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Poster presentation

P16-03. Persistence of robust cross-reactive group M consensus T-cell responses in a chronic HIV-1 clade A1 and D-infected Ugandan population

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Background

HIV-1 group-M exhibits extraordinary genetic variation, cross-reactivity of immunogens based on consensus clades could be continuously diminishing as the AIDS epidemic progresses. Characterisation of cross-reactive T-cell responses to more central group M consensus peptides in this multi-clade population has not been performed; and could be pertinent for global vaccine

Methods

Fifty, randomly selected, HIV-1 chronically infected, ART-naïve, Ugandan adults with CD4 ≥ 350 cells/μl were screened for consensus group-M Gag and Nef-induced IFN-γ using ELISpot. Gag sequence diversity was evaluated and correlated with IFN-γ.

Results

Clades A1, D, and inter-subtype recombinants A1/C, A1/D occurred at frequencies 44%, 51%, 2.4% and 2.4%, (n = 41), respectively. Infecting gag sequences highly diverged from consensus group-M (median 9.2: inter-quartile range (IQR) 8.6–10%), and reveled evidence of immunological pressure. Inter-clade divergence was above the 3% threshold in clades A1 (5.3: 4.8–5.8%) and D (6.1: 5.8–6.9%). High avidity Gag (96: 19–267 ng/ml) and Nef-induced IFN-γ responses (74: 12–159 ng/ml) were detected. All gag regions were recognized, highest magnitudes were to p24. Gag was more targeted than Nef (44/50[88%] vs. 32/50[64%]; p = 0.014, Fisher's Exact); and induced higher IFN-γ magnitude (2420, 625–6445 vs. 475: 0–2000 SFU/106 PBMCs; p = 0.0003) and breadth (2: 1–3 vs. 1: 0–1 epitopes; p = 0.0001, Mann-Whitney), respectively, with no detectable difference between clades. Nef-induced IFN-γ responses targeted the conserved core region, and depicted lower magnitude (0: 0–765 vs. 1090: 275–2310 SFU/106 PBMCs; p = 0.04) and breadth in clade A1 than D (0: 0–1 vs. 1: 1–2 epitopes; p = 0.03), respectively.

Conclusion

Robust, cross-reactive, HIV-1 consensus group-M cellular responses in this highly diverse virus population implies a potential for a vaccine using immunogens based on these sequences despite the increasing diversity over time. Nef responses correlated with clade D known to be linked with faster disease progression; data suggests particular focus on Gag previously also shown to correlate with protection in this population.