Poster #615

Using the Bio-Rad Geenius™ HIV1/2 Supplemental Assay for Detecting Recent HIV Infection and Calculating Population Incidence

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Introduction

Assays that measure biomarkers during HIV seroconversion are being used in cross sectional studies for HIV incidence estimation.

The Bio-Rad Geenius™ HIV 1/2 Supplemental Assay has been developed for HIV-1 and HIV-2 differentiation and confirmation. Recently an algorithm was developed to perform HIV-1 recency estimations using this same technology.

It is a 3 step protocol, easy to perform and takes less than 30 minutes. It can use serum, plasma, finger stick or whole blood specimens.

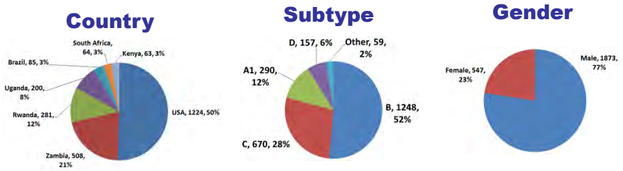
This immunochromatographic test detects antibodies to HIV-1 (p31, gp160, p24, p41), HIV-2 (gp36, gp140) antigen bands and protein A (control band) bound to the membrane solid phase and uses protein A conjugated to colloidal gold dye particles for band detection.

The HIV band intensity during IgG antibody evolution in HIV infection is captured by the camera in the Geenius™ reader and analyzed using Bio-Rad proprietary image analysis software .



Methods

An evaluation of a 2500 member HIV-1 plasma panel was performed using the Geenius™ HIV1/2 Supplemental assay. This panel consisted of specimens from 918 individuals from the United States, Brazil and Africa with many HIV-1 subtypes represented. It is comprised of longitudinal seroconversion series, long-term infected, treated, AIDS, and elite controllers.



Age (at draw) : 18-76 (median 37)

Results I

BIO-RAD Geenius™ HIV-1/2 Supplemental System: A new Unitary HIV supplemental assay was developed by Bio-Rad. The HIV-specific band intensity can be used to calculate an antibody index (p31+gp160+gp41/control band: diversity and quantity Index) to determine titer and specificities of anti-HIV Ab that evolve after

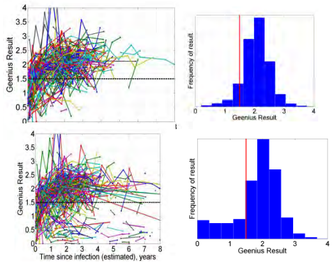


Figure 1. Antibody results from longitudinal specimens.

a) **excluding elite controllers and treated subjects**
Results are plotted as time since estimated 'infection', where infection refers to being positive on Western Blot throughout
418 subjects, 1376 data points

b) **Including elite controllers and treated subjects**
Antibody responses from some elite controllers and treated individuals fall under the recent infection Index cutoff. These samples will impact false recent rate.

Results II

Geenius Algorithm utilizes: (p31 band intensity + gp160 band intensity + gp41 band intensity) / CTRL band intensity = Antibody Index (AI). Geenius cutoff = 1.5 AI (AI result ≤ 1.5 classified as 'recent' and >1.5 classified as 'longstanding" or 'non-recent') is currently calculated off line using the Geenius band intensities.

The **Mean Duration of Recent Infection (MDRI)** is the average time spent alive and 'recently' infected, while infected for less than a time cut-off T=1 year.

We calculated an estimated mean duration of recent infection (MDRI) for the Antibody Index cutoff of ≤1.5 to be 141 days (124-159) using a binomial regression model.

The **False-Recent Rate (FRR)** is the probability that a randomly chosen subject, who is infected for longer than T, will produce a 'recent' result.

Subject Group	Number of Subjects	False-Recent Rate (95% CI), as %
Excluding treated subjects and elite controllers	456	6.1 (4.1-8.8)
Treated subject (for at least 3 months)	142	72.5 (64.4-79.7)
By time from estimated infection to treatment		
(0, 0.5) years	70	90 (80.5-95.9)
0.5+ years	37	40.5 (24.8-57.9)
Elite controllers	31	30.6 (15.4-49.7)
Low viral load (<75 copies/ml)	184	63.6 (56.2-70.5)
Low CD4 cell count (<200)	141	1.4 (0.2-5)

Table 1. False recent rate estimations with subjects stratified into various subject groups. The proportion of 'recent' results amongst the subjects is measured (the most frequent classification is used if the subject has more than one result over time). Clopper-Pearson binomial confidence intervals are provided. Low viral load after treatment or elite control impact the false recent rate the most. Low CD4 counts do not impact false recent rate calculations.

Results III

Using the intensity values from each of the HIV-1 antibody band measurements, we investigated antigen-specific antibody evolution of each antigen band combination as compared to the others. We see that the antibody band intensities evolve at different kinetics.

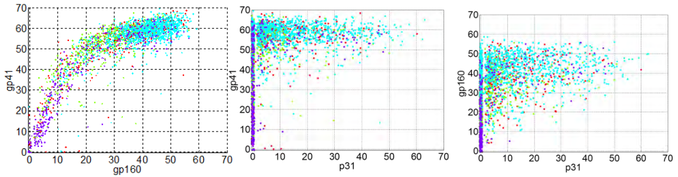


Figure 2. Antibody profile from the different HIV-infection subgroups.
Each dot represents the intersection of antigen-specific antibody expression. **Green**: Specimen drawn within a year of infection, excluding treated subjects and elite controllers. **Blue:** Specimen drawn more than a year after infection, excluding treated subjects and elite controllers. **Purple:** Specimen drawn more than a year after infection, treated subjects and elite controllers only. **Red:** Everything else.

Summary/Conclusions

This is the first external laboratory evaluation of the Geenius™ assay as a method for identifying recent HIV infection.

The Geenius FRR and MDRI presented here are similar to other currently used methods for detecting recent HIV infection. Geenius recency estimates are impacted by low viral loads after ARV treatment or in patients who are elite controllers.

The Geenius test format not only allows for HIV1/2 antibody confirmation and HIV1/2 differentiation, but also can be used to inform newly diagnosed individuals and their health care providers of the likely duration of infection and to understand recent infection in a population.

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