DEVELOPMENT OF PAN-FILOVIRUS VACCINE AGAINST EBOLA AND MARBURG VIRUS CHALLENGES

Xiangguo Qiu, National Microbiology Laboratory, Public Health Agency of Canada; Department of Medical Microbiology, University of Manitoba, Canada
Md Niaz Rahim, ational Microbiology Laboratory, Public Health Agency of Canada; Department of Medical Microbiology, University of Manitoba, Canada
Edmund G. Wee, The Jenner Institute, Nuffield Department of Medicine, University of Oxford, United Kingdom;
Shihua He, National Microbiology Laboratory, Public Health Agency of Canada, Canada;
Jonathan Audet, National Microbiology Laboratory, Public Health Agency of Canada, Canada;
Bette M. Korber, Los Alamo National Laboratory, Theoretical Biology and Biophysics; The New Mexico Consortium, United States of America
Tomáš Hanke, The Jenner Institute, Nuffield Department of Medicine, University of Oxford; International Research Center for Medical Sciences, Kumamoto University, Japan

Filoviruses such as Ebola (EBOV) and Marburg (MARV) viruses cause deadly viral hemorrhagic fever in humans with high case fatality rates. To date, no licenced therapeutic or vaccine has been clinically approved to prevent infection. Several vaccine candidates are under development against the few most common filoviruses targeting the virus glycoprotein (GP). However, protective antibodies induced by such GP vaccines are usually limited to the same species. In contrast, T-cell vaccines offer an opportunity to design a single pan-filovirus vaccine protecting against all members of the Filoviridae family. In this study FILOcepX vaccines were constructed targeting the four most conserved regions among the viral proteomes with the aim to induce protective T-cell responses against different filoviruses. BALB/c mice were immunized with FILOcep 1 and 2 vaccines vectored by non-replicating engineered simian adenovirus and poxvirus MVA. Groups of 20 BALB/c mice were primed and boosted with either the FILOcep1 and FILOcep2 vaccines or control ChAdOx1- and MVA-vectored vaccines. Four animals in each group were sacrificed after 1 week of boosting to detect T-cell response for the FILOcepX antigen. High frequency T cells specific responses were detected in mice receiving the test vaccines by IFN-γ ELISPOT kits. Of the remaining 16 animals in each group, 8 were challenged with mouse-adapted EBOV and 8 were challenged with mouse adapted MARV in Containment Level 4 laboratory. All the mice in the control group either died or had to be euthanized between 4 and 6 days post challenge. On the other hand all the FILOcepX vaccinated mice maintained their normal body mass and survived till the end of the scheduled protocol on day 29 post challenge. These FILOcepX vaccines provided 100% protection against the lethal challenges with filoviruses of two different genera. Further evaluation the efficacy of this vaccine in non-human primates (NHPs) is warranted.