

Single-dose monomeric HA subunit vaccine generates full protection from influenza challenge

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Abstract

Recombinant subunit vaccines are an efficient strategy to meet the demands of a possible influenza pandemic, because of rapid and scalable production. However, vaccines made from recombinant hemagglutinin (HA) subunit protein are often of low potency, requiring high dose or boosting to generate a sustained immune response. We have improved the immunogenicity of a plant-made HA vaccine by chemical conjugation to the surface of the Tobacco mosaic virus (TMV) which is non infectious in mammals. We have previously shown that TMV is taken up by mammalian dendritic cells and is a highly effective antigen carrier. In this work, we tested several TMV-HA conjugation chemistries, and compared immunogenicity in mice as measured by anti-HA IgG titers and hemagglutination inhibition (HAI). Importantly, pre-existing immunity to TMV did not reduce initial or boosted titers. Further optimization included dosing with and without alum or oil-in water adjuvants. Surprisingly, we were able to stimulate potent immunogenicity and HAI titers with a single 15µg dose of HA as a TMV conjugate. We then evaluated the efficacy of the TMV-HA vaccine in a lethal virus challenge in mice. Our results show that a single dose of the TMV-HA conjugate vaccine is sufficient to generate 50% survival, or 100% survival with adjuvant, compared with 10% survival after vaccination with a commercially available H1N1 vaccine. TMV-HA is an effective dose-sparing influenza vaccine, using a single-step process to rapidly generate large quantities of highly effective flu vaccine from an otherwise low potency HA subunit protein.