Retrovirology

Poster presentation

P16-41. Evidence for in vivo immune selection pressure exerted by HLA class I restricted CTL responses to anti-sense encoded HIV sequences

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Background

Past studies have suggested that certain portions of the integrated HIV-1 proviral genome can be transcribed in the anti-sense direction, resulting in novel viral protein products that may provide alternative targets for the host anti-viral immune response. Little is known whether immune responses exist against antisense HIV peptides, whether they can recognize HIV infected cells and whether CTL-driven escape mutations within antisense peptides may be detectable on a population level.

Methods

Anti-sense sequences with potential start codons (Methionine) that preceded well-conserved genome sequences of at least 50 nucleotide triplets without stop codon were identified in 261 aligned HIV whole-genome sequences. Plasma HIV gag, pol and nef sequences from >500 treatment-naive, chronic infected patients were analyzed for HLA class I allele-specific viral polymorphisms in all three possible reading frames in the anti-sense direction. A maximal false-discovery rate of 20% (q value < 0.2) was applied to correct for multiple tests. Polymorphisms in the anti-sense direction that affected the original coding sequence were excluded from study.

Results

Five potential anti-sense encoded proteins, including the previously described HIV anti-sense protein (ASP) were identified. Each putative protein sequence was synthesized as overlapping peptide set and was targeted by at least 2 individuals (range 2–22) of 40 HIV infected subjects tested. HLA-footprint analyses revealed 67 HLA-associated imprints (37 gag, 6 nef, 34 pol). For each imprint, the predicted epitopes were tested in individuals expressing the appropriate HLA allele. Several frequently-targeted antisense epitopes were identified.

Conclusion

CTL responses targeting anti-sense derived epitopes in HIV may be relatively common and may have an impact on viral evolution at the population level. Thus, T cell specificities to anti-sense encoded epitopes may be a biologically relevant mechanism contributing to immune control of HIV and may represent interesting vaccine immunogen candidates.