

ORAL ABSTRACT SESSION 04: ACUTE INFECTION / VIRAL DIVERSITY

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HIV-1 acute infection: evidence of selection?

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Background: Characterizing HIV-1 populations in acute infection is critical to help devise HIV-1 vaccines.

Methods: We sequenced near-full-length genome (nflg) from 3-12 time points during the first year of HIV-1 infection of 11 individuals.

Results: HIV-1 subtype B evolution was primarily stochastic before signs of adaptive selection emerged about five weeks post-infection. Nonetheless, several findings suggested that selective processes may play a role at transmission or in acute infection. Using additional data, we found that 75% of homosexual transmissions of HIV-1 were established by a single lineage. Examining four transmission pairs, we noted that the restriction to a single founder was not due to a lack of variation in transmitter viruses, suggesting that the mucosal barrier impedes the establishment of infection by multiple variants. Additionally, although one would expect that sequences in the seroconverter would correspond to the most frequent variant in the transmitter, when the transmitter was in chronic infection (three pairs) we saw that rare variants established infection, leaving open the possibility that selection may affect the outgrowth of particular variants. When comparing mean pairwise nucleotide diversity across nflg, we observed a slight dip in nucleotide diversity that temporally overlapped with peak viremia. Interestingly, the dip in diversity paralleled a dip in the mean number of APOBEC-specific mutations per nflg. This suggests that the sequences found at the earliest time points may have been relatively enriched with APOBEC-induced mutations (yet not hypermutated), and that the viral population may have subsequently undergone a clonal purification related to these mutations.

Conclusion: Neither diversifying nor directional selection was detected in acute infection. Thus, it appears unlikely that the founder strain has adapted rapidly to its new host. Yet, perplexing evidence of selective pressure in acute infection warrant further evaluation of the selective forces governing the transition from a localized to a systemic infection.