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

Yersinia Pestis Nlp Subunit Vaccine Platform: Protective Efficacy And Immunological Profile

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Yersinia pestis (Yp) is the etiological agent of plague, a disease that remains a concern as demonstrated by recent outbreaks in Madagascar. Infection with Yp results in a severe and rapidly progressing illness that can only be treated with antibiotics. There are no FDA-approved vaccines. Live attenuated or whole-cell inactivated vaccines confer short-lived protection against bubonic but not pneumonic plague. Subunit vaccine formulations may circumvent some of these shortfalls. Here we compare the immunogenicity generated by the most advanced subunit vaccine formulation (rF1V), against a nanolipoprotein particle (NLP)-based vaccine. BALB/c mice were immunized twice, four weeks apart. Four weeks after the last immunization, splenocytes and sera were collected for immune profiling and animals were aerosol challenged with Yp CO92. Both vaccine formulations induced a strong total IgG response against F1 and V proteins along with a robust memory B cell response against F1V. Additionally, both formulations induced a strong cell-mediated immune response with induction of Th1- and Th2-related cytokines. However, the NLP-based vaccine induced a stronger cytokine response against F1, V, and F1V proteins relative to the rF1V vaccine. As with rF1V, the inclusion of Alhydrogel in the NLP vaccine formulations was critical for enhanced immunogenicity and protection following challenge. Addition of F. tularensis antigens to the Yp NLP vaccine platform did not result in deleterious effects on vaccine efficacy based on the level of protection following challenge and antibody response. The modularity and lipid bilayer structure of NLPs allows for incorporation of many protective antigens with variable ratios against multiple pathogens.

The opinions, interpretations, conclusions, and recommendations presented are those of the authors and are not necessarily endorsed by the U.S. Army or the Department of Defense Health Agency.

Research was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations relating to animals and experiments involving animals and adheres to principles stated in the Guide for the Care and Use of Laboratory Animals, National Research Council, 2011. The facility where this research was conducted is fully Accredited by the Association for Assessment and Accreditation Of Laboratory Animal International.