PRE-CLINICAL EVALUATION OF AN INTRANASAL HIV VACCINE STRATEGY.

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Introduction: Pox viral vector-based HIV vaccines co-expressing IL-13Rα2 or IL-4R antagonist that transiently inhibit IL-4/IL-13 activity at the vaccination site have shown to recruit unique antigen presenting cells to the vaccination site, responsible for the induction of high avidity HIV-specific CD8 T cells with better protective efficacy in murine models. In the current study, the efficacy of these vaccines was evaluated in non-human primates (NHP).

Methods: Juvenile *Macaca nemestrina* were primed intranasally using a Teleflex mucosal atomization device with $2x10^8$ pfu recombinant fowl poxvirus co-expressing macaque IL-13Rα2 or IL-4R antagonist together with SIV gag/pol/env antigens and boosted intramuscularly with $2x10^8$ pfu recombinant Modified Vaccinia Ankara expressing the same adjuvants together with SIV gag/pol antigens. Another two groups were also vaccinated with the unadjuvanted HIV vaccines and the empty viral vectors. At different time intervals pre and post high dose intra-rectal SIVmac239 challenge, immunogenicity and protective efficacy were evaluated.

Results: The intranasal rFPV priming was highly successful. In the context of T cell immunity: i) highly poly-functional mucosal/systemic gag-specific CD84 and CD8 T cells were detected, ii) IL-13Rα2 and IL-4R antagonist vaccines induced broaden T cell responses to both gag and pol. The vaccines also induced good SIV-gag antibody responses and a single rFPV gag/pol/env intranasal prime generated excellent env-specific antibodies post challenge. Three out of fourteen macaques were fully protected (unadjuvanted and IL-4R antagonist vaccinated groups), and the remaining showed varying degrees of protection. Animals that received empty vector were not protected.

Conclusion: Complete protection was mainly associated with multi-functional CD4 and CD8 T cell immunity. Out of the two adjuvanted vaccines tested IL-4R antagonist adjuvanted vaccine induced superior responses. Our finding suggest that similar to what has been observed in murine models, the level of IL-13 in the milieu, plays an important role in regulating T and B cell immunity.

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