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HLA-B molecules target more conserved regions of HIV-1 proteome

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Background: HLA-B alleles of HIV-infected individuals have been shown to have a major impact on their rate of progression towards AIDS, and the T-cell responses they restrict are immunodominant.

Objective: We sought to identify if the association of HLA-B alleles with rate of progression towards AIDS is due to targeting of more restricted and thus more conserved regions of the HIV-1 proteome.

Methods: Each residue of the HIV-1 consensus subtype B sequence was coded according to the presence/absence of an epitope, using the compiled epitope data available in the HIV-LANL Immunology database. The Shannon entropy for each HXB2 position was calculated using pre-aligned HIV-1 clade B sequences, as a measure of its degree of conservation. We then compared the entropy of empty *versus* epitope-containing positions, and HLA-B *versus* HLA-A restricted-positions.

Results: Positions containing $CD8^+$ epitopes were significantly more conserved than corresponding empty positions. Moreover, residues targeted by HLA-B alleles in the HIV-1 proteome were significantly more conserved than the ones targeted by A alleles. Analysing a recent dataset by Wang et al [1], we found that B epitope regions contain significantly more escape mutations and reversions, which might be the reason why we find them to be more conserved.

Conclusions: Our results suggest that epitopes in HIV-1 targeted by HLA-B alleles lie in more constrained regions of its proteins, in which mutations might have a higher fitness cost and tend to revert. Consequently, HLA-B-restricted cytotoxic T-lymphocyte (CTL) responses may persist longer. This may be one of the factors contributing to the immunodominance and impact of HLA-B-restricted CTL responses on disease progression.

Keywords: Human immunodeficiency virus, HLA-A, HLA-B, Cytotoxic T lymphocyte, viral mutation