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Poster presentation

P04-43. Neutralizing antibody responses against conformational envelope epitopes in early HIV-1 infection

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Background

Identification of the transmitted/founder virus in HIV-1 infection allows a unique opportunity to explore the earliest processes of immune pressure and escape. Through single genome amplification (SGA), we can identify the transmitted envelope (env), characterize the diversity of plasma viral quasispecies at subsequent time points, and characterize neutralizing antibody (Nab) responses.

Methods

SGA of HIV-1 plasma viral RNA from CHAVI subjects 040 (CH040) and 077 (CH077) was performed. The transmitted env and site-directed mutants representing the dominant mutations occurring over the first year of infection were cloned. Pseudotyped viruses were generated and neutralization susceptibility to autologous plasma was tested. Adsorption assays using linear peptides and conformationally intact gp120 and gp140 Env monomers were performed.

Results

In CH040, a single amino acid (AA) mutation arising in V1 by week 12 post-infection conferred complete escape from plasma Nab. A two AA mutation at the base of V3 arising at week 24 also conferred escape from week 12 and week 24 plasma Nab pressure. Neither linear V1 peptides nor conformationally intact Env monomers were able to adsorb neutralizing antibody. In CH077, mutations in both V2 and C2 cause escape from the plasma Nab response at week 24. Linear V2 peptides were not able to adsorb away neutralization.

Conclusion

SGA allowed determination of the transmitted virus and subsequent variants and enabled detailed analysis of early Nab epitopes and viral escape pathways. In CH040, V1 and V3 mutations each confer total escape from autologous plasma Nab. This early Nab likely recognizes a conformational epitope involving protomer-protomer interaction since the autologous monomeric gp120 adsorbed b12 Nab activity but not the Nab in CH040 plasma. Similarly, in CH077, we observe that the earliest Nab likely recognizes a conformational epitope involving V2 and C2. Elicitation of Nab against conformational epitopes may be a common theme in early HIV-1 infection.