

Poster presentation

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PI9-46. Co-delivery of mucosal chemokine plasmids in a systemically delivered DNA vaccine elicits systemic and mucosal immune responses in mice and macaques

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Background

The induction of mucosal immunity is a crucial goal for HIV vaccines. DNA vaccines which are non-live/non-proliferating have had limited success in this area. Mucosal immune cell homing is in part controlled by a subset of chemokines (CCL27, CCL28 and CCL25). We hypothesized that a DNA vaccine encoding antigen and chemokine could induce mucosal immunity.

Methods

Mice were systemically co-immunized with pHIV-1gag/pol and chemokine adjuvants. Rhesus macaques (n = 5/group) were immunized intramuscularly with antigenic plasmids plus/minus each chemokine. For rhesus optimized CCL27, CCL25, and CCL28 plasmids, optimized/consensus macaque pol and sooty mangabey consensus gag/env plasmids were generated.

Results

Mice: Co-immunization with chemokines induced significant enhancement of HIV-1 specific CD8+ T cell IFN-gamma secretion in the periphery and TNF-alpha, IL-2 and IFN-gamma by gut lymphocytes. Co-immunization with mucosal chemokines augmented HIV-1-specific sIgA in sera/fecal samples. Similar immunogenicity data was

observed to Influenza A/PR8/34 hemagglutinin plasmid including responses that neutralized virus and protected mice from morbidity/mortality associated with lethal mucosal challenge. Macaque: In the periphery, we observed significant IFN-gamma in all groups (~6,000 SFU each). However intracellular cytokine staining on mucosal lymphocytes showed a trend toward an increase in CD8+T cells secreting TNF and IL-2 in CCL27 co-immunized macaques, levels greater than those observed in infected animals. Enhanced antigen-specific IgA was also detected in sera of chemokine-vaccinated macaques. A mucosal challenge is scheduled to determine if the functionality and phenotype of vaccine-induced immunity, either at the mucosa or periphery, is a driving determinant of protection.

Conclusion

The results of this study will be critical to the development of an effective vaccine against HIV. This is the first example of the use of mucosal chemokines to influence a DNA vaccine strategy, suggesting a novel approach for manipulation of vaccine-induced immune responses. This work is supported by NIH funding (HIVRAD).