Retrovirology

Poster presentation

P04-02. Increased breadth and potency of the neutralizing antibody response among dually-HIV-1-infected individuals

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Background

Neutralizing antibodies (nAbs) generated during HIV-1 infection are insufficient to protect against a 2nd (dual) infection; yet, little is known regarding the effect of a 2nd infection on the anti-HIV-1 nAb response. Therefore, the objective of this study was to analyze the effect of dual infection by subtype-discordant HIV-1 strains on the potency and breadth of this nAb response.

Methods

Two sequential plasma samples from 4 dually-intersubtype-infected subjects, obtained ~6 months before and >12 months after the 2nd infection was identified, were tested against 7 heterologous viruses (5 primary isolates and 2 Tier1 viruses) representing subtypes A1, B, F2, G, and CRF02_AG in the GHOST cell neutralization assay. Additionally, 23 singly-infected control subjects matched for disease stage, CD4 counts, and time between samples were studied. Plasma was assayed at 1:80 dilution to compare each plasma pair; subsequently, plasma from dually-infected subjects and 6 control subjects were assessed for magnitude and specificity of neutralization using plasma serial dilutions, 1:20–1:640.

Results

At 1:80 plasma dilution, 3 of the 4 dually-infected subjects' plasma obtained after dual infection exhibited significantly increased neutralization compared to initial plasma. Increases in percent neutralization for all 3 plasma pairs against all 7 heterologous viruses were significant ($0.05 > p > 0.001$), with the 2nd sample exhibiting 65%–96% neutralization. No control plasmas exhibited >30% neutralization of any of the heterologous viruses; thus, there was an overall significant difference between case and control subject-sets ($p = 0.009$). Fifty percent neutralization titers (IC50) of plasma obtained after dual infection from the 3 dually-infected subjects exhibited ~6X–100X increases compared to the initial samples ($0.05 > p > 0.0001$). No differences in the magnitudes of neutralization were observed for any of the singly-infected, control sample pairs.

Conclusion

These data propose that re-infection by a subtype-discordant virus broadens the anti-HIV-1 immune response, suggesting that vaccines incorporating and/or boosting with subtype-discordant immunogens may generate significantly improved anti-HIV-1 immunity.