

Oral presentation

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## OA06-05. Adaptation of HIV-1 to the human immune system at the population level is driven by protective HLA-B alleles

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### Background

HIV undergoes extensive within-host adaptation to HIV-specific Cytotoxic T Lymphocyte (CTL) responses. However, the full extent and importance of CTL escape mutations in driving HIV evolution at the population level remains to be established.

### Methods

We included 27 individuals from the Amsterdam Cohort Studies on HIV infection and AIDS with a known seroconversion date in 1985 or 2005/06 (12 and 15 individuals, respectively), of which HIV sequences were derived within a year after seroconversion. CTL epitopes were predicted using a proteasomal cleavage/TAP transport/MHC class I combined predictor. HLA-binding epitopes from the proteins P17, P24, Nef, Protease and RT were predicted for 5 common HLA-A and 3 common HLA-B alleles, as well as for HLA-B27 and HLA-B57, the HLA-B alleles most strongly associated with slow progression to AIDS. To avoid the possibility that observed CTL escape mutations were due to within-host evolution rather than adaptation at the population level, individuals expressing the particular HLA allele under investigation were excluded from the analyses.

### Results

HIV strains isolated from recent seroconvertors were found to contain significantly less 9-mers predicted to

bind to the 5 HLA-B alleles under investigation compared to historical HIV strains, which was not observed for the 5 HLA-A alleles. Remarkably, the reduction in the number of CTL epitopes during the epidemic was not due to adaptation to the most common HLA-B alleles, but instead to the alleles associated with slow disease progression, HLA-B27 and B57.

### Conclusion

These data show that, over the past 20 years, HIV has adapted to the human immune system by decreasing the number of potential CTL epitopes presented via HLA-B, but not HLA-A, alleles, and that such adaptations can become fixed in the population. Adaptation was not related to the population frequency of the HLA alleles, but instead seemed driven by the immune selection pressure of the HLA alleles.