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# Cohort-specific adaptation of the Intact Proviral DNA Assay (IPDA) to HIV-1 subtypes A1, D, and recombinants

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**EDITION** 

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HIV Persistence During Therapy, 2022





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# **Conflicts of Interest:**

None to report.



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# **IPDA on HIV Subtype B**



Q2: Intact proviruses are Ψand env- double positive

Q1: 3' defective proviruses are Ψ- single positive

Q4: 5' defective proviruses are env- single positive

Q3: Contain no HIV or highly defective proviruses that are Ψand env- double negative

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## **Distribution of HIV-1 Subtypes**



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# Psi detection failure in a Genome-Intact Subtype D Amplicon from our cohort







# The goal of this project was to adapt the existing IPDA primers/probes for use in the **Rakai Health Sciences Program (RHSP) clinical study Cohort.**

(Therefore their application/use for A1D sequences outside of this cohort, and all other subtypes, is unknown)

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## Study Cohort: Rakai Health Sciences Program (RHSP), Uganda

### 90 people living with HIV (PLWH), ART-suppressed

Heterosexual transmission, chronic infection, 63% female, NNRTI/NRTI

Single genome amplification (SGA): Near-full-genome viral sequencing (FLIP-Seq) → 607 sequences from 23 individuals



Pragya Khadka

VIAMIUSA



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### Bruner *et al.,* IPDA regions [HXB2 692-797 and 7736-7851] were > 96% predictive.



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### **Degeneracy does not Affect Primer/Probe Detection**



- pNL4-3 (Subtype B HIV-1)
- Amplitude reduction

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\*All values have been normalized to 20000 droplets.

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### A1D-Adapted IPDA:

• Positive controls using HIV molecular clones from our cohort



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### A1D-Adapted IPDA:

\*All values have been normalized to 20000 droplets.

• Single-region defective amplicons from the Rakai cohort



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### **A1D-Adapted IPDA:**

\*All values have been normalized to 20000 droplets.

Hypermutated amplicons from the Rakai cohort ٠





# Take Home Message/Community Summary:

### High-throughput assay needed

- Distinguish intact provirus, contributing to viral rebound, versus defective
- IPDA designed for subtype B

IPDA regions [HXB2 692-797 and 7736-7851] were >96% predictive in A1D cohort

• Degeneracy had minimal impact on detection, but shifted amplitude

Test on A/D molecular clones; clinical samples; human cell line infected with HIV subtypes A/D?

• Long-term goal: RHSP longitudinal cohort (n=90 individuals)

Quantifying the reservoir in non-B subtypes can help us better understand the LVR and guide more diverse HIV cure efforts.

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# Thank you to all of the participants.





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Los Alamos Subtype D Full length



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psiR LosAlamos A1 Uganda psiR COTACO DE LOS DE LOS





5′

Rakai



2 3′

8 3′

rkelev edu

8 <sub>3′</sub>

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10 10

#### psiPv1

#### envP



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# Los Alamos

5′

5′

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Subtype A1 Full length

Los Alamos Subtype D Full length

Rakai cohort