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OA06-03. Dynamics of CTL epitope escape and reversion in an African subtype C cohort

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Background

HIV immune escape follows a predictable mutational path in response to the HLA alleles carried by an individual. The kinetics of CTL epitope escape and reversion in subtype B HIV-1 infected individuals have recently been reported, however, the inferences drawn from them were limited by the absence of information about the transmitted sequence. To address these issues, we examined Gag, Pol and Nef sequences in both partners of 148 epidemiologically-linked transmission pairs from an African subtype C cohort.

Methods

Cohabiting HIV-1 discordant heterosexual couples from Lusaka, Zambia were followed longitudinally. Despite counseling and condom provision, 7% of uninfected partners became infected each year. At this time and at three-month follow-up intervals, blood and PBMC samples were collected from both the donor (D) and recipient (LR). The *gag*, *pol* and *nef* genes were amplified and sequenced from virus in plasma obtained from both partners. CTL epitopes were identified using previously published HLA-linked polymorphisms.

Results

Analyses of the viruses in the linked transmission pair recipients indicated that a surprising fraction of those transmitted had polymorphisms relevant for the HLA of the LR. Specifically, 29% of LR had viruses with escaped Gag epitopes at the time of seroconversion and these escaped epitopes were present in the D virus at the time of transmission. Thus, we find that Gag escape occurs more slowly than previously reported, with only 5–15% of Gag epitopes exhibiting *de novo* escape within the first year, and that a majority of HLA-linked polymorphisms at one year were transmitted from the donor.

Conclusion

The study of epidemiologically-linked transmission pairs demonstrates the high rate of transmission of escaped epitopes and that this directly impacts the calculated rates of escape, which could not be accounted for in previous studies. The potential for these non-donor driven mutations to impact viral pathogenesis is under investigation.