VACCINATION WITH RECOMBINANT NEURAMINIDASE PROTECTS AGAINST INFLUENZA VIRUS INFECTION IN MICE

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While the efficacy of most influenza virus vaccines is measured by the ability to induce antibodies against the hemagglutinin (HA), antibodies against the viral neuraminidase (NA) are also correlated with less severe disease in humans and animal models. Yet, neither the amount nor the enzymatic activity of NA is standardized in current seasonal vaccines, and the breadth of NA-based protection is unknown. In the present study, different subtypes of recombinant NA were expressed in a baculovirus system and used to vaccinate mice prior to homologous, heterologous, or heterosubtypic virus challenge. Additionally, pre- and post-vaccination human serum samples from vaccinees that received TIV were studied to compare induction of antibodies against the HA and NA. Finally, the amounts of NA in 4 different vaccine formulations from 2013-2014 were quantified using ELISA. Mice immunized with N2 were 100% protected from morbidity and mortality in a homologous challenge and displayed significantly reduced viral lung titers. Heterologous challenge with a drifted strain resulted in morbidity but no mortality. Mice immunized with B/Yamagata/16/88 NA were 100% protected from morbidity and mortality when lethally challenged with a recent Victoria lineage strain. In our human cohorts, the increase in endpoint titers against N1 NA post-vaccination was less robust than that against HA and, as our quantification data suggests, the N1 NA amounts in seasonal vaccine formulations is quite variable. To confirm the broad protective effects of anti-influenza B NA antibodies on a monoclonal level, a panel of mouse monoclonal antibodies was generated against influenza B virus NA; several of these displayed broad reactivity in ELISA to whole virus and recombinant NA and protected against lethal influenza B virus challenge in mice when delivered at a dose of 5 mg/kg prophylactically, or therapeutically, 48 hours post-infection. Analysis of the protective epitopes is currently in progress. The demonstrated protective capacity of anti-NA antibodies suggests that targeting the NA through vaccination may offer increased protection against influenza virus infection.