Recombinant murine gammaherpesvirus 68 (MHV-68) as challenge virus to test efficacy of vaccination against chronic virus infections in the mouse model.

Abstract:

Efficient vaccines against AIDS, Hepatitis C and other persistent virus infections are urgently needed. Vaccine development has been especially hampered by the lack of suitable small animal models to reliably test the protective capacity of candidate vaccines against such chronic viral infections. A natural mouse pathogen such as MHV-68 that persists lifelong after infection, appears to be a particularly promising candidate for a more relevant model system. Here, we investigated infections with recombinant MHV-68 as novel mouse challenge model to test the efficacy of heterologous vaccines based on recombinant modified vaccinia virus Ankara (MVA). To apply ovalbumin (OVA) as a model antigen, we constructed the recombinant virus MHV-68-OVA by BAC technology and characterized genetic stability and replicative capacity of the virus in vitro and in vivo. We demonstrated the ability of MHV-68-OVA to produce ovalbumin upon tissue culture infection. Moreover, the use of MHV-68-OVA-infected target cells allowed for efficient ex vivo amplification of OVA-specific, MHC class I-restricted CD8 T cells derived from MVA-OVA-vaccinated C57BL/6 mice. Finally, we immunized C57BL/6 mice with MVA-OVA and challenged the animals with MHV-68-OVA testing different time points and routes of infection. Vaccinated mice were
infected with MHV-68-OVA but showed reduced viral loads in the acute and latent phase of challenge infection. These data strongly suggest the usefulness of the MHV-68 challenge model for further evaluation of recombinant vaccines against persisting virus infections.