B cell depletion, CD4 counts and viral load impact on ADCC, binding antibodies and neutralizing antibody profiles in HIV-1 subtype A chronically infected Ugandans

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Abstract

Background: HIV-1 may cause B-lymphocytopenia and impaired antibody responses. Mechanisms that may modulate the immune response and alter disease progression, include binding antibody production, as well as functional antibodies that neutralize HIV or mediate antibody-dependent cellular cytotoxicity (ADCC).
Methods: A rural cohort of 50 chronically infected, treatment-naïve Ugandan patients with HIV-1 subtype A infection was characterized to assess the relationship between B cell depletion and disease progression (assessed by CD4 absolute counts and viral load). Immunophenotyping was performed using the FACS MultiSET system and HIV antibodies assessed using the TZM-bl neutralization assay, a conventional ADCC assay and ELISA.
Results: B cell lymphocytes exhibit significant lower frequency in HIV-1 subtype A chronic infection as compared to community matched negative controls ($p<0.0001$). CD4 counts and viral load showed an inverse correlation ($p < 0.01$. $r = -0.3675$). Functional and binding antibody titers showed no direct correlation with viral load or CD4 count. ADCC responses did not correlated with B cell counts but B cell absolute counts correlated with neutralizing antibody titers against two clade A pseudoviruses ($p=0.02$, $r = -0.44$ and $p = 0.03$, $r = -0.43$ respectively). A strong correlation was observed between gp120 binding antibody titers and neutralizing antibody breadth ($p=0.004$, $r =0.4$) and titer ($p=0.011$, $r=0.5$). In addition, subtype A sera showed higher neutralization against subtypes D,A and CRF02_AG, with some cross-neutralization of B and C.
Conclusions: Our findings suggest that in chronic HIV-1 subtype A infection, B cell depletion may lead to a failure to generate functional antibody responses against HIV-1. Furthermore, subtype A infected patients preferentially neutralize subtype A viruses or subtype A-containing recombinants