THE HARTWELL FOUNDATION

2023 Nominee Individual Biomedical Research Award

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Improving Vaccine-Induced Protection Against Streptococcus Pneumoniae by Harnessing Nanoscale Structure

Children are at high risk for bacterial pathogens like Streptococcus pneumoniae (Spn), that colonize the upper respiratory tract to frequently cause pediatric infections and lead to serious medical conditions, including meningitis, bacteremia, and pneumonia. Spn is the leading cause of meningitis and pneumonia among children in the US, and pneumonia is the most common cause for pediatric hospitalization nationally. Unfortunately, even though vaccines have been developed, Spn continues to cause life-threatening disease in vulnerable children. Moreover, there remains a constant threat of "breakthrough" disease in vaccinated children, where a vaccine does not protect against all bacterial variants or serotypes (distinct variations of bacteria), some of which "escape" and reemerge. The threat is especially concerning, as these variants have also become resilient to many antibiotics. Therefore, vaccines that protect children effectively and broadly from all Spn serotypes are direly needed. Accomplishing this goal will better protect children in the US, especially immunocompromised ones, from infection and disease. Overall, there are minimal design considerations for vaccines, as development has focused mainly on selecting the bacterial target, rather than considering interactions between the target and immune cells. I hypothesize that this narrow focus has caused critical limitations, where vaccines only raise protection against a subset of serotypes causing infections; rely on protection through antibodies, excluding other beneficial immune interactions; elicit minimal immunity in the lung, the site of infection. I have observed that these limitations can be directly overcome by controlling the delivery and presentation of vaccine components to immune cells. Indeed, in prior research — against various cancers and infectious diseases — I observed that rationally structured vaccines that elevate delivery of immune cues, coordinate the timing of immune signals, and synchronize multifaceted interactions, will generate robust immunity. By considering how immune cells process external cues, my research has the potential to transform how vaccines are designed. By broadening vaccine design to include both target selection and structural arrangement, I will maximize a vaccine's ability to raise protective immunity. I will synthesize highly modular, tunable vaccines that incorporate targets against Spn, and will benchmark this platform against current alternatives. If I am successful, a rapidly deployable vaccine platform for protecting US children against Spn will significantly improve robust immunity and provide better protection for infants and neonates from influenza infection and disease.