Retrovirology

Oral presentation

Induction of HIV-specific T-cell responses by gag

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Objectives

In order to suppress HIV and delay evolution to AIDS, antigen-loaded DC might be useful to boost and broaden HIV-1-specific T-cell responses, which are dysfunctional in HIV infection.

Methods

DC (from 15 treatment-naïve and 15 HAART-treated HIV-1-infected patients) were electroporated with codon-optimized mRNA encoding consensus HxB-2 Gag. These DC were co-cultured for 1 week with autologous peripheral blood leucocytes. Expansion of specific T-cells was measured by ELISPOT, using a pool of overlapping peptides, spanning HxB-2 Gag.

Results

Expansion of specific T cells producing IFN-γ, IL-2 and perforin was seen. Comparing the response between 12 treated and 12 naïve patients, matched in absolute CD4+ T-cell count, showed that the response was higher in treated subjects for IFN-γ and IL-2 but not for perforin. HxB-2 peptides induced IFN-γ in CD4+ and CD8+ T-cell subsets purified following coculture, IL-2 was only secreted by CD4+ T-cells and perforin was dominantly secreted by CD8+ T-cells. Remarkably, the perforin response in naïve persons was negatively correlated with the absolute CD4+ and CD8+ T-cell count. The nadir CD4+ T-cell count in treated subjects was positively correlated with the IL-2 response and negatively correlated with the perforin response.

Conclusion

HxB-2 gag mRNA-transfected DC from treated and naïve subjects have the capacity to induce secondary T-cell responses. These results of this and another study, where we showed that T-cells from naïve HIV-infected subjects can be triggered by DC electroporated with autologous gag mRNA (Blood 2006;107:1818-27), open the perspective for a DC immunotherapy of HIV disease.