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

Protective Vaccination Of Nonhuman Primates Against Aerosol Exposure To Marburg Virus Using A Vesicular Stomatitis Virus-vectored Vaccine – Implications For Mucosal Vaccine Strategies And Unpredictable Filovirus Transmission

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Recent increases in outbreaks caused by filoviruses, including Marburg virus (MARV) pose a serious global health threat due to a lack of countermeasures shown to be effective in people. Zoonotic spillover of MARV likely from Rousettus bat virus reservoirs followed by human-to-human transmission through contact with infected body fluids, has been associated with outbreaks. However, lethal infection by aerosol exposure, an unnatural route, has been demonstrated in preclinical models, which further establishes MARV as having the potential to become a significant bioweapon and threat to military personnel. We have previously shown that a single intramuscular (IM) injection with a clinical-ready replication-competent recombinant vesicular stomatitis virus vaccine vector encoding the MARV glycoprotein GP (rVSVDG-MARV-GP) was highly efficacious in protecting cynomolgus macaques exposed to MARV-Angola by systemic infection. Here, we demonstrate that either IM or mucosal intranasal (IN) rVSVDG-MARV-GP vaccination regimens can elicit immunity that protects cynomolgus macaques following MARV-Angola aerosol exposure. We found that all rVSVDG-MARV-GP vaccinated macaques developed potent systemic immunity as measured by anti-MARV GP binding titers and viral neutralization responses, regardless of the route of vaccine delivery and that the humoral responses appeared to be predictive of MARV aerosol protection. Moreover, macaques vaccinated by the IN route displayed superior protection against MARV aerosol exposure as indicated by improved control of MARV viremia, decreased clinical pathologies and increased survival. Together, these results support that rVSV-based vaccines have broad utility as effective countermeasures against natural and unpredictable pathogen exposures. Moreover, this work highlights that rVSV-based vaccines can be safely deployed within the mucosal environments and can provide significant benefits for protection of the warfighter and the general population against potential respiratory pathogen exposure in the advent of military and bioterrorist scenarios respectively.