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Poster presentation

P17-28 LB. The antiviral efficacy of HIV-specific CD8+ T-cells to a conserved epitope is heavily dependent on the infecting HIV-1 isolate

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Background

The greatest challenge to developing an effective T-cell based vaccine against HIV-1 is its high genetic variability. We hypothesised that efficient CTL antiviral activity is not only dependent on conserved epitopes but is also heavily modulated by the infecting HIV strain, with virus specific polymorphisms altering the efficiency of antigen processing and presentation.

Methods

CTL Lysis Assays, ELISPOT assay, Live Virus ELISPOT (LVE), Viral Suppression Assay (VSA), Intracellular Antigen Processing Inhibition Assay (IAPIA) and Proteasomal Digestion Assay (PDA) were used.

Results

We examined whether an invariant HLA-B8 restricted Nef90-97 epitope FL8 shared between five high titre viruses and eight recombinant vaccinia viruses expressing Nef from different viral isolates (clades A-H) could activate antiviral activity in FL8-specific cytotoxic T-lymphocytes (CTL). Surprisingly, despite epitope conservation, we found that CTL antiviral efficacy is heavily dependent on the infecting viral strain. Only a small proportion of HIV strains tested were correctly processed, whilst 77% were impaired or abolished. This occurred independently of clade-grouping and was associated with virus-specific polymorphisms in the epitope flanking region altering patterns of immunoproteasomal cleavage, to increase or inhibit epitope generation.

Conclusion

we demonstrate that CTL antiviral efficacy to this conserved immunodominant epitope is impaired in a strikingly high proportion of viral isolates. These findings have implications for evaluating the antiviral efficacy of dominant T-cell responses in patients and the effectiveness of vaccine-induced T-cells.