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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⁺T cells controlling HIV

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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.