Retrovirology

Poster presentation

P18-02. Peptide pulsed dendritic cells allows for induction of polyfunctional CD4+ T cell responses and help CD8+ T cell targeting subdominant CTL epitopes

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P311 doi:10.1186/1742-4690-6-S3-P311

This abstract is available from: http://www.retrovirology.com/content/6/S3/P311

Background

To target HIV-1 specific CTL epitopes that are subdominant in the context of natural infection we designed a peptide based vaccine in order to induce a balanced CD4+ and CD8+ cellular immune response. We believe that inducing CD4+ T cell responses would provide help and allow for responses against sub-dominant epitopes to come forward.

Methods

In a phase I/II therapeutic HIV-1 vaccine trial 12 treatment naïve HIV-1 infected Danish individuals received 1 × 10e7 autologous monocyte derived dendritic cells s.c. (week 0, 2, 4 and 8) pulsed with 10 different peptides, 7 CTL epitopes from conserved regions of HIV-1 and two HIV-1 derived and one universal T helper epitope. Novel T cell responses were evaluated by intracellular cytokine staining for IFN-γ, TNF-α and IL-2.

Results

This mode of vaccination generated robust polyfunctional vaccine specific CD4+ T cell responses sustained at the last evaluation, 6 months after the last immuniza-tion. Cytokine responses were dominated by TNF-α and IL-2 production, indicative of long-lived central memory cells. Moreover, in 12 out of 12 patient's vaccine specific CD8+ T cell responses were detected.

Conclusion

This suggests that this mode of vaccination, dendritic cells loaded with a combination of T helper and CTL epitope peptides, is a successful approach to target subdominant epitopes and the possibility to re-direct the immune response towards selected epitopes during chronic HIV-1 infection is an important proof of concept.