

Poster presentation

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## PI6-11. HLA-B57/5801 induces preferential CD27 expression on HIV-Gag but not Nef specific central memory CD8<sup>+</sup>T cells controlling HIV

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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>

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### Background

The HLA-B57/5801 allele and characteristics of HIV-specific CD8<sup>+</sup>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<sup>+</sup>T cells in HLA-B57/5801<sup>+</sup> individuals, we compared the frequency, cytokine production, differentiation, and functional avidity of HIV-specific CD8<sup>+</sup>T cells in B57/5801<sup>+</sup> and B57/5801<sup>-</sup> nonprogressors.

### Methods

This study investigated in 53 untreated nonprogressors whether CD8<sup>+</sup>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<sup>+</sup> and 11 B57/5801<sup>-</sup>, with simultaneous positive responses to Gag and Nef detected by ELISpot assays, were selected for analyzing whether antigen specificity and HLA-restriction trigger CD8<sup>+</sup>T cell profiles that could explain the association between HLA-B57/5801 and virus control.

### Results

The frequency of Gag-specific CD8<sup>+</sup>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<sup>+</sup>T cells did not differ for IL-2 production in two HLA groups. In B57/5801<sup>+</sup> group, the IFN- $\gamma$ -producing Gag-specific central memory (CD45RA<sup>-</sup>CCR7<sup>+</sup>) CD8<sup>+</sup>T cells showed a significantly higher proportion of CD27<sup>+</sup> cells than their Nef-specific counterparts ( $p = 0.007$ ). This differentiation pattern was not observed in B57/5801<sup>-</sup> 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- $\gamma$ <sup>+</sup>TCM CD8<sup>+</sup>T cells negatively correlated with HIV-DNA in the B57/5801<sup>+</sup> group ( $r = -0.683$ ,  $p = 0.042$ ) but not in the B57/5801<sup>-</sup> 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<sup>+</sup> individuals HIV-Gag induces a preferential CD27<sup>+</sup> central-memory differentiation profile distinct from that caused by Nef and that this profile may contribute to the protective effect of Gag-specific CD8<sup>+</sup>T cells in HLA-B57/5801<sup>+</sup> nonprogressors.