A NOVEL MUCOSAL HIV VACCINATION REGIMEN INVOLVING LIVE RECOMBINANT HUMAN RHINOVIRUS AND DNA VACCINES TO ELICIT PROTECTIVE HIV-SPECIFIC IMMUNITY

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**Background:** Human immunodeficiency virus (HIV)-1 has either killed (~39 million) or infected (~37 million) over 76 million people, and infection rates are rising worldwide. Thus, cost-effective vaccines that will elicit robust mucosal immunity are needed given that vast majority of HIV-1 transmissions occur via exposure of the genitoreal mucosa. Herein we report the efficacy of innovative vaccines pioneered in our laboratory to evoke T cell immunity to Gag and non-classical neutralizing antibodies (NAb) to Tat in mucosal and systemic compartments.

**Methods:** The vaccines used in this study include DNA vaccines encoding Gag and a cytolytic protein viz. perforin (PRF) (pVAX-Gag-PRF) or a secreted version of Tat (sTat) and IMX313 (pVAX-sTat-IMX313), and a cocktail of recombinant human rhinoviruses (HRV) encoding Gag and Tat (rHRV). PRF and IMX313 are strategically encoded in DNA to act as adjuvants. Female Balb/c mice (n=7 per group) were vaccinated with 2 IN doses (2 weeks apart, 5 X10\textsuperscript{6} TCID\textsubscript{50} per dose) of rHRV and then intradermally (ID) boosted for 2 weeks with 50 µg of pVAX-Gag-PRF and pVAX-sTat-IMX313. Subsequently, Gag- and Tat-specific immunity were analysed in mucosal (gut and vagina) and systemic (splenocytes and blood) compartments using various immunological assays. For protective efficacy studies, rHRV-DNA or control vaccinated mice were challenged intraperitoneally with EcoHIV (murine HIV challenge model). 7 days after the challenge viral loads in various EcoHIV replication sites were measured.

**Results:** rHRV-DNA vaccination significantly elevated Gag-specific T cell immunity and Tat-specific NAb in mucosal and systemic compartments which correlated with 10-fold reductions in EcoHIV viral loads in rHRV-DNA vaccinated mice compared to control mice.

**Conclusion:** These data provide the first evidence that a rHRV-DNA vaccination regimen has high potential for eliciting protective HIV-specific immunity and warrants further testing of the rHRV-DNA regimen in higher animal models.

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