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S011-06 OA. HIV specific T cell responses and response patterns associated with viral control independent of classical non-progessor HLA class I alleles

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Background

Although specific HLA alleles and single epitope-specific CTL responses have been implicated in mediating effective control of viral replication, effective HIV vaccine design will depend on broader assessments of the cellular immunity that overcome host genetic limitations and consider the entire viral proteome.

Methods

Here, 223 HIV clade B and 631 clade C infected subjects in Lima, Peru and Durban South Africa were tested for responses to a set of 410 overlapping peptides (OLP) spanning the entire HIV protein sequence. A cohort of 50 individuals in Barcelona Spain was included to confirm the clade B findings in the Peruvian clade B cohort. Median viral loads between OLP-non-responders and OLP-responders were compared and defined as the OLP-specific protective ratio (PR).

Results

In both cohorts, negative correlations between this PR and the entropy of the OLP sequence were observed, suggesting that responses towards conserved portion of the viral genome mediate superior viral control. The number of responses to OLP with elevated PR values was cumulatively related to reduced viral loads, indicating that multiple responses take part in *in vivo* viral control. Individuals responding to OLP with highest PR values showed a broad HLA class I allele heterogeneity, indicating that beneficial responses were not limited to few HLA alleles previously associated with relative *in vivo* control of HIV. In fact, T cell response patterns across the entire set of tested OLP, more so than individuals' HLA types, were predictive of HIV viral loads. These findings were confirmed in a second clade B infection cohort in Spain, again demonstrating the largely HLA-independent relative protection of these responses.

Conclusion

Together, the data are in strong support of inclusion of conserved regions of the viral proteome in vaccine design and identify sequence candidates for a minimalistic, yet still largely HLA-independent HIV vaccine immunogen approach.