Retrovirology

BioMed Central

Oral presentation

S04-06 OA. Polyvalent Gag-specific CD8 T-cells with enhanced functional properties are enriched in HIV-1 clade C infected individuals with lower viral loads

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):O48 doi:10.1186/1742-4690-6-S3-O48

This abstract is available from: http://www.retrovirology.com/content/6/S3/O48

Background

Gag-specific CD8 T-cell responses have repeatedly been associated with lower viremia. However, no functional mechanism has been determined thus far. By using an array of cellular assays we aimed to identify characteristics of CD8 T-cells, which are associated with enhanced antiviral control.

Methods

26 patients with broad (> 6) or narrow (< 1) gag responses assessed by IFN-γ Elispot were selected from 288 untreated HIV-1 clade C-infected South Africans. We controlled for disease progression and total numbers of HIV specific CD8 T-cells. Infected or uninfected CD4 T-cells from both groups were co-cultured with autologous unstimulated CD8 T-cells. HIV-1 replication was measured by p24 ELISA. Phenotypes and cytokine profiles were assessed by flow. Proliferation was measured by CFSE dilution.

Results

Viral load was lower in individuals that generate broad gag responses compared to persons with few or no Gag-specific responses. CD8 T-cells from high gag responders suppressed HIV-1 replication more potently than those from low gag responders (mean Log10 inhibition: 1.38 vs 0.5, $p < 0.004$). Furthermore, CD8 T-cells from high gag responders secreted a more 2 and 3- functional cytokine profile than low gag responders, who mainly exhibited mono-functional CD8 T-cells. The ability to respond polyfunctionally was significantly correlated with the ability to inhibit viral replication *in vitro*. Furthermore, CD8 T-cells from high gag responders showed a stronger proliferative capacity. However, no difference in the maturation status of HIV-specific CD8 T-cells was observed.

Conclusion

Subjects who target more epitopes in gag exhibit lower viral loads than subjects who target this protein less. This enhanced viral control is associated with an elevated CD8 T-cell inhibitory capacity, enhanced proliferation, polyfunctional cytokine secretion, but no difference in the maturation status of CD8 T-cells. This data indicates that it is not the phenotype but the specificity and functional capacity that are indicative of effective antiviral CD8 T-cell function.