P16-11. HLA-B57/5801 induces preferential CD27 expression on HIV-Gag but not Nef specific central memory CD8+T cells controlling HIV

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Retrovirology

BioMed Central

Poster presentation

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P240 doi:10.1186/1742-4690-6-S3-P240

This abstract is available from: http://www.retrovirology.com/content/6/S3/P240

Background

The HLA-B57/5801 allele and characteristics of HIV-specific CD8+T cells play a key role in controlling HIV. To gain novel insight into the nature of the protective effect mediated by HIV-specific CD8+T cells in HLA-B57/5801+ individuals, we compared the frequency, cytokine production, differentiation, and functional avidity of HIV-specific CD8+T cells in B57/5801+ and B57/5801- nonprogressors.

Methods

This study investigated in 53 untreated nonprogressors whether CD8+T cells specific for Gag, Nef and RT differed in their relations to plasma HIV-RNA and cell-associated HIV-DNA loads. Twenty-two patients, 11 HLA-B57/5801+ and 11 B57/5801-, with simultaneous positive responses to Gag and Nef detected by ELISpot assays, were selected for analyzing whether antigen specificity and HLA-restriction trigger CD8+T cell profiles that could explain the association between HLA-B57/5801 and virus control.

Results

The frequency of Gag-specific CD8+T cells negatively correlated with HIV-DNA loads (r = -0.395, p = 0.004), while that of Nef- and RT-specific cells did not. None of these frequencies correlated with plasma HIV-RNA levels. The HIV-Gag and Nef-specific CD8+T cells did not differ for IL-2 production in two HLA groups. In B57/5801+ group, the IFN-γ-producing Gag-specific central memory (CD45RA-CCR7+) CD8+T cells showed a significantly higher proportion of CD27+ cells than their Nef-specific counterparts (p = 0.007). This differentiation pattern was not observed in B57/5801- individuals. These distinct profiles were not explained by the functional avidity against Gag or Nef epitopes. The percentage of CD27 expression on Gag-specific IFN-γ+TCM CD8+T cells negatively correlated with HIV-DNA in the B57/5801+ group (r = -0.683, p = 0.042) but not in the B57/5801- group. The same subset specific for Nef was not correlated with HIV burden whatever the HLA group considered.

Conclusion

Our findings indicate that in HLA-B57/5801+ individuals HIV-Gag induces a preferential CD27+ central-memory differentiation profile distinct from that caused by Nef and that this profile may contribute to the protective effect of Gag-specific CD8+T cells in HLA-B57/5801+ nonprogressors.