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 (Eksitsson PLoS Pathogens 2013, No Cell 2013).

There is a need for scalable assays that reflect the latent HIV reservoir to measure the success of HIV cure treatments.

Our group has previously demonstrated that anti-HIV antibody levels differentiate HIV patient groups (Burbelo JID 2014).

We performed a pilot study to assess whether anti-HIV antibody levels reflect the size of the HIV reservoir and may be a sensitive measure of HIV persistence.

Do Anti-HIV Antibody Levels Reflect the Size of the Latent HIV Reservoir?

Methods

•61 HIV+ SCOPE participants who initiated antiretroviral therapy (ART) during chronic infection.

•12 HIV-1 reservoir measures from two studies:
  - Study 1: total, integrated, 2-LTR DNA (by nPCR, N=48); unspliced RNA (by rPCR, N=44).
  - Study 2: total, 2-LTR DNA (by droplet digital PCR, N=27); integrated DNA (by aluPCR, N=16); infectious units (by viral outgrowth assay, VOA, N=27); and plasma HIV RNA (by single copy assay, SCA, N=27).

•7 anti-HIV antibody measures using a novel luciferase immunoprecipitation systems (LIPS) assay.

•We performed permutation testing to analyze the association between antibody and reservoir measures, adjusted for multiple comparisons.

•Univariate correlations and multivariate linear regressions were performed using log-transformed, standardized predictor and outcome variables. Multivariate analyses included covariates for age, proximal CD4+ T cell count, nadir CD4+ T cell count, years of ART suppression, and pre-ART viral load.

Novel Luciferase Immunoprecipitation Systems (LIPS) Assay Detects Conformational Antibodies

Results

Descriptive Statistics of Study Participants

Characteristics N=61

Gender (M/F) 55 (90.2)
Age (years) 54 (44-63)
Pre-ART HIV RNA (log, copies/mL) 8 (1.8-3.1)
Nadir CD4+ T cell count (x10^3) 700 (410-1280)
Duration of ART (years) 8 (4-18)
Mean CD4+ T cell count (x10^3) 570 (410-900)

Measures of CA HIV-1 DNA and RNA but Not Plasma RNA are Correlated with Anti-HIV Antibody Levels

The observed maximum correlation (0.82) than the samples studied using the other eight HIV reservoir measures (Study 2). The four HIV reservoir measures marked with an asterisk (*) were performed on a subgroup of different patient samples with permuted p-values below.

The correlation coefficients between HIV reservoir measures and anti-HIV antibody levels shown in bold font. Permuted p-values shown below.

CA= Cell-Associated

The Observed Maximum Correlation is Greater Than Expected by Chance

Conclusions/Implications

•We observed a strong association between measures of the latent HIV reservoir and anti-HIV antibody levels.

•Anti-HIV antibody levels against RT, gp120, gp41, had the observed maximum correlation of R=0.82 is shown at the tail of the distribution of permuted correlations, P=0.04.

•There is a preferential B cell response against certain HIV antigens?

•Can viral RNA or proteins be produced in cells with defective proviruses?

•Is there a preferential B cell response against certain HIV antigens?

•Are certain anti-HIV antibody levels more “stable over time”/decelay slower?

•Why are measures of cell-associated HIV DNA and RNA but not plasma HIV RNA correlated with anti-HIV antibody levels? Do antibody levels more closely quantify the latent tissue HIV reservoir?

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