Retrovirology

Poster presentation

P16-07. HLA-B1302 is associated with viral control in clade CRF01_AE HIV-1 infection in Thailand

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Background

Little is known about the role of different HLA class I alleles in the control of HIV-1 CRF01_AE infections, which dominate in South and Southeast Asia, or the CD8+ T-cell responses that might be mediating this effect.

Methods

We studied a cohort of 250 chronically HIV-1 infected, HAART naïve individuals in Bangkok, Thailand. Viral load and CD4 data were collected for all individuals as well as 4-digit HLA typing and viral sequences. A comprehensive screen of CD8+ T-cell responses was conducted using an IFN-gamma ELISpot assay and overlapping clade AE-specific peptides (OLP) spanning the entire HIV-1 proteome.

Results

Of HLA alleles previously associated with control, namely B5701, B27, B51 and B1302, only HLA-B1302 was associated with significantly lower viral loads (n = 14, p = 0.029, q = 0.115) and with HIV-1 'controllers' (VL<2000/ml; p = 0.016). In examining which CD8 responses might be mediating this protective effect, we found that the majority of frequently targeted OLPs in HLA-B1302+ subjects were located in Gag and Pol (7 of top 9 responses; avg. 753 spot forming cells (SFC/106 PBMC). In addition, we found frequent (avg. 58% recognition) and strong (avg. 872 SFC) responses against 3 of 6 previously described clade C HLA-B1302 epitopes in Gag and Pol (Gag-VV9, Pol-GI9, and Gag-RI9), versus infrequent (avg. 12% recognition) and weak (avg. 316 SFC) responses to the other described epitopes in Pol, Nef and Gag (Pol-RI10, Nef-GI11, Gag-GI11). In analyzing for CTL escape mutations in the 3 targeted epitopes or OLPs in Gag, we found no evidence of viral escape.

Conclusion

HLA-B1302 is correlated with virus control in CRF01_AE infection and appears to predominantly target highly conserved regions of Gag and Pol. These data extend the observation that maintenance of CD8+ T-cell responses against highly conserved regions of HIV may also be critical to long-term control of CRF01_AE.