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Novel matrix protein virus-like particle (M2e VLP) subunit vaccine for influenza

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Introduction: The purpose of this study was to design a universal influenza vaccine. Thus we investigate the efficacy and protection of the common M2e protein which is common to all influenza virus. We formulated M2eVLP particulate vaccine and administered them transdermally in a pre-clinical mouse model for influenza.

Methods: The M2e VLP was adsorbed onto Alhydrogel® and encapsulated into a polymer matrix along with the adjuvant, MPL-A®. This combination was then formulated into microparticles using a spray drying method. For animal experiments, 4-6 week old male C57BL/6 mice (Charles River Laboratories, Wilmington, MA) were used. One prime (Week 0) and two booster (Week 3, 6) doses were administered to mice intramuscularly (I.M.) or transdermally (T.D.) using microneedles. Mice were intranasally (i.n.) challenged with A/Phillipines/2/82 (H3N2) (4x103 PFU) live influenza virus on week 12. Blood samples were obtained for detection of antibody titers every 3 weeks (Weeks 1, 4, 7 and 10). Animals were sacrificed at week 14 and T cell phenotypes were examined in the primary (bone marrow) and secondary lymphoid organs (spleen and lymph node). The whole lung tissue was isolated after challenge and homogenates were examined for determination of viral load.

Results: The microparticle yield and encapsulation efficiency was 92% and 84% respectivels, with a size of 1.85µm. The M2e VLP, M2e VLP MP and M2e VLP MP + MPL-A® + Alhydrogel® relulted in elevated levels of IgG, and IgG1 beginning at week 7, demonstrating that the M2e VLP is immunogenic. The adjuvant group showed increased levels of Th1 related subclass IgG2a compared to M2e VLP MP and M2e VLP formulations. Mice that were immunized with the M2e VLP MP and M2e VLP MP + MPL-A® + Alhydrogel® demonstrated high expression of CD4+ T cells in the spleen and the lymph node. The M2e VLP MP + MPL-A® + Alhydrogel® showed high levels of CD8+ cells in the lymph node. The lung viral titer was 10-fold lower in the M2e VLP MP + MPL-A® + Alhydrogel® vaccinated mice compared to M2e VLP and M2e VLP MP.

Conclusion: Since the current licensed vaccines against influenza are facing numerous challenges associated with production time, antigenic changes, route of administration, etc, we developed a universal flue vaccine with an extracellular domain matrix 2 protein virus-like particle (M2e VLP) micro particulate vaccine that is easy to formulate and is stable, immunogenic, safe and protective.

Translational Impact: Our universal Influenza VLP microparticulate vaccine could potentially serve as a feasible alternative to the currently available trivalent and quadrivalent influenza vaccines in humans since we use the M2e membrane protein, which is conserved in all strains of the disease. Furthermore, since the vaccine is administered through the microneedle route, it iwl also non-invasie and very stable.

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