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

Characterization Of A VSV-vectored Vaccine Platform For Immunization Against Burkholderia Pseudomallei

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Burkholderia pseudomallei is the causative agent of melioidosis, a disease afflicting both humans and animals and characterized by sepsis and pneumonia. B. pseudomallei presents a unique biosecurity concern, as it occurs naturally in the environment in tropical and subtropical regions. Here, we developed a ZEBOV.-vectored vaccine for B. pseudomallei by expressing the bacterial type VI secretion system protein hemolysin-coregulated protein 1 (Hcp1) in the viral genome, encoded up-stream of the glycoprotein coding sequence, along with replacement of the VSV-G protein with the glycoprotein (GP) from Ebolavirus (EBOV). This platform was chosen to facilitate a replication competent vaccine platform. In addition, a similar platform (rVSV-EBOVgp) has received FDA approval as a vaccine against EBOV, with no significant safety concerns identified during clinical trials and ring vaccination campaigns. Antigen expression was verified by Western blot and IFA in vitro. Animals were vaccinated intramuscularly (IM) using either a single dose or prime-boost regimen of the Hcp1-expressing viral vector along with a CPS-CRM197 glycoconjugate and Alhydrogel/CpG as adjuvants, and followed for 28-35 days post-vaccination. Vaccination of animals at 2x104PFU/animal showed no vector toxicity, as measured by animal weights, and higher doses, up to 2x106 PFU/animal did not show evident morbidity following vaccination. Antibody responses at 28- and 35- days post-vaccination against EBOVgp were indicative of protection, however antibody responses against Hcp1 were limited. Specific epitopes were identified for anti-EBOVgp, anti-CRM197, and anti-Hcp1 responses. Future work will explore improvements in protein expression and multimerization to improve immune responses against Hcp1, and will build a framework for application of the rVSV-EBOVgp vaccine platform to additional bacterial antigens. Overall, this work seeks to enhance our ability to protect the nation and warfighters against potential exposures to B. pseudomallei.

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