Retrovirology

Poster presentation

P16-04. Cryptic CTL epitopes derived from antisense transcription are frequently recognized in HIV-1 infection

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Background

Of the six potential reading frames encoded by a gene, cryptic epitopes are derived from the translation of any of the five alternate reading frames (ARF) including two sense and three antisense reading frames. The latter has not been evaluated as a potential source of CTL epitopes in HIV infection.

Methods

Using MHC-I associated HIV-1 polymorphisms in gag, pol and nef sequences from 730 South Africans with chronic infection; over 957 potential ARF epitopes were predicted. Of these, 25 potential cryptic epitopes (CE) were selected for testing using the standard overnight IFN-γ ELISpot assay in PBMC from 61 HIV clade B infected US patients and 14 seronegative controls. In a subset of HIV infected patients: chronic (N = 6) and acute (N = 9), the polyfunctionality of the CE responses was measured using an ICS assay. CTL clones were derived for three antisense cryptic pol epitopes by limiting dilution cloning. The CD8 clones were characterized using 51Cr release and ICS assay.

Results

Pol is highly enriched in potential ARF epitopes predicted by HLA-I associations ($p < 1.1 \times 10–15$); with the majority of these derived from antisense transcripts ($p = 0.002$). CE responses were were readily detected by IFN-γ ELISpot in acute and chronically HIV infected patients (range = 50–250 SFC/106 PBMC). The CD8 T-cell CE specific responses elicited IFN-γ, TNF-α, CD107, and perforin as measured in an ICS assay. Three pol antisense derived CD8 clones specific for HLA-A*3002 AL9, HLA-A*0205 SL10 and HLA-Cw*0702 were lytic to HLA matched CE pulsed BLCL targets in 51Cr release assay and did not cross react with known conventional epitopes.

Conclusion

This data demonstrates the existence of a novel repertoire of HIV-1 specific CTL that are common in HIV-1 infection. CE responses can therefore be exploited as targets to increase the breadth of T-cell based HIV vaccines.