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

Multivalent Outer Membrane Vesicle (omv) Vaccine For Melioidosis And Glanders Disease

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Abstract: The objective of this research project is to develop a multivalent outer-membrane vesicle (OMV) vaccine targeting melioidosis and glanders, severe infectious diseases caused by Burkholderia pseudomallei (Bp) and B. mallei (Bm), respectively. These pathogens are classified as Tier-1 select agents due to their potential to be used in a bioterrorism event, and their resistance to antibiotic therapy. Despite previous efforts, there are currently no effective vaccines against these biothreat agents. Recently, the Centers for Disease Control and Prevention (CDC) declared Bp to be endemic in the state of Mississippi based on melioidosis reported in three patients with no travel history to an endemic country. Soil sampling in the immediate vicinity of these individuals revealed clonal populations of pathogenic Bp. Environmental modeling suggests that the entire Gulf Coast of the United States may be conducive to the growth of Bp in the soil and is an emerging threat in the United States. These pathogens have the ability to evade the host immune system, leading to acute pulmonary infection and sepsis, with chronic infection and relapse being common in melioidosis. Most vaccines developed so far have failed to provide long-term protection, particularly against different serotypes or genotypes of Bp. We hypothesize that OMVs derived from the less pathogenic related bacteria B. thailandensis (Bt) and biosafe attenuated Bp strains can offer better protection against melioidosis and glanders compared to those from a single Bp strain. We also suspect that OMV antigens from Bt may be less immunosuppressive than those from pathogenic Bp. This research project strives to design a multivalent OMV vaccine containing different O-antigen types to enhance protection and reduce regulatory T-cell responses. The study will involve in vitro, in vivo, and ex vivo experiments to identify OMV composition, assess protection in mice, study T cell responses, assess for cellular toxicity of the OMV, and design vaccination strategies. The goal is to develop OMV vaccines that provide broad protection against diverse strains and serotypes of Bp and Bm, ultimately achieving sterilizing immunity and long-term protection against these biothreat agents.