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Poster presentation



# P20-10. Differences in patterns of Gag-induced immunogenetic pressure occur between clades A and D chronic HIV-1 infection in a Ugandan population

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## Background

We previously reported slow HIV-1 disease progression in this population to be associated with the inherent host HLA B allele-mediated ability to induce broader Gag T-cell responses and faster disease progression to be more associated with clade D than A. Since Gag escape mutations often reduce viral fitness leading to significant reduction in virus replication, in this study, we evaluated the immunogenetic characteristics of clades A and D-associated escape mutations that could be harnessed for vaccine design.

## Methods

The HIV-1 gag gene was sequenced to determine genetic variability in 55 HIV-1 chronically infected, ART-naive adults previously screened for Gag T-cell responses. The proportion of individuals in which Gag-induced immune escape occurred was determined in 46 individuals that had sequence data. The proportion of B57/5801-driven substitutions: A→P in p17 AISPRTLNAW and T242N in p24 TSTLQEQIAW (TW10) both known to confer protection in early infection; and substitution A163G in p24 KAFSPEVIPMF (KF11) known to confer protection in chronic infection was correlated with the infecting gag clade.

## Results

Clades A1, D, and inter-subtype recombinants A1/C, A1/D occurred at frequencies 43%, 52%, 2.2% and 2.2%, (n = 46), respectively. Substitution A→P occurred in 3/41 (1 vs.2), A1 and D respectively; T242N occurred in 5/41 (1 vs. 1 vs. 3), A1, A1/C and D, respectively. Immununogenetic substitution A163G in the Gag KF11 epitope, known to confer protection in chronic HIV-1 infection, was absent in the two recombinants, but occurred in 11/44 (11/20 clade A vs. 0/24 clade D); p = 0.00012, Fisher's Exact.

## Conclusion

These data suggest preferential, clade A-associated, immunogenetic selection of a dominant Gag escape mutation known to have an impact on virus replication in chronic HIV-1 disease; this may partly account for the differential disease progression we have observed in clade A and D infection, this is also relevant to HIV vaccine development.