P16-45. High avidity CD4+ T cell response directed to an immunodominant Gag epitope in HIV controllers: an ANRS EP36 study

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Poster presentation

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Background

Emerging evidence indicates that HIV controllers contain HIV-1 replication through very active cellular immune responses, though how such responses can persist over time without exhaustion or waning is not yet understood. To investigate the nature of memory CD4+ T cells responsible for sustained anti-HIV responses, we characterized their capacity to generate primary cell lines specific for immunodominant Gag peptides.

Methods

CD4+ T cell lines were derived from patients who spontaneously controlled HIV replication (HIV controller group, n = 17) and patients who achieved viral control following successful antiretroviral therapy (HAART group, n = 20). Cell lines were compared for growth kinetics, Vβ repertoire, and sensitivity to antigen.

Results

Specific cell lines were obtained at high rate for both HIV controllers (16/17) and efficiently treated patients (19/20) in response to the immunodominant Gag293 peptide. However, lines from controllers showed faster growth kinetics than those of treated patients. After normalizing for growth rates, IFN-γ responses directed against the immunodominant Gag293 peptide showed higher functional avidity in HIV controllers, while responses to Gag161, Gag263, or CMV peptides did not differ between groups. Characterization of Gag293-specific CD4+ T cells through MHC class II tetramer labeling revealed a diverse Vβ repertoire, suggesting that multiple clones contributed to the high avidity CD4+ T cell population in HIV controllers. The high functional avidity of the Gag293-specific response could be explained, at least in part, by a high avidity interaction between the TCR and the peptide-MHC complex, as demonstrated by class II tetramer binding.

Conclusion

This study provides evidence that HIV controllers harbor a pool of high avidity memory CD4+ T cell precursors directed against an immunodominant Gag peptide. The capacity to mount a rapid CD4 response in the presence of minimal amounts of Gag antigen helps explain how HIV controllers maintain an active antiviral response in the face of very low viremia.