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

A Nanolipoprotein Particle Platform Vaccine Targeting Ebola Virus Elicits A Robust Immune Response In Vivo

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Ebola virus (EBOV) disease (EVD), caused by Zaire ebolavirus and related viruses, is a rare but often deadly illness where recovery depends on the patient's immune response, quality supportive care, and more recently, administration of monoclonal antibody therapies. A vesicular stomatitis virus (VSV)-vectored vaccine, ERVEBO®, was approved for use in 2019 and is considered the gold-standard for pre-exposure prophylactic use in the US among high-risk populations, including deployed military personnel and health-care workers at risk for occupational exposure to EBOV. While remarkable progress has been made in EBOV vaccine development, challenges associated with vaccine efficacy, potency, durability and cost remain. We have developed a nanolipoprotein (NLP) particle-based EBOV vaccine consisting of the EBOV glycoprotein (GP) and a cholesterol-tagged CpG (2006) adjuvant conjugated to the NLP platform (EBOV GP:NLP + cCpG). Alhydrogel (Alh) adjuvant was also assessed in combination with CpG. C57BL/6 mice were vaccinated intramuscularly (IM) using a prime-boost regimen 4 -weeks apart. Animals were bled prior to the boost and 4 weeks after to quantify GP-specific antibody responses. Seven days after the boost, a cohort of animals were euthanized to assess cell-mediated immune responses induced by vaccination. Vaccinated animals elicited robust GP-specific IgG antibody titers, with animals receiving both CpG and Alh showing higher titers over CpG alone. Pseudovirion neutralization assays (PsVNA) demonstrated low but detectable serum antibody titers. Interestingly, splenocytes isolated from vaccinated animals showed significant levels of IFN- g production upon restimulation by ELISpot compared with PBS control animals. Taken together, these data suggest that EBOV GP:NLP + cCpG and/or Alh does induce robust humoral and cell-mediated immune responses in vivo and may further enhance the tools we have to protect warfighters and other at-risk populations from EVD.

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