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Poster presentation

P17-24. Interfering overlapping epitopes contribute to the subdominance of an HLA-A2-restricted HIV Gag-specific epitope

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Background

Recapitulating immunodominant A2-restricted HIV-specific CTLs that do not suppress virus *in vivo* is unlikely to be an effective vaccine strategy.

Methods

To detect novel subdominant determinants in HIV-1 Gag, we primed CD8+ T cells from eight seronegative donors with autologous dendritic cells transduced to express Gag. T cells were re-stimulated weekly with monocytes pulsed with 123 15-mer overlapping peptides (OLPs) spanning Gag. Responses were identified with OLP matrix pools followed by interrogation at the single OLP level in responsive pools using IFN-γ ELISPOT assays.

Results

One OLP (Gag145-159) was recognized by all donors. Of note, this reactivity predominated in five of eight T cell cultures. Fine mapping with progressively truncated peptides revealed three overlapping epitopes: RTLNAWVKV (RV9), RTLNAWVKVV (RV10) and TLNAWVKVV (TV9). TV9 is a known epitope that is rarely recognized *in vivo*. In contrast, RV9 and RV10 are novel. Although the latter bound with lower affinities to HLA-A2 than TV9, RV9- and RV10-cultures were readily generated. RV9- and RV10-T cells were cytotoxic, secreting cytokines and suppressive of HIV replication *in vitro*.

Conclusion

In sum, we report two novel naturally processed and presented epitopes in HIV p24 that are recognized by pre-infection T cell repertoires. Further studies are needed to explain why these reactivities are rare during infections and more importantly, whether this conserved region of the HIV proteome has value as a prophylactic vaccine for A2 individuals.