LONGITUDINAL QVOA AND IPDA MEASUREMENTS IN CD4 T CELLS FROM ART-SUPPRESSED DONORS

00313

Shane D. Falcinelli[1,2], Jenna Read[1], Ross Murtagh[1], Sam Raines[1], Morgan Dewey[1], Nancie M. Archin[1,3], David M. Margolis[1,2,3]
[1]UNC HIV Cure Center, [2]Dept. of Microbiology and Immunology, [3]Dept. of Medicine University of North Carolina, Chapel Hill, NC, USA;

BACKGROUND

- The intact proviral DNA assay (IPDA) is a novel method to quantify intact, latent provirus using minimal cell input relative to the gold standard quantitative viral outgrowth assay (QVOA)
- As IPDA sensitivity and specificity may be affected by viral diversity, prior to implementation in experimental medicine trials it is critical to evaluate the relationship between the IPDA and QVOA measurements across different participants
- As latent provirus can decay over time, a comparison of the IPDA to QVOA longitudinally is also needed

METHODS

- We conducted the IPDA on stored resting CD4 T cells from a cohort of 68 ART-suppressed individuals in whom QVOA had been measured (Sex: n=22 XX, n=46 XY)
- In 27 of these individuals, we performed the IPDA on two to six longitudinal samples, with matched QVOA data
- Longitudinal sampling spanned a range of 1 to 33 years after ART initiation

IPDA measurements correlated with QVOA measurements over time.

The precision of correlation of IPDA with QVOA may vary across individuals.

CONCLUSIONS

- This study provides a key comparison of QVOA and IPDA measurements longitudinally in a large cohort of ART-suppressed participants
- In general, intact proviral DNA measurements correlated with QVOA measurements over time; some correlation was also seen in measurements of defective DNA species
- The precision of correlation of IPDA with QVOA may vary across individuals. The recent description of proviral clones that contract and expand over time may explain some changes seen in IPDA over time
- These findings suggest an advantage for the IPDA over traditional single-target assays that measure predominantly defective DNA
- The utility of IPDA to monitor cure interventions designed to deplete persistent infection deserves further study

ADDITIONAL KEY INFORMATION

Author Contact Information: shane_falcinelli@med.unc.edu
Acknowledgements: The authors thank the study participants for their collaboration. This work was supported by Collaboratory of AIDS Researchers for Eradication (NIH UM1AI126619) and NIH F30AI145588.

RESULTS

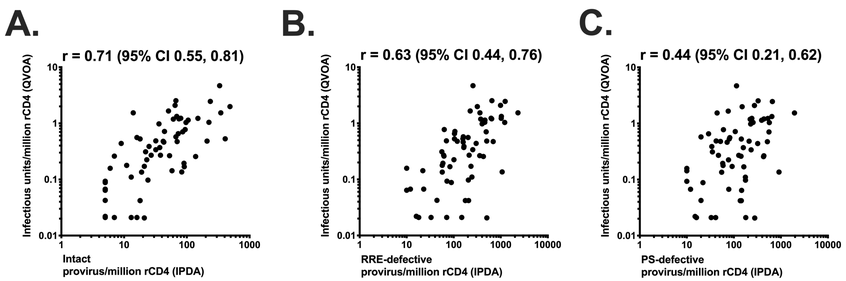

Figure 1: Correlation of intact and defective proviral DNA frequency with QVOA measurements. 62/68 participants had provirus assessable by the IPDA.

Table 1: IPDA Assay Performance Parameters.

Performance Category	Fraction of Participants
No PCR amplification issues	62/68
Env/RRE probe amplification failure	3/68
PS probe amplification failure	2/68
Env/RRE **and** PS probe amplification failure	1/68

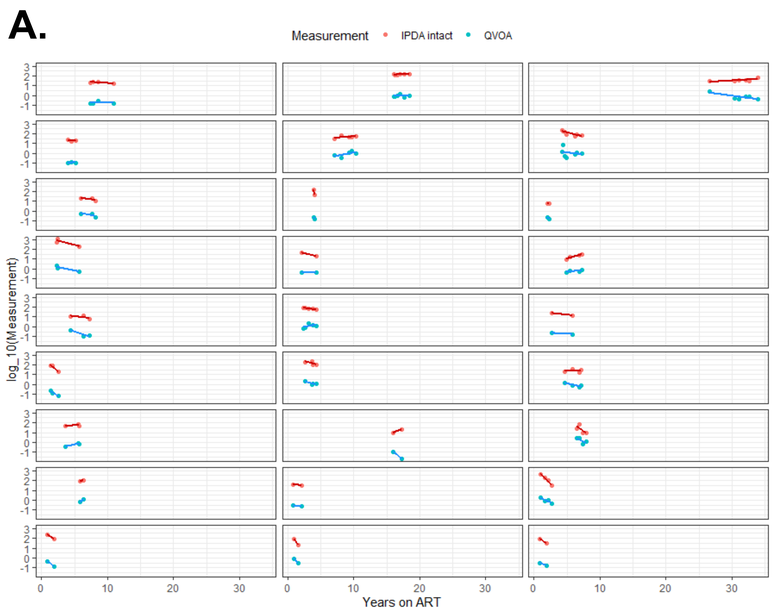

Figure 2: Intact DNA and QVOA measures correlate over time in ART-suppressed participants. Each plot represents data from a distinct participant. Red dots = IPDA Intact; Blue dots = QVOA. Lines represent ordinary least squares regression.

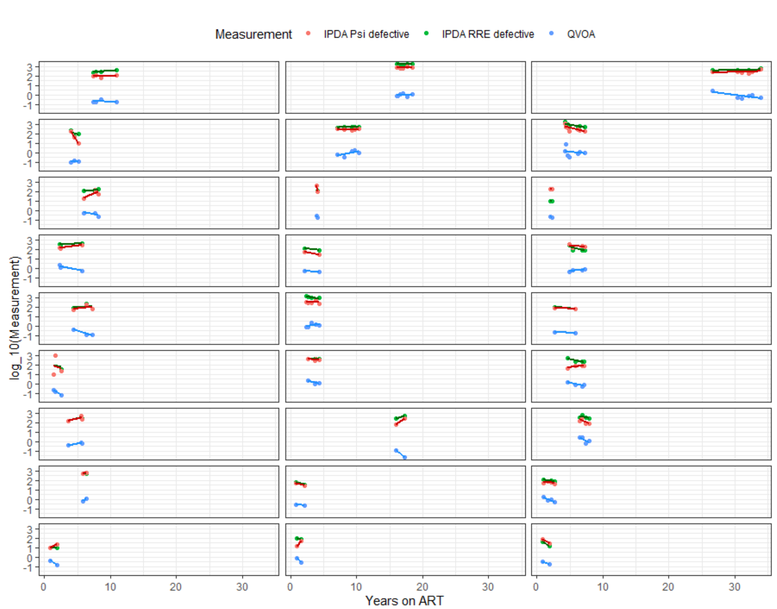

Figure 3: Defective DNA tracked with QVOA frequency in some individuals. Each plot represents data from a distinct participant. Red dots = IPDA Packaging Signal (Psi)-defective; Green dots = IPDA RRE-defective; Blue dots = QVOA. Lines represent ordinary least squares regression.