A RECOMBINANT VACCINIA VIRUS-BASED T CELL VACCINE AGAINST INFLUENZA VIRUS REDUCES LUNG VIRAL LOAD UPON VIRUS CHALLENGE

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Currently, there are only two approved vaccines against influenza virus, one containing killed virus and the other containing live, attenuated virus. Each year, there is a reformation of the vaccine formulation, depending on which strains are thought to become most dangerous in the upcoming season. Numerous groups and pharmaceutical companies are developing universal vaccines that would not require changing every year. Many of these vaccine strategies target strain-conserved influenza virus proteins, such as the matrix, polymerase, and nucleoproteins, rather than the surface hemagglutinin and neuraminidase proteins. In addition, non-disease-causing viral vectors are a popular choice as a delivery system for the influenza virus antigens. We have developed a DNA-prime/vaccinia virus-boost vaccine strategy utilizing recombinant, multi-epitope influenza virus proteins, based on the nucleoprotein backbone, the N-terminal of neuraminidase, and the C-terminal of hemagglutinin, which were mainly expressed in the cytosol of recombinant vaccinia virus-infected cells. Upon vaccination, we observed an increase in the number of splenocytes secreting IFNγ when stimulated with influenza virus peptide, as compared to vaccination with wild-type vaccinia virus. The regime also elicited an increased adaptive immune response, marked by CD4+ and CD8+ T cells producing IFNγ or TNFα. Finally, upon challenge with influenza virus, mice vaccinated with recombinant vaccinia virus exhibited decreased viral load in the lungs. These findings suggest that vaccination with multi-epitope recombinant influenza virus proteins provide protection against viral replication during heterologous challenge.