P16-29. HIV Nef-specific T cells: Th1/CTL, Th2 and Th17 responses

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Retrovirology

Poster presentation

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Background

Identification of promiscuous antigenic regions is crucial for the design of an epitope-based vaccine. Still, the quality of the responses has been under estimated in most cases when only IFN-γ is used to measure anti-HIV cellular immunity. Luminex multiplexing system allows the identification of T cell responses characteristic of T cell subtypes through their secretion of not only Th1/CTL but other important sets of cytokines, including IL-5, Il-10, Il-13, IL-21 and IL-17.

Methods

We have studied the full spectrum of Nef-specific T cell memory recall responses in chronically infected HIV patients on HAART expressing a broad spectrum of HLA types. Briefly, short-term PBMC cultures were stimulated with 15-mer overlapping peptides from Nef in the presence of IL-2, conditions which favor expansion of antigen-specific T cells. Luminex analysis of the culture supernatants were used for simultaneous identification of a diverse array of peptide-specific cytokine profiles.

Results

We observed strong Th1/CTL responses against two previously described highly immunogenic regions in the central Nef sequence: Nef 67–101 and Nef 103–148. All of the 16 patients that we analyzed responded to peptides from one or both regions by secreting IFN-γ and TNF-α. However, Th2 responses (IL-5, IL-13) against peptides covering the Nef 67–97 were observed in half of the patients. This region is also able to stimulate Th1/CTL specific cells. Interestingly, we also observed high levels of IL-17 secretion in 7 out of 16 patients in response to at least one peptide, yet no specific region in the protein could be associated with IL-17 responses.

Conclusion

In order to design new vaccines we need a deep understanding of both the quantity and quality of the responses induced by any antigen. A more complete study of T cell responses to HIV antigens is essential for the selection of epitopes that should be included in future trials.