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DEVELOPMENT OF AN ORAL PROTEIN SUBUNIT COVID-19 VACCINE TO INDUCE MUCOSAL AND SYSTEMIC IMMUNE RESPONSE

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It is widely recognized that mucosal immunization is the most efficient route of delivery to offer protective immunity. Oral administration can boost the economic value of vaccines, make needle-free delivery possible, and allow for safe and convenient self-administration. Despite these critical advantages, there are very few oral or nasal COVID-19 vaccine in development, and none on the market. The main challenge for an efficacious vaccine administered orally is the need for an efficient antigen delivery system into the mucosa. VaxForm has developed a technology that consists of co-adsorbing antigen(s) and a C-type lectin (CTL) receptor agonist to an aluminum delivery particle and encapsulating the vaccine with an enteric polymer to protect it from the stomach acidic environment and enhance stability. Once in the intestines, the protective polymer dissolves, and the CTL agonist targets the microfold (M) cells in the gut associated lymphoid tissues (GALT), allowing efficient delivery of the antigens adsorbed to aluminum particle. In this study, funded by NSF SBIR Phase I grant (#2031281), VaxForm developed an oral protein subunit COVID-19 vaccine using receptor binding domain (RBD) as the antigen target. The oral vaccine was developed as a liquid suspension as well as spray dried and freeze-dried powder versions. All three versions of the vaccine were stored at 60°C for 14 days to force degrade the vaccines, and immunogenicity in mice was compared to vaccines stored at 25°C. Figure 1 shows serum IgG and mucosal IgA (from intestinal lavage samples) titers normalized to untreated group. Results show that different immune response profiles were induced from the 3 types of vaccines. Liquid suspension vaccine resulted in a balanced serum IgG/mucosal IgA response, spray dried vaccine induced a strong mucosal response/no serum IgG, and freeze-dried vaccine a strong serum IgG and weak mucosal IgA. Three different particle distribution were also observed between the three vaccine presentations. Other studies have shown that particles less than 5 µm in diameter tend to result in a systemic response due to their propensity to disseminate to systemic lymphoid tissues, whereas particles larger than 5 µm induce a predominant mucosal IgA response as they remain in the intestinal mucosa for longer periods of time. Figure 2 shows the particle size distribution of the vaccines after exposure to simulated intestinal fluid: the spray dried vaccine’s particles were all larger than 5µm, which explains the high mucosal IgA response. The red distribution shows the liquid suspension particle distribution between 2 and 10 µm, with about 50% of particles below 5 µm and 50% above 5 µm, which explains the balanced mucosal IgA serum IgG detected in mice. And the blue distribution represents the freeze-dried vaccine, with a mean particle size of 3.5 µm and 60% of particles below 4 µm in freeze dried, which matches the high systemic/ serum IgG response detected in mice. Additionally, the 14 days at 60C storage did not reduce the immunogenicity of the liquid suspension, demonstrating an incredible stability profile. VaxForm’s oral vaccine strong antibody and stability profile, in addition to the many advantages that the oral platform technology brings, show great potential to contribute to the fight against the global pandemic.

Figure 1 – RBD specific serum IgG and mucosal IgA titers normalized to untreated group. N=10 mice per group.

Figure 2 – Particle size distribution of liquid suspension vaccine (red) vs spray dried (green) vs freeze dried (blue) by laser diffraction in µm.