Poster #402

Using Antibodies to Detect HIV Persistence in Treatment Intensification and Eradication Studies

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Introduction

Quantifying the degree of HIV persistence during therapy is challenging due to low viral burden and the intracellular sequestration of virus in tissue reservoirs.

An alternative or complementary approach is to quantify the host immune response to HIV.

HIV incidence assays have been developed to measure antibody (Ab) evolution during HIV seroconversion.

HIV incidence assays can be used to investigate the association between HIV Ab levels, avidity and HIV antigen specificities in diverse cohorts of treated and untreated adults.

Methods: Samples Tested

We measured antibodies in plasma samples from:
-280 long-term infected HIV+ untreated
-280 HAART-treated and virally suppressed HIV+ individuals
-100 non-treated but virally suppressed HIV+ elite controllers (ELITE)
-one potentially HIV-eradicated individual.

We used HIV antibody diagnostics with or without modification to measure avidity, quantity and diversity of HIV Abs.

Methods: Assays and analyses

Less-sensitive (LS) and Avidity-modified VITROS® Anti-HIV1+2: A chemiluminescent assay to detect HIV-1/2 Ab approved by FDA for diagnosis of infection. To measure anti-HIV Ab quantity and binding ability, the assay was modified to be LS by using dilution (1:400 dilution in buffer) and increasing the cutoff. To measure the avidity of anti-HIV Ab, sample treated with guandidine was compared to sample treated with PBS. An avidity index was calculated (guanidine-incubation/buffer-incubation).

Avidity modified BIO-RAD GS HIV-1/HIV-2 *PLUS O* EIA: An FDA-licensed ELISA to detect HIV-1/2 Abs and to diagnose infection was subjected to avidity modification by treatment of plasma with DEA (DEA-incubation/PBS-incubation; avidity index) to measure anti-HIV Ab binding ability.

Bio-Rad Geenius™ HIV 1/2 Supplemental Assay: Geenius™ is a supplemental assay. It is a 3 step protocol, easy to perform and takes less than 30 minutes. The HIV-specific band intensities can be used to calculate an index (p31+gp160+gp41/control band: diversity and quantity Index) to determine titer and specificities of anti-HIV Ab.

These assays measure antibody evolution in titer, avidity and antigen-specificity during seroconversion after infection or seroreversion after treatment or eradication protocols.

We compared the overall results from each of the HIV groups for each assay used and looked for decline in reactivity over time on treatment.

Result I: There is a decline antibody measurement in elite control and after successful HIV treatment.

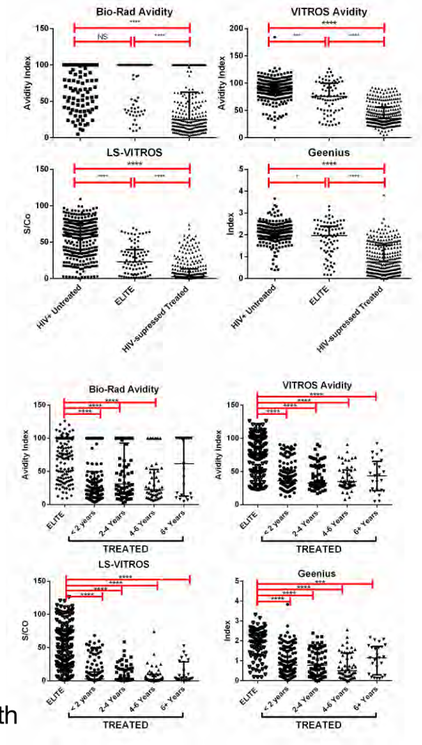


Figure 1. Lower levels of anti-HIV Ab concentration and avidity in ELITE controllers and HIV suppressed. Assays to detect HIV infection can be modified and reanalyzed to explore the reduction in Ab concentration in ELITE individuals who control virus or are HIV-suppressed during treatment. There is significant reduction in Ab and avidity in ELITE control and suppressed groups compared to HIV untreated. There were fewer significant differences in the ELITE compared to untreated in Bio-Rad avidity and Geenius Index. This may suggest that continued antigenic stimulation maintains concentration and avidity of anti-HIV Ab in ELITE.

Figure 2. Antibody concentrations continue to decline with time on treatment. There is significant reduction in antibody measurements after long term treatment compared to individuals who control virus without ART. This suggests that there is continual antigenic boosting of responses in ELITE that maintains higher concentrations of circulating antibodies. Loss of circulating virus corresponds to reduction in anti-HIV antibody.

Result II: Antibody concentrations continue to decline after stem cell transplant during eradication protocols.

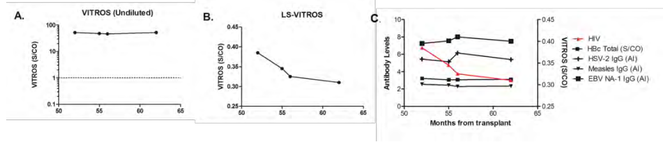


Figure 3. Reduction in anti-HIV Ab concentration after stem cell transplant in potential eradication (Berlin Patient). Compared to highly sensitive VITROS HIV assay (A), less sensitive VITROS HIV assay shows continual Ab decline (B), and this is HIV-specific (C).

Summary/Conclusions

There are progressive reductions in Ab titer but less decline in avidity in treated compared to untreated individuals that correlates with time on treatment.

Although ELITE had undetectable or very low VL, Ab levels remained elevated compared to individuals on ART, demonstrating maintenance of Ab stimulation from persistent viral replication in reservoirs.

Measuring the quantity, quality and diversity of Ab to HIV may be used as a marker for monitoring viral persistence in studies of eradication and treatment.

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