PE17

Anti-HIV antibody responses reflect the quantifiable HIV reservoir size

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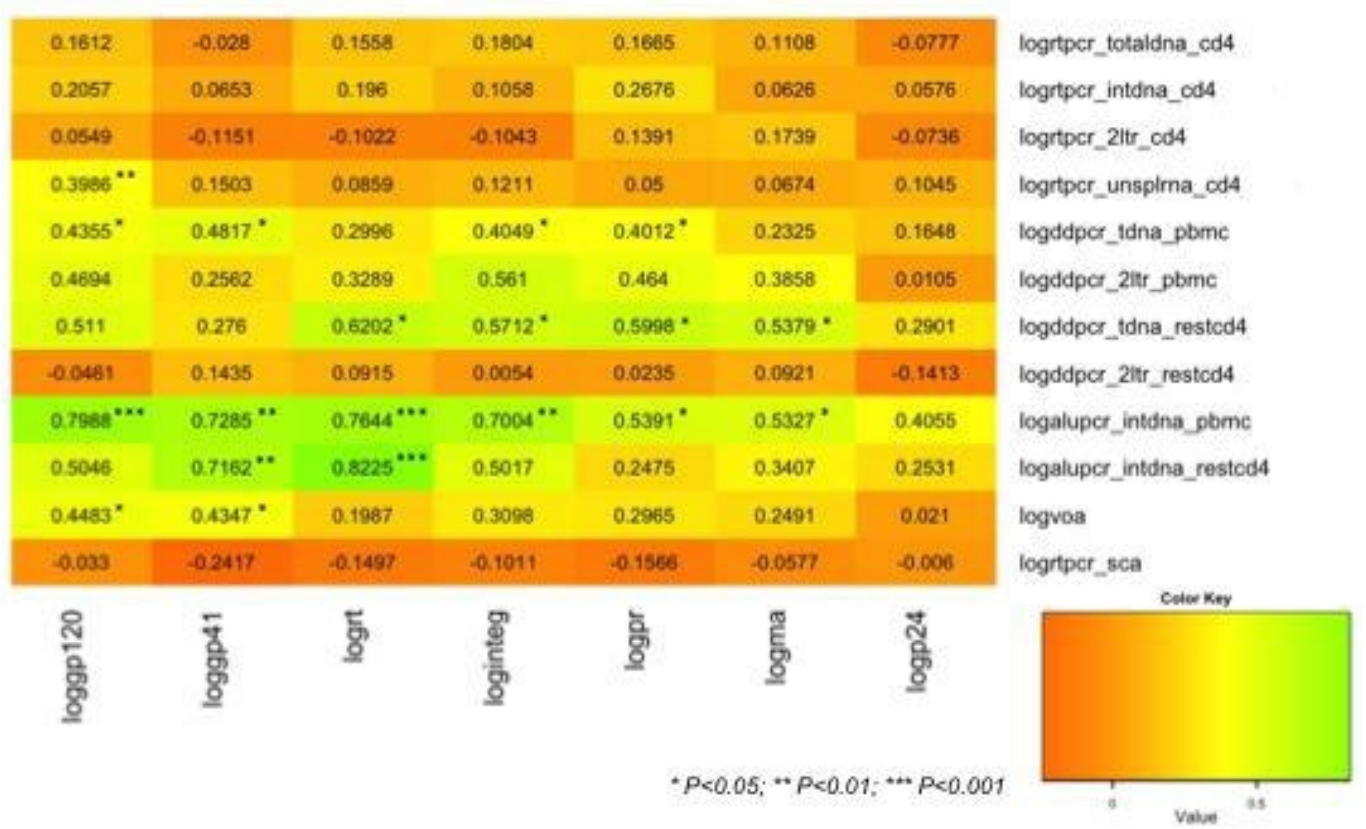
Background: A major challenge to HIV eradication strategies is accurate measurement of the latent HIV reservoir. We assessed whether the host response to residual virus may be a sensitive measure of reservoir size by comparing anti-HIV antibody profiles in relation to several HIV reservoir assays.

Methods: Using a luciferase immunoprecipitation systems (LIPS) assay, we quantitatively analyzed seven anti-HIV antibody profiles from 61 patients who initiated long-term (>3 years) antiretroviral therapy (ART) during chronic HIV infection. HIV antibody levels were evaluated in relation to twelve HIV reservoir measures: total, integrated, and 2-LTR DNA (rtPCR, N=48); unspliced RNA (rtPCR, N=44), total and 2-LTR DNA (droplet digital PCR, N=27); integrated DNA (aluPCR, N=16); viral outgrowth assay (VOA, N=27), and plasma HIV RNA (single copy assay, SCA, N=27). Summary estimates of the overall association between HIV reservoir measures and HIV antibody levels adjusted for multiple comparisons were obtained using permutation testing.

Results: Participants were mostly male (96%) with a median age of 56, median nadir and proximal CD4+ T cell counts of 210 and 670 cells/mm3, respectively, and ART-suppression for a median of 11 years. Individual correlations showed that integrated and total HIV DNA levels by aluPCR and ddPCR were significantly associated with all antibody levels except p24 (nor matrix, for ddPCR, Figure 1). HIV reservoir size measured by VOA was associated with gp120 and gp41 levels (R=0.45, P=0.02; R=0.43, P=0.02) while HIV RNA by SCA and HIV DNA by rtPCR were not correlated with any HIV antibody responses. Permutation testing demonstrated a strong overall association between HIV reservoir size and anti-HIV antibody responses (R=0.82, P=0.04, Table 1), in particular with gp120 (R= 0.80, P=0.009), gp41 (R=0.73, P=0.04), and reverse transcriptase (R=0.82, P=0.007). Further adjustment for age, proximal CD4+ T cell count, and years of ART suppression did not significantly alter these results.

Conclusions: Anti-HIV antibody responses correlate with quantifiable reservoir size during chronic ART-mediated suppression. Epitope location (envelope proteins and reverse transcriptase, an enzyme involved in the early steps of viral replication) may determine the strength of this association. Future studies are needed to evaluate whether viral RNA or proteins are produced in cells with defective proviruses.



[Figure 1. Individual correlations matrix.]

Anti-HIV Antibody Response	R	P
loggp120	0.80	0.009
loggp41	0.73	0.042
logrt	0.82	0.007
logintegrase	0.70	0.053
logpr	0.60	0.199
logma	0.54	0.340
logp24	0.41	0.679
All	0.82	0.039

[Table 1. Adjusted summary correlations.]

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