Retrovirology

Poster presentation

P19-46. Co-delivery of mucosal chemokine plasmids in a systemically delivered DNA vaccine elicits systemic and mucosal immune responses in mice and macaques

KA Kraynyak*[1], MA Kutzler[2], B Pahar[3], A Sylvester[2], J Yan[1], D Carnathan[1], AS Khan[4], N Sardesai[4], Z Moldoveanu[5], J Mestecky[5], MR Betts[1], P Marx[3] and DB Weiner[1]

Address: [1]Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA, USA, [2]Drexel University College of Medicine, Philadelphia, PA, USA, [3]Tulane National Primate Research Center, Covington, LA, USA, [4]VGX Pharmaceuticals, The Woodlands, USA and [5]University of Alabama at Birmingham, Birmingham, AL USA

* Corresponding author

from AIDS Vaccine 2009
Paris, France. 19–22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P366 doi:10.1186/1742-4690-6-S3-P366

This abstract is available from: http://www.retrovirology.com/content/6/S3/P366

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 hemagglutanin 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).