



Virulent HIV-1B: Clinical Challenges and Proteomic Insights

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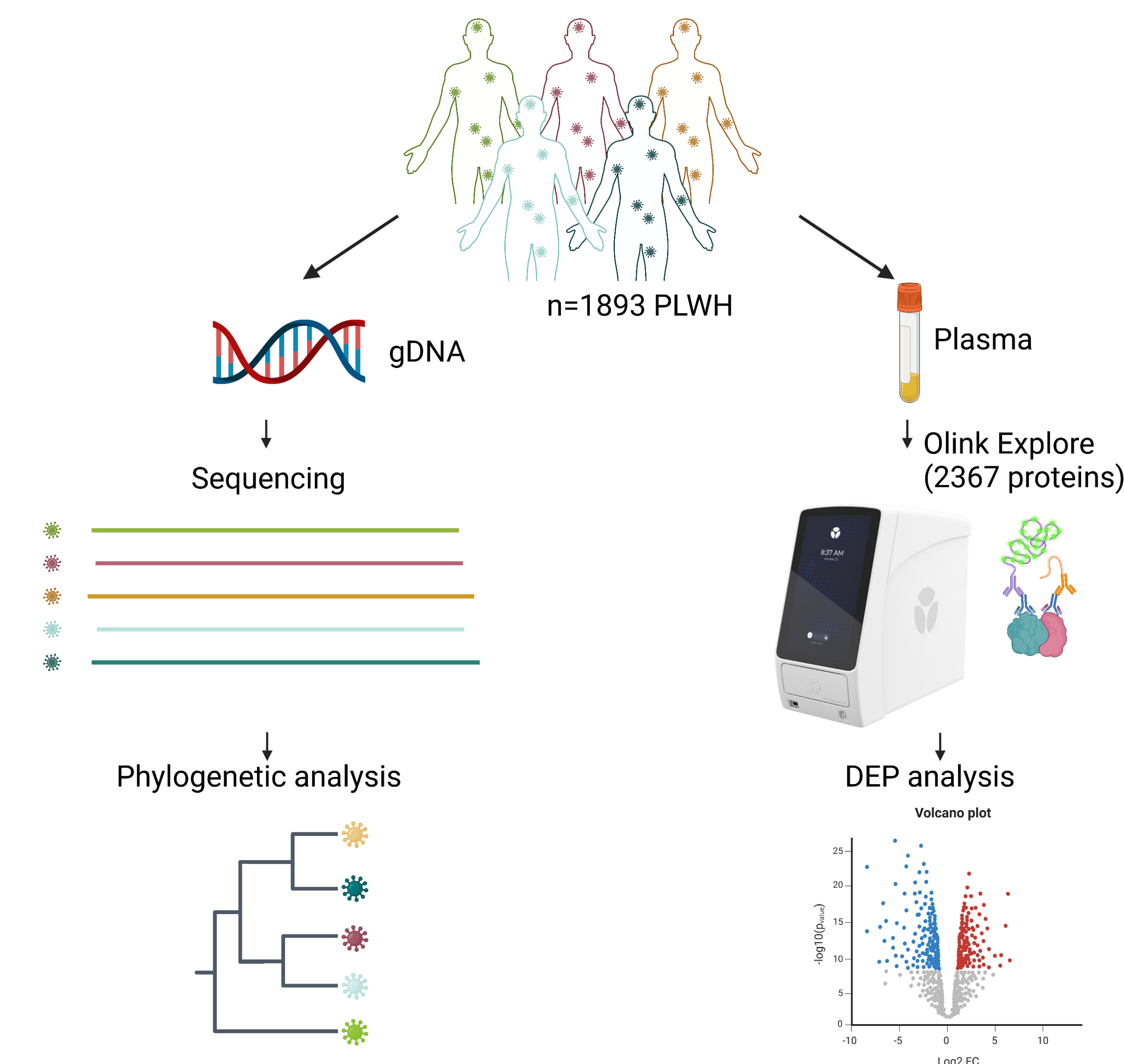
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BACKGROUND

A virulent HIV-1 subtype B clade (VB) first reported in 2022 (Wymant et al. 2022), is linked to higher plasma viral loads (pVL) and two-fold faster CD4+ T-cell decline. This study aims to elucidate the effects of VB on clinical outcomes and host proteomic profiles.

METHODS

Genetic analysis was conducted on 1,893 people living with HIV (PLWH) from the 2000HIV cohort on ART, using partial *env* and *pol* sequencing of genomic DNA from CD4+ T-cells.

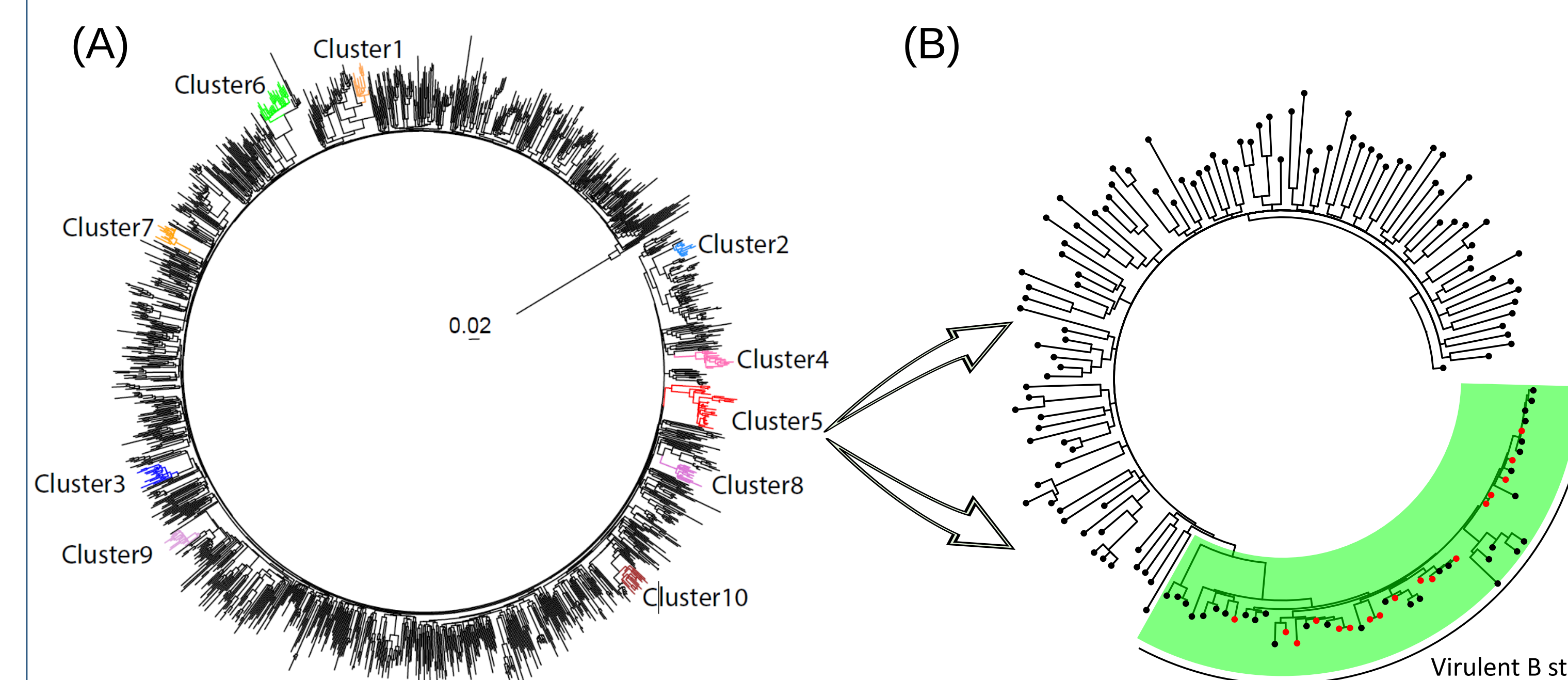


Phylogenetic analysis with IQ-TREE (subtype B; 80% of cohort) identified **32 participants** belonging to the VB clade. Proteomics analysis comparing VB and non-VB groups was conducted using a linear regression model, adjusting for covariates such as age, smoking status, and other factors that explained at least 3% of the variance in the plasma proteome.

VB is linked to more severe clinical outcomes and distinct proteomic changes. Notably, proteomic profile changes persist even after a decade of ART.

RESULTS

Virulent B clade in 2000HIV cohort

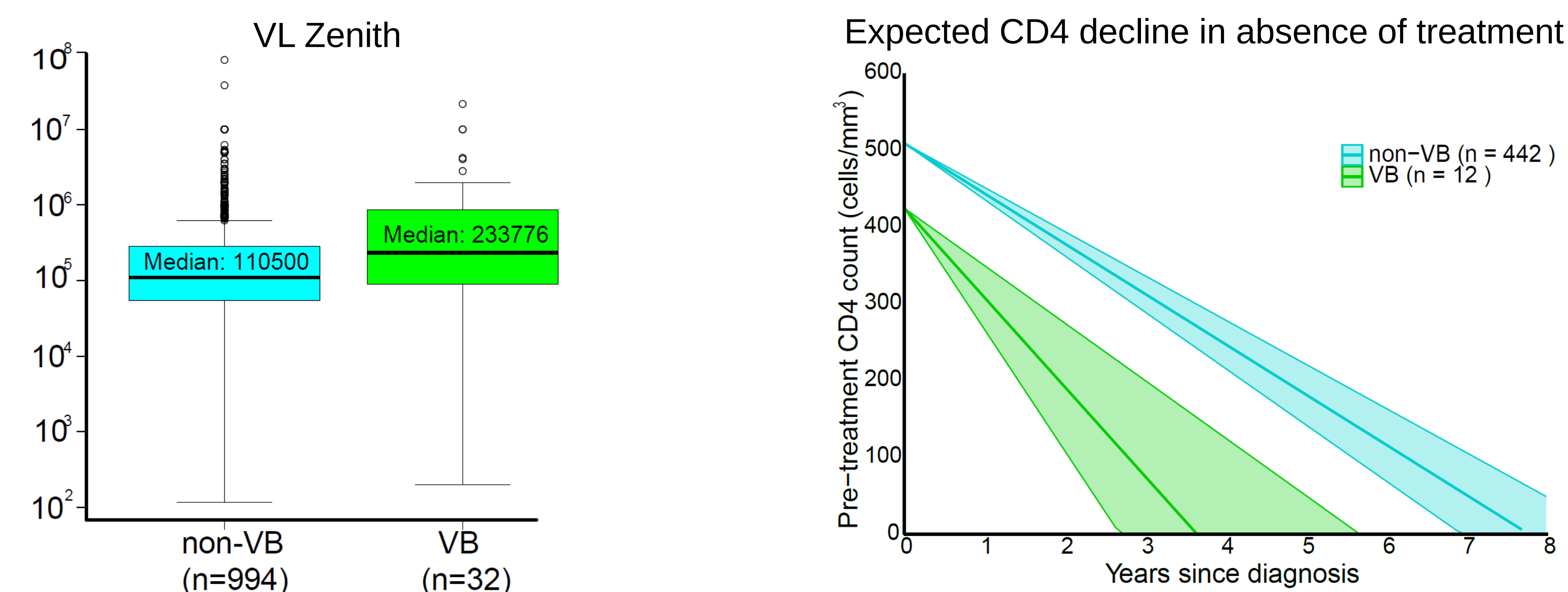


Characteristics of VB clade (n=32):

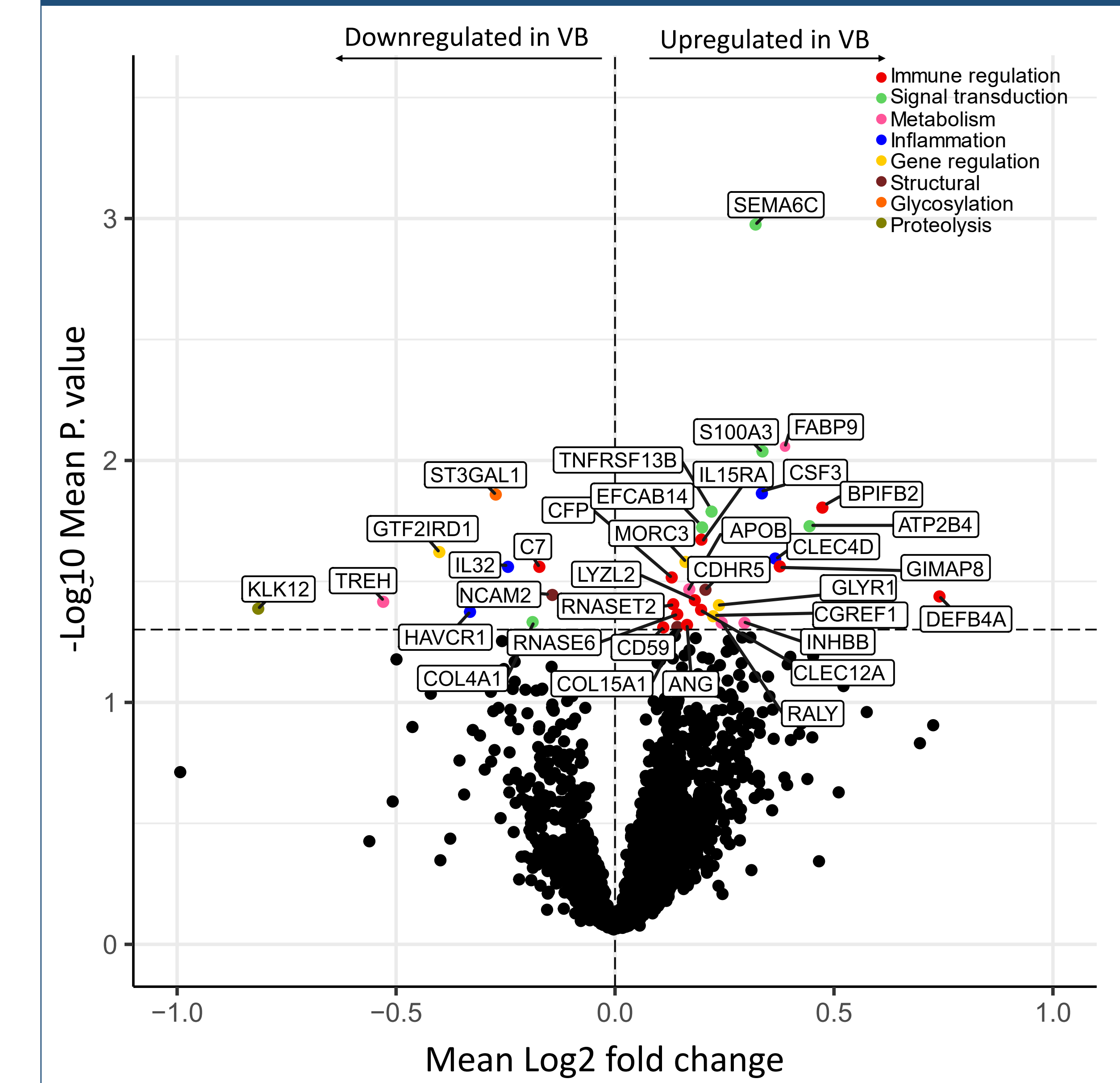
- All males, MSM
- Diagnosed between 2004-2019
- Median ART duration: 9.93 years
- R5 (n=22), X4 (n=3), and mixed-tropic (n=2)
- 1 immunological non-responder
- 7 rapid progressors
- Drug resistance mutation (DRM): singleton M41L in 27 participants

Fig: (A) Phylogenetic tree from *pol* sequences (1.7 kb); 10 clusters identified (4.5% genetic distance) using clusterpicker. (B) Phylogeny of VB clade sequences and 100 background subtype-B sequences; red tips mark VB reference genomes.

Higher pVL and faster CD4 decline in VB vs non-VB participants



Proteomic Differences in VB vs non-VB



CONCLUSIONS

- The VB clade shows faster disease progression.
- The virulence of the clade is not mediated by coreceptor usage and DRMs.
- Perturbations in circulating immune and inflammation proteins were identified that related to accelerated disease progression observed in the VB clade. IL-32 is an antiviral cytokine that seems to be lower and therefore could lead to a more aggressive disease.

ACKNOWLEDGEMENT

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ADDITIONAL KEY INFORMATION

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ClinicalTrials.gov Identifier: NCT03994835