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Development of Ebola virus glycoprotein Fc fusion proteins as a vaccine candidate

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Ebola virus is a Filoviridae that causes severe hemorrhagic fever in humans and results in high morbidity and mortality rates. Filoviruses are classified as "Category A" bioterrorism agents, and currently there are no licensed therapeutics or vaccines to treat and prevent infection. Immunization with the Filovirus glycoprotein (GP) is sufficient to protect individuals against infection, and several vaccines based on GP are under development including recombinant adenovirus, parainfluenza virus, Venezuelan equine encephalitis virus, vesicular stomatitis virus (VSV) and virus-like particles. Here we describe the development of an Ebola virus subunit vaccine based on GP fused to the Fc fragment of human IgG. We expressed the extracellular domain of the Zaire Ebola virus (ZEBOV) GP fused to the Fc fragment of human IgG1 (ZEBOVGP-Fc) in mammalian cells and showed that GP undergoes the complex furin cleavage and processing observed in the native membrane-bound GP. Mice immunized with ZEBOVGP-Fc developed T-cell immunity against ZEBOV GP and neutralizing antibodies against replication-competent VSV-G deleted recombinant VSV containing ZEBOV GP. The ZEBOVGP-Fc vaccinated mice were protected against challenge with a lethal dose of ZEBOV. These results show that vaccination with the ZEBOVGP-Fc fusion protein alone is sufficient to induce protective immunity against ZEBOV in mice. We are currently extending our studies to the guinea pig model of Ebola virus. Our data provide a basis for further studies of Filovirus GP Fc fusion proteins as a potential vaccine against Filovirus infection.

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