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Michelle Lam M.S. Advisor(s): Thomas Postler Ph.D.

Co-author(s): -

Investigating Mucosal Immunity with Dual-Immunogen VSV-based Vaccines

The mucosal immune system serves as the body's first line of defense, utilizing secretory IgA, mucins, antimicrobial peptides, and cytokines to combat infection. Intranasal vaccines leverage this system to induce localized immune responses thereby reducing viral replication, preventing infection, and limiting transmission. This strategy is particularly relevant for mucosally transmitted pathogens like human immunodeficiency virus (HIV). A key question is whether immune responses generated in lung mucosa can disseminate protection to other mucosal sites with VSV-based vaccinations, which we explore in this study.

The VSV platform is highly immunogenic and adaptable, allowing for the expression of diverse antigens by replacing its glycoprotein (G) with those from other pathogens. Our research focuses on developing dual-immunogen VSV vectors that express a stabilized HIV envelope glycoprotein (Env) alongside a functional glycoprotein to enable viral infection. We are evaluating several VSV vector candidates incorporating glycoproteins from Lassa virus (LASV GPC), SARS-CoV-2 (SCV2 Spike), and Marburg virus (MARV GP), selected for their ability to facilitate mucosal infection and their proximity to human trials. Our studies include dual constructs combining LASV GPC and SCV2 Spike, alongside constructs expressing Env with or without a transmembrane domain addition (EnvG), which enhances stability and infectivity.

Using a hamster model, we aim to identify the most effective vector candidates capable of eliciting strong mucosal immune responses and protective immunity. This research advances our understanding of mucosal vaccine strategies and informs the development of novel vaccines against mucosally transmitted pathogens.