B-cell proliferation and differentiation, as well as the generation of plasma cells, which secrete large amounts of antibodies, and memory B-cells. Initially, the model was fitted to a rich data set of antibody and immune cell concentrations in a SARS-CoV-2 vaccine experiment. This demonstrated the utility of this mechanistic modeling. We then used machine learning, in particular transfer learning techniques, to apply the same model to multiple other systems involving different pathogens, vaccine platforms, and booster dose use/timing. This transfer learning involved fixing most parameter values relating to the dynamics of the immune system. Overall, the model describes antibody generation in all systems tested extremely well and shows that the main differences across platforms are related to the dynamics of antigen presentation. Thus, we conclude that knowing these dynamics is critical to differentiate vaccine platforms. This model can be used to predict antibody generation in pairs of vaccine platform/pathogen, allowing for the use of in silico results to narrow experimental burden in vaccine development. This approach has the potential to accelerate medical countermeasures targeting the host immune system's response to infectious diseases of interest to JSTO's mission.

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