Retrovirology

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Oral presentation

S01-04 OA. Phenotypic analyses of CD8+ T cells that mediate virus inhibition from HIV-1 vaccinees and HIV-1+ virus controllers

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):O1 doi:10.1186/1742-4690-6-S3-O1

This abstract is available from: http://www.retrovirology.com/content/6/S3/O1

Background

CD8-mediated virus inhibition can be detected in HIV-1+ subjects controlling virus replication in the absence of ART. Characterizing the CD8+ T cells that mediate virus inhibition is important for determining the nature of CD8+ T cells that need to be elicited by an HIV-1 vaccine.

Methods

We used a 3-day CD8+ T cell mediated virus inhibition assay (CD8 VIA) to assess CD8+ function. Primary CD4+ enriched lymphocytes were infected with reporter viruses expressing transmitted/founder envelopes in the presence of serial dilutions of autologous CD8+ T cells. We examined activated CD8+ T cells from 22 HIV-1+ subjects (of which 15 were virus controllers (VC)), 37 HIV-1 vaccinees (DNA prime, rAd5 boost encoding HIV-1 Env and Gag-Pol) and 6 seronegative donors. Phenotypic analysis of HIV-1 specific CD8+ cells was determined by 13 color flow cytometry. Phenotypically-defined CD8+ T cell subsets from selected donors were sorted by flow cytometry and tested for virus suppression.

Results

VCs had robust antiviral activity against both transmitted/founder and NL4-3 enveloped viruses (1.43 +/- 0.67 log reduction). Among vaccinees, CD8 VIA correlated with HIV-1 specific CD107a expression; and weakly with IFN-gamma expression. No correlations were observed with CD8+ cell expression of IL-2, TNF-alpha, or MIP-1 beta. Virus inhibition by sorted cells was absent from naive CD8+ T cells; the predominant activity was from central and early effector memory populations.

Conclusion

CD8-mediated virus inhibition, as measured in a 3-day assay with early transmitted reporter viruses, was present in HIV-1+ subjects and vaccinees. Among HIV-1+ subjects, the activity was most robust in virus controllers. Virus suppression correlates most strongly with CD107a, and may come primarily from central memory populations. These data provide insight into the mechanisms of viral inhibition, and suggest that functional analyses of CD8+ T cell mediated virus inhibition could identify benchmarks for successful T-cell directed vaccine strategies.