M2SR, a novel live influenza vaccine, protects mice and ferrets against highly pathogenic avian influenza

Abstract

The emergence of highly pathogenic avian influenza H5N1 viruses has heightened global concern about the threat posed by pandemic influenza. To address the need for a highly effective universal influenza vaccine, we developed a novel M2-deficient single replication (M2SR) influenza vaccine virus and previously reported that it provided strong heterosubtypic protection against seasonal influenza viruses in mice. In the current study, we assessed M2SR induced protection against H5N1 influenza in mice and ferrets.

Mice were intranasally inoculated with M2SR viruses containing the HA and NA from A/Vietnam/1203/2004 (M2SR H5N1) or A/California/07/2009 (M2SR H1N1). All M2SR vaccinated mice survived lethal challenge with influenza A/Vietnam/1203/2004 (H5N1), whereas 40% of mice vaccinated with recombinant H5 HA and none of the naïve controls survived. M2SR H5N1 provided sterile immunity, whereas low levels of virus were detected in the lungs of some M2SR H1N1 vaccinated mice. In contrast, recombinant H5 HA vaccinated mice and naïve controls showed systemic infection.
M2SR H5N1 induced strong serum and mucosal antibody responses (IgG and IgA classes) against H5 HA, with high hemagglutination inhibition (HAI) titers. In contrast, while M2SR H1N1 elicited crossreactive antibodies recognizing the H5 HA2 stalk region or the neuraminidase, no HAI activity against H5N1 virus was detected after M2SR H1N1 immunization.

Both M2SR H5N1 and H1N1 also protected ferrets against lethal challenge with A/Vietnam/1203/2004. A prime–boost regimen provided optimal protection with no virus detected in the respiratory tract or brain after challenge. As in the mouse model, only the M2SR H5N1 vaccine induced HAI antibodies against the challenge virus in ferrets, while the M2SR H1N1 was able to provide protection without the induction of HAI antibodies.

In summary, effective protection against highly pathogenic H5N1 influenza virus was provided by both homologous H5N1 M2SR and heterologous H1N1 M2SR demonstrating the cross-protective attributes of the M2SR platform.