Heterologous neutralization breadth persists despite B-lymphocyte dysfunction in chronic HIV-1 infection

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Journal Title: Retrovirology
Volume: Volume 9, Number Suppl 2
Publisher: BioMed Central | 2012-09-13, Pages P103-P103
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1186/1742-4690-9-S2-P103
Permanent URL: https://pid.emory.edu/ark:/25593/s5f1m

Final published version: http://dx.doi.org/10.1186/1742-4690-9-S2-P103

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Accessed April 9, 2019 9:38 AM EDT
Heterologous neutralization breadth persists despite B-lymphocyte dysfunction in chronic HIV-1 infection

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From AIDS Vaccine 2012
Boston, MA, USA. 9-12 September 2012

Background
Of the millions globally infected with HIV-1, only 20-30% will develop broadly neutralizing antibodies. To date, no one has measured this phenomenon in a cohort of subjects for which multiple aspects of B-lymphocyte dysfunction have been evaluated in parallel.

Methods
In 16 viremic seroconverters, the cross-clade neutralizing activity of plasma was investigated using a panel of thirteen clade A, B, and C HIV-1 envelope (Env) pseudotyped virions, which represented three tiers of sensitivity. The neutralization IC50 was calculated for each plasma-Env combination, and these data were used to determine a breadth (how many Envs were neutralized) and potency (the strength of neutralization) score for each seroconverter. Additionally, the level of plasma antibodies that bound to the monomeric form of a subtype B Env gp120 (HIV-1 BaL) was quantitated.

Results
A range of neutralization breadth emerged: three plasma samples (19%) demonstrated widespread neutralizing activity against this panel of Envs, while five subjects (31%) exhibited a complete lack of detectable neutralization at the lowest dilution of plasma tested (1:100). No correlation was observed between neutralization breadth or potency and parameters of B-lymphocyte dysfunction (PD-1, BTLA), immune activation (Ki-67, CD95), or disease progression (CD4 T cell count, plasma viral load). The level of total IgG in each plasma sample, however, did significantly correlate with both neutralization breadth and potency. Like total IgG, anti-gp120 binding antibodies also positively correlated, but, in this case, the correlations only trended toward significance. Anti-gp120 binding antibodies did not correlate with parameters of B-lymphocyte dysfunction, immune activation, disease progression, or total IgG level.

Conclusion
These findings demonstrate that even in chronically HIV-1-infected subjects in whom B-lymphocytes display multiple indications of dysfunction, antibodies that mediate cross-clade neutralization breadth (particularly anti-gp120 binding and other IgG antibody specificities) continue to circulate in plasma.

Published: 13 September 2012

doi:10.1186/1742-4690-9-S2-P103
Cite this article as: Murphy et al. Heterologous neutralization breadth persists despite B-lymphocyte dysfunction in chronic HIV-1 infection. Retrovirology 2012, 9(Suppl 2):P103.