Reservoir and Phylogenetic Signatures Identify Distinct Subsets of HIV Nonsuppressible Viremia

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BACKGROUND

- Nonsuppressible HIV viremia is a phenomenon where ART adherent individuals with no drug resistance have a detectable viral load
- NSV represents an area of clinical research relevant to understanding the mechanisms of HIV persistence

METHODS

- 15 NSV participants with high ART adherence and ≥2 active ART were clinically and phylogenetically evaluated via IPDA, near-full length proviral single genome sequencing, and pol-env extended-length plasma sequencing

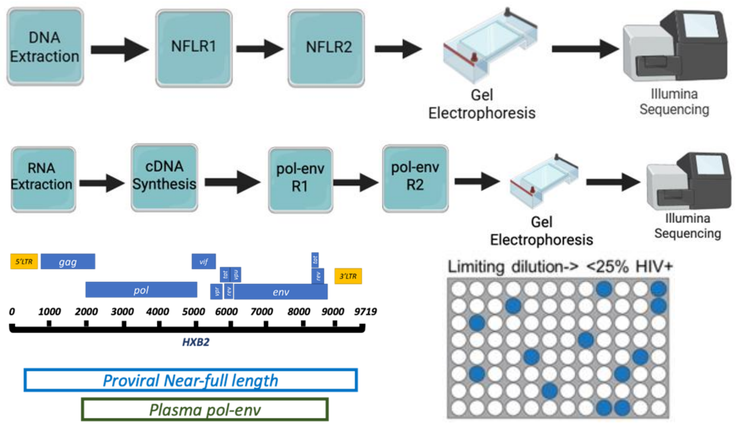


***Fig 1**. Overview of the methodology utilized.*

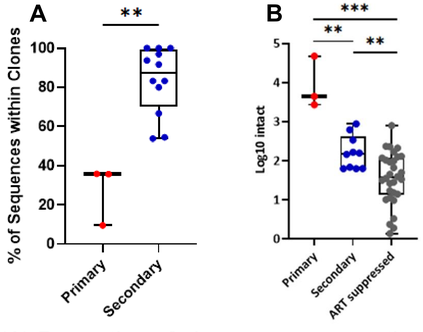


***Fig 3**. (A) Proportion of plasma sequences that belonged to expanded clonal lineages in primary (red) and secondary (blue) NSV. (B) Level of intact proviruses per million PBMCs as measured by intact proviral DNA assay. Statistical test Mann-Whitney U test * P<0.05 ** P<0.01 *** P<0.001*

RESULTS

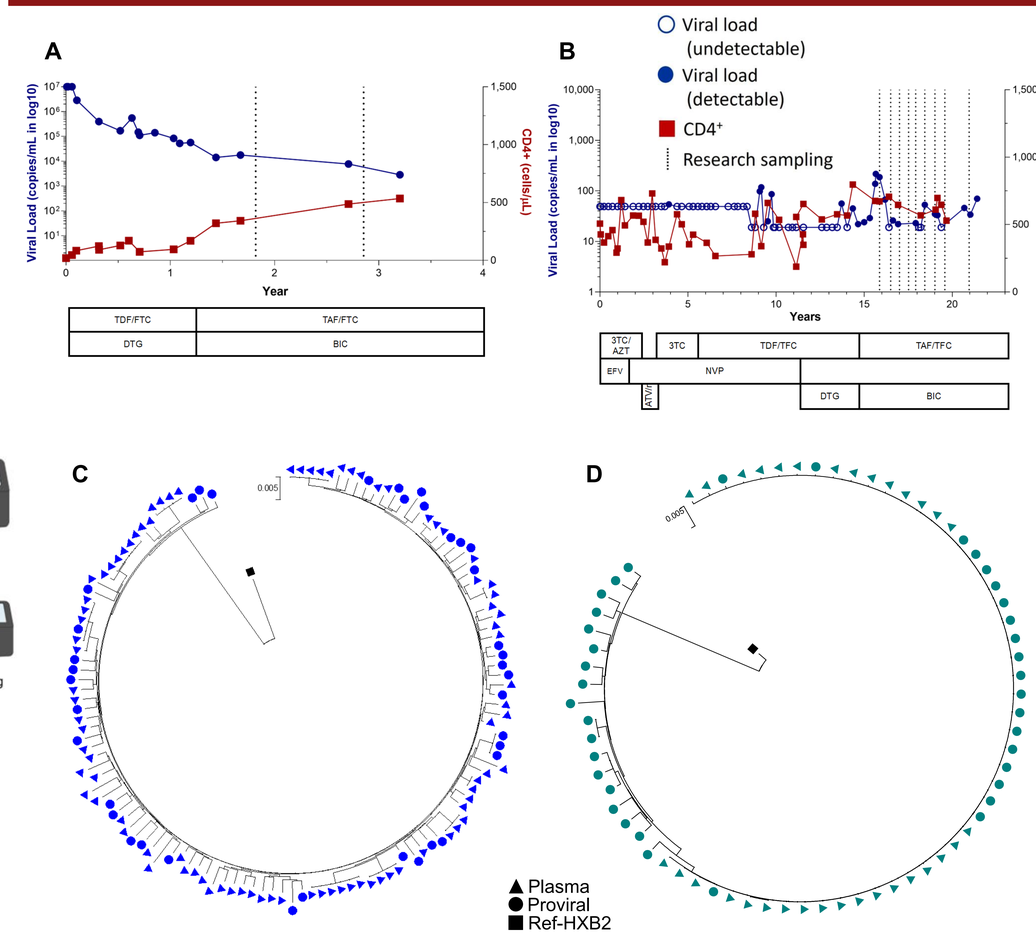


***Fig 2**. (A-B) Viral load & CD4+ count graph of primary (A) and secondary (B) NSV participant. (C-D) Phylogenetic tree of plasma and proviral sequences from primary (C) and secondary (D) NSV.*

Primary NSV is a novel category of NSV that is characterized by lack of viral suppression, low CD4 nadir, exceptionally large intact proviral reservoir, and high plasma diversity.

- Primary NSV is defined by never being virologically suppressed (**Fig 2)**
- Secondary NSV participants were previously suppressed before experiencing viral rebound.
- Primary NSV individuals have a significantly higher proportion of intact proviral reservoir as indicated by intact proviral DNA assay (**Fig 3**) and have much more diverse plasma than the clonally expanded secondary NSV group (**Fig 2,3**).
- Plasma viremia in secondary NSV is more clonally expanded (**Fig 2**).

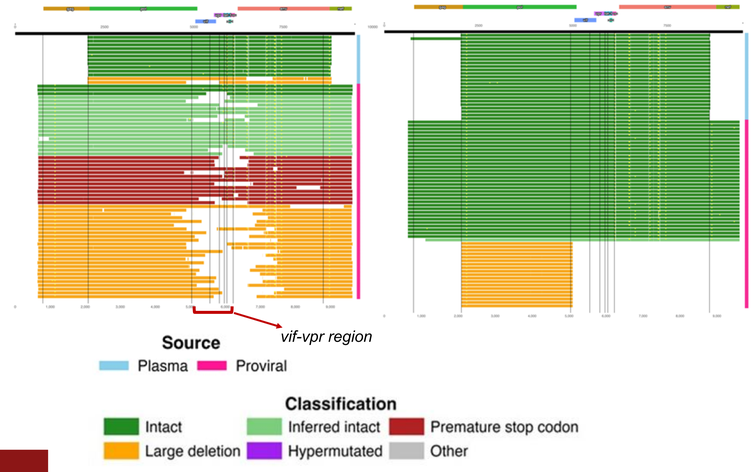


***Fig 4.** Virogram of two primary and secondary NSV participants*

- Primary NSV individuals harbor deletions in the *vif-vpr* region of plasma and proviral sequences (**Fig 4**) that is not seen in secondary NSV.

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