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Evaluation of a matrix protein virus-like particle (m2e vlp) subunit vaccine for influenza

Kimberly Braz Gomes[1], **Sang-Moo Kang**[2] and **Martin J D'Souza**[3]
[1]McMaster University, Canada
[2]Georgia State University, USA
[3]Mercer University, USA

The purpose of this study was to investigate the efficacy and protection of the M2e VLP particulate vaccine administered transdermally in a pre-clinical mouse model for influenza. The M2e VLP was adsorbed onto Alhydrogel® and encapsulated into a polymer matrix with MPL-A®. 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 the AdminPatch® 1200 microneedle array. Mice were intranasally (i.n.) challenged with A/Phillipines/2/82 (H3N2) ($4x10^3$ PFU) live influenza virus on week 12. Blood samples were collected 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. The microparticle yield was found to be 92% and the encapsulation yield was around 84% with a size of approximately 1.85µm. The M2e VLP, M2e VLP MP and M2e VLP MP + MPL-A® + Alhydrogel® showed elevated levels of IgG beginning at week 7, demonstrating that the M2e VLP is immunogenic. IgG1 antibodies were elevated in the M2e VLP MP + MPL-A® + Alhydrogel® and there were also levels of IgG 1 present in the M2e VLP and inactivated H1N1 vaccinated groups. 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® had 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 and there were very low levels of effector $CD4^+$ and $CD8^+$ T cells present in the bone marrow. The viral titer was shown to be 10-fold lower in the M2e VLP MP + MPL-A® + Alhydrogel® vaccinated mice compared to M2e VLP and M2e VLP MP. Since the current licensed vaccines against influenza are facing numerous challenges associated with production time, antigenic changes, route of administration, etc, we developed 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.

Biography

Kimberly Braz Gomes has completed her BSc in Neuroscience at Brock University and did her PhD in Pharmaceutical Sciences at Mercer University. She is currently a Post-doctoral fellow at McMaster University.

Kimberly.Braz-Gomes@live.mercer.edu

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