

ACTIVE AND PASSIVE IMMUNIZATION AGAINST AVIAN INFLUENZA VIRUSES

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Highly pathogenic avian influenza A H5N1 viruses have been circulating in avian species since 1997 and have caused more than 380 human infections and more than 240 deaths since 2003. The outbreaks of human infection by H5 subtype avian influenza viruses along with sporadic reports of infections by H7 and H9 subtype avian influenza viruses underscore an urgent need to develop novel prophylactic and therapeutic interventions to protect humans in the event of a pandemic. Vaccination is the key strategy to prevent severe illness and death from pandemic influenza. We have generated and evaluated live attenuated influenza vaccines (LAIV) against 4 avian influenza virus subtypes (H5, H6, H7 and H9). The intranasally administered candidate LAIV vaccines were attenuated and immunogenic in mice and ferrets. The vaccines protected mice and ferrets from challenge with homologous and heterologous virus infection. We have also evaluated the efficacy of neutralizing human monoclonal antibodies (Mabs) for prophylaxis and treatment of H5N1 virus infection in BALB/c mice. The Mabs were generated from memory B cells from patients who had recovered from highly pathogenic H5N1 virus infections. Our data indicate that fully human Mabs with neutralizing activity generated from the peripheral blood mononuclear cells of convalescent patients can effectively prevent and treat H5N1 virus infection in vivo. The promising findings of efficacy against antigenically diverse viruses with these two approaches suggest that active and passive immunization approaches may be useful for prophylaxis and/or adjunctive treatment of human infections by avian influenza viruses.