BACKGROUND: Efficient vaccines against hepatitis C virus (HCV) infection are urgently needed. Vaccine development has been hampered by the lack of suitable small animal models to reliably test the protective capacity of immunization.

METHODS: We used recombinant murine gammaherpesvirus 68 (MHV-68) as a novel challenge virus in mice and tested the efficacy of heterologous candidate human vaccines based on modified vaccinia virus Ankara or adenovirus, both delivering HCV non-structural NS3 or core proteins.

RESULTS: Recombinant MHV-68 expressing NS3 (MHV-68-NS3) or core (MHV-68-core) were constructed and characterized in vitro and in vivo. Mice immunized with NS3-specific vector vaccines and challenged with MHV-68-NS3 were infected but showed significantly reduced viral loads in the acute and latent phase of infection. NS3-specific CD8+ T cells were amplified in immunized mice after challenge with MHV-68-NS3. By contrast, we did neither detect a reduction of viral load nor an induction of core-specific CD8+ T cells after core-specific immunization.

CONCLUSIONS: Our data suggest that the challenge system using recombinant MHV-68 is a highly suitable model to test the immunogenicity and protective capacity of HCV candidate vaccine antigens. Using this system, we demonstrated the usefulness of NS3-specific immunization. By
contrast, our analysis rather discarded core as a vaccine antigen.