

Broad Protection against Avian Influenza Virus by Using a Modified Vaccinia Ankara Virus Expressing a Mosaic Hemagglutinin

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Abstract : A critical failure in our preparedness for an influenza pandemic is the lack of a universal vaccine. Influenza virus strains diverge by 1 to 2% per year, and commercially available vaccines often do not elicit protection from one year to the next, necessitating frequent formulation changes. This represents a major challenge to the development of a cross-protective vaccine that can protect against circulating viral antigenic diversity. We have constructed a recombinant modified vaccinia virus Ankara (MVA) that expresses an H5N1 mosaic hemagglutinin (H5M) (MVA-H5M). This mosaic was generated in silico using 2,145 field-sourced H5N1 isolates. A single dose of MVA-H5M provided 100% protection in mice against clade 0, 1, and 2 avian influenza viruses and also protected against seasonal H1N1 virus (A/Puerto Rico/8/34). It also provided short-term (10 days) and long-term (6 months) protection post vaccination. Both neutralizing antibodies and antigen-specific CD4+ and CD8+ T cells were still detected at 5 months post vaccination, suggesting that MVA-H5M provides long-lasting immunity.

Keywords : modified vaccinia Ankara, MVA, H5N1, hemagglutinin, influenza vaccine

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