

Poster presentation

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PI9-44. Priming with a DNA vaccine encoding HIV CD4+ T cell epitopes enhances responses against subsequent immunization with plasmid encoding Vif

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Background

Since none of the developed candidate vaccines against HIV has been effective, novel vaccine concepts are needed. Our group has identified conserved HIV CD4+ T cell epitopes binding promiscuously to multiple HLA-DR molecules, and frequently recognized by HIV-1-infected patients. A DNA vaccine encoding such epitopes (pVAX-HIVBr18) showed strong cellular responses in mice. An early CD8+ T cell response against Vif is associated with control of SIV infection in primates. A vaccine capable of stimulating both CD4+ and CD8+ T cells can be useful to establish an appropriate immune control of HIV. We aim to test whether preimmunization with pVAX-HIVBr18, which contains the CD4/CD8 Vif (144-158) epitope, can boost Vif-specific CD8+ T cell responses after immunization with a plasmid encoding Vif (pVAX-Vif).

Methods

Synthetic genes encoding either 18 HIV-1 CD4+ T cell epitopes or HIV-1 Vif were subcloned in the pVAX vector to obtain pVAX-HIVBr18 and pVAX-vif. BALB/c mice were immunized with pVAX-vif (3 doses) or preimmunized with pVAX-HIVBr18 before receiving pVAX-vif (2 doses) every 2 weeks. T cell responses were assessed by IFN-gamma ELISPOT, Cytometric Bead Array, intracellular cytokine staining and CFSE based proliferation assay.

Results

Immunization with pVAX-vif induced proliferation of CD4+ and CD8+ T cells against different pooled Vif pep-

tides. Preimmunization with pVAX-HIVBr18 enhanced the magnitude and breadth of the proliferative response of central and effector memory CD4+ and CD8+ T cells against Vif peptide pool 9, containing the homologous peptide, and, surprisingly, to Vif pools 2, 3 and 7, which did not contain the epitope. Moreover, preimmunization with pVAX-HIVBr18 also increased the number of CD4+ and CD8+ T cells producing TNF- α and IFN-gamma.

Conclusion

Our data suggest that preimmunization with a plasmid encoding CD4+ T cell epitopes induces proliferative and cytokine responses of CD4+ and CD8+ T cells to multiple Vif peptide pools, suggesting an epitope spreading mechanism.