# HIV-1 reservoir size and diversity among acute-infected individuals

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## INTRODUCTION

- Early combined antiretroviral treatment (cART) of HIV infection aims to limit the seeding of the viral reservoir in the initial phase of infection, and, consequently, decreasing the intrahost viral diversity.

## OBJECTIVE

- To measure the effect of the cART in the size and complexity of the proviral reservoir.

## MATERIAL AND METHODS

- Peripheral blood mononuclear cell (PBMC) and plasma samples were obtained from ten HIV-infected individuals, diagnosed at the acute phase (Fiebig II-V) of infection, before ($Pre_{ART}$) and 12 months ($M12_{ART}$) after suppressive cART beginning.
- HIV proviral reservoir size was determined by quantitative real time PCR while the intrahost viral diversity of the *env* C2-V3 region was assessed by single genome amplification or next-generation sequencing in PBMC and plasma, respectively.
- The mean nucleotide diversity (π) and the normalized Shannon entropy ($H_{SN}$) were used to infer the complexity of the viral population.

## RESULTS

- The patients presented immunological recovery after 12 months under cART, with $CD4^+$ T cell gain (~200 cells) and $CD4^+/CD8^+$ ratios normalization (~1.0) (Fig. 1A & B).
- We observed significant decreases of HIV-1 RNA (~4 log) and DNA (~1 log) levels (Fig. 1C & D). The median time to achieve viral suppression was ~3 months (Fig. 2).
- The high intermixing between the sequences from both visits suggests that the HIV-1 DNA reservoir remained remarkably stable under cART (Fig. 3A).
- There was a slightly reduction in proviral π ($Pre_{ART}$=0.20 vs $M12_{ART}$=0.10) and a significant decrease in $H_{SN}$ ($Pre_{ART}$=0.41 vs $M12_{ART}$=0.25) after one year of cART (Fig. 3B).
- We found no correlation between π or $H_{SN}$ at $Pre_{ART}$ with the rate of HIV DNA decay, T $CD4^+$ cell change or $CD4^+/CD8^+$ ratios presented at $M12_{ART}$ (Fig. 4).

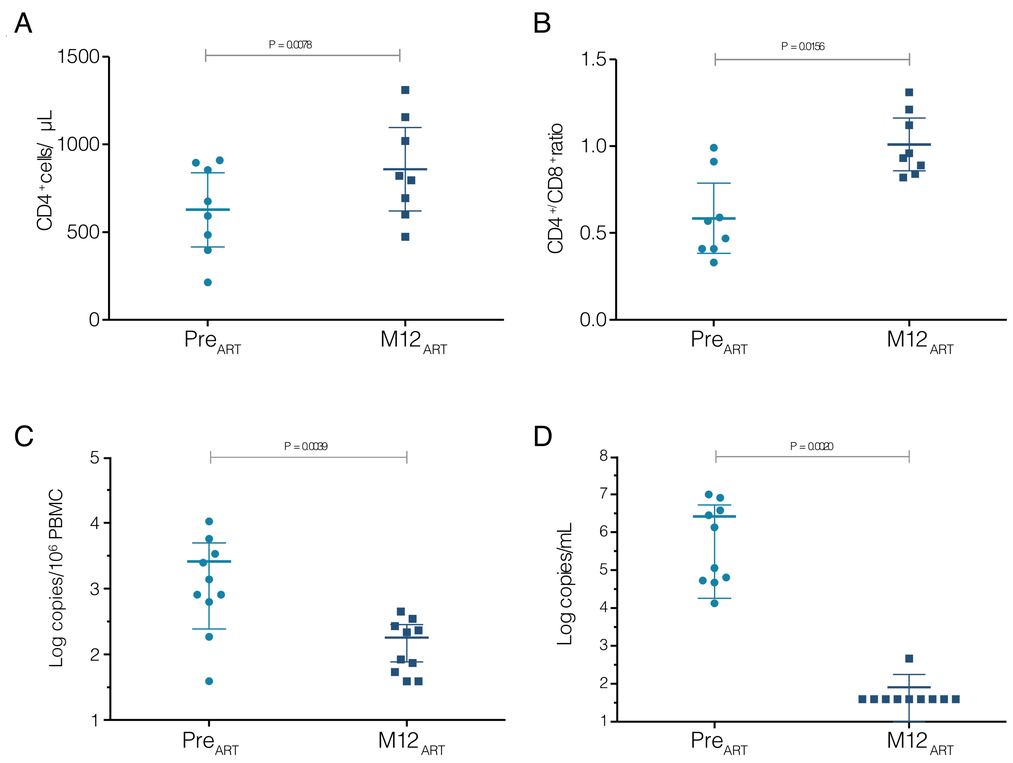


**Figure 1 – Immunologic and virologic measurements before and after cART initiation.** $CD4^+$ T cell counts (A), $CD4^+/CD8^+$ ratios (B), HIV-1 proviral load in PBMC (C) and HIV-1 plasmatic viral load (D) were measured at $Pre_{ART}$ and $M12_{ART}$ visits (colored light and dark blue, respectively). P values < 0.05 were considered statistically significant.

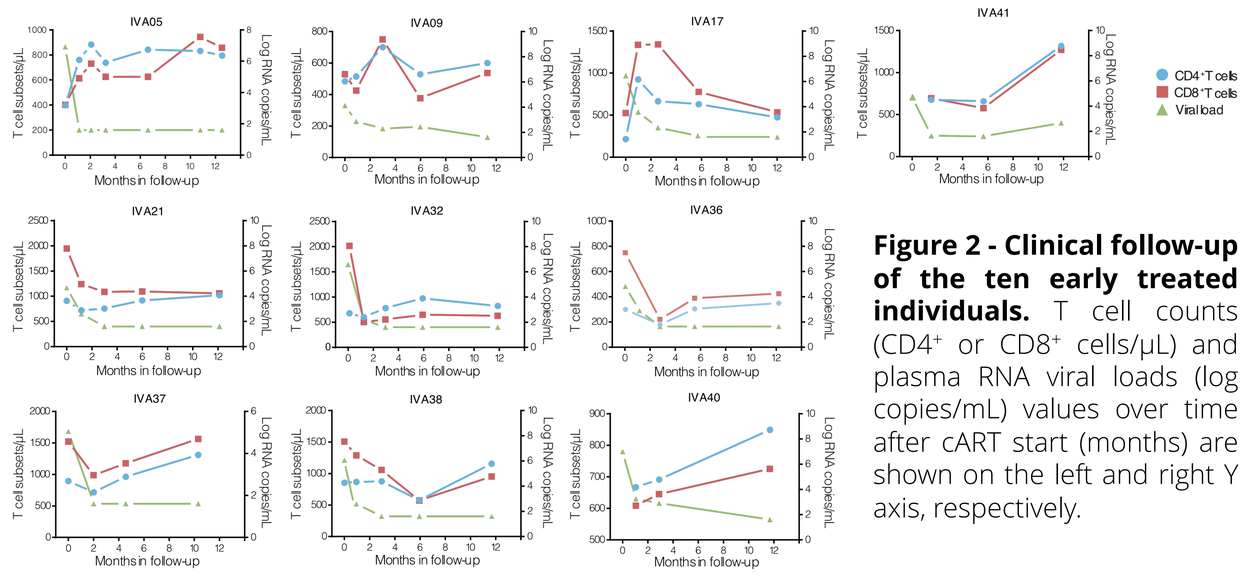


**Figure 2 - Clinical follow-up of the ten early treated individuals.** T cell counts ($CD4^+$ or $CD8^+$ cells/µL) and plasma RNA viral loads (log copies/mL) values over time after cART start (months) are shown on the left and right Y axis, respectively.

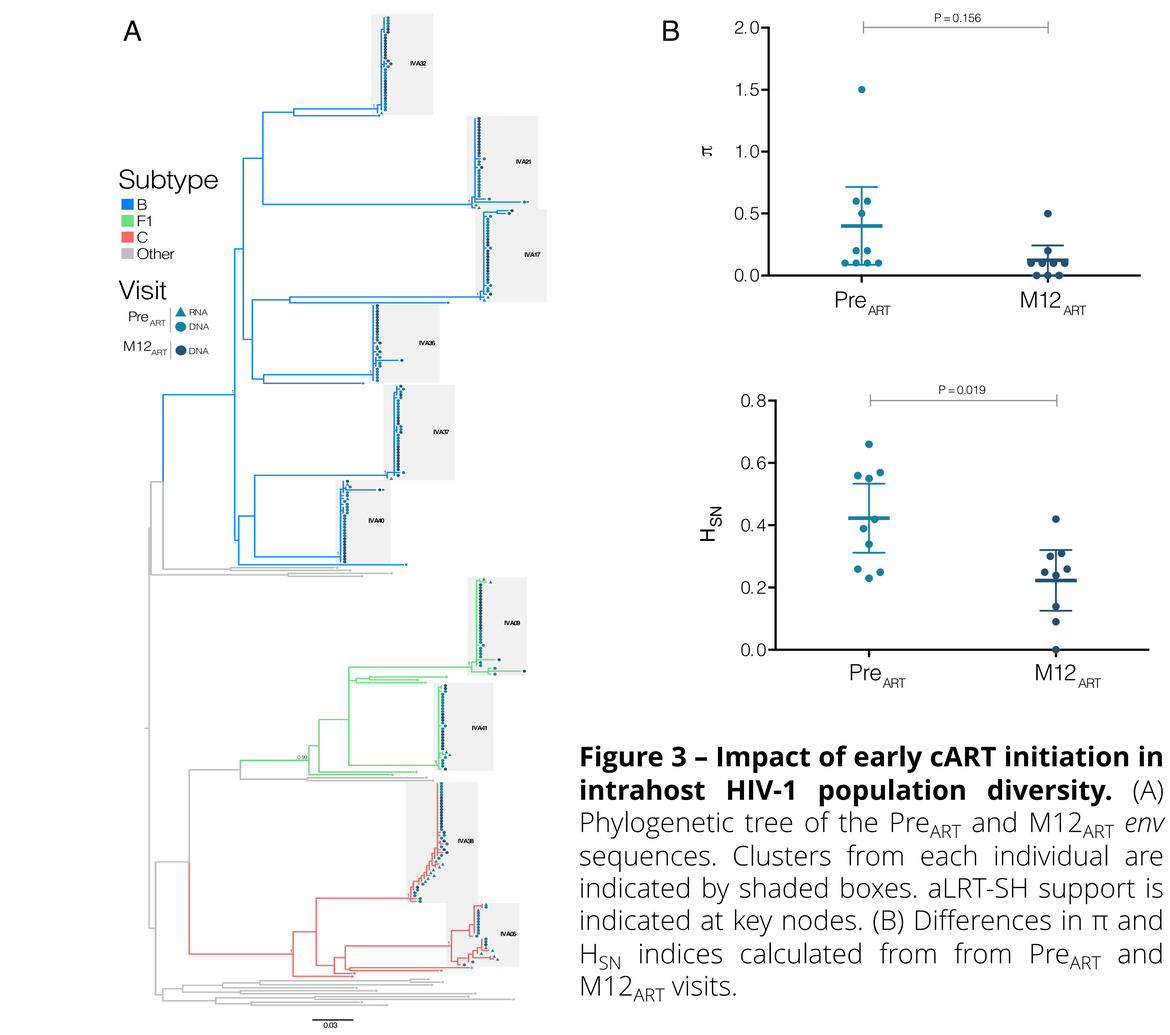


**Figure 3 – Impact of early cART initiation in intrahost HIV-1 population diversity.** (A) Phylogenetic tree of the $Pre_{ART}$ and $M12_{ART}$ *env* sequences. Clusters from each individual are indicated by shaded boxes. aLRT-SH support is indicated at key nodes. (B) Differences in π and $H_{SN}$ indices calculated from from $Pre_{ART}$ and $M12_{ART}$ visits.

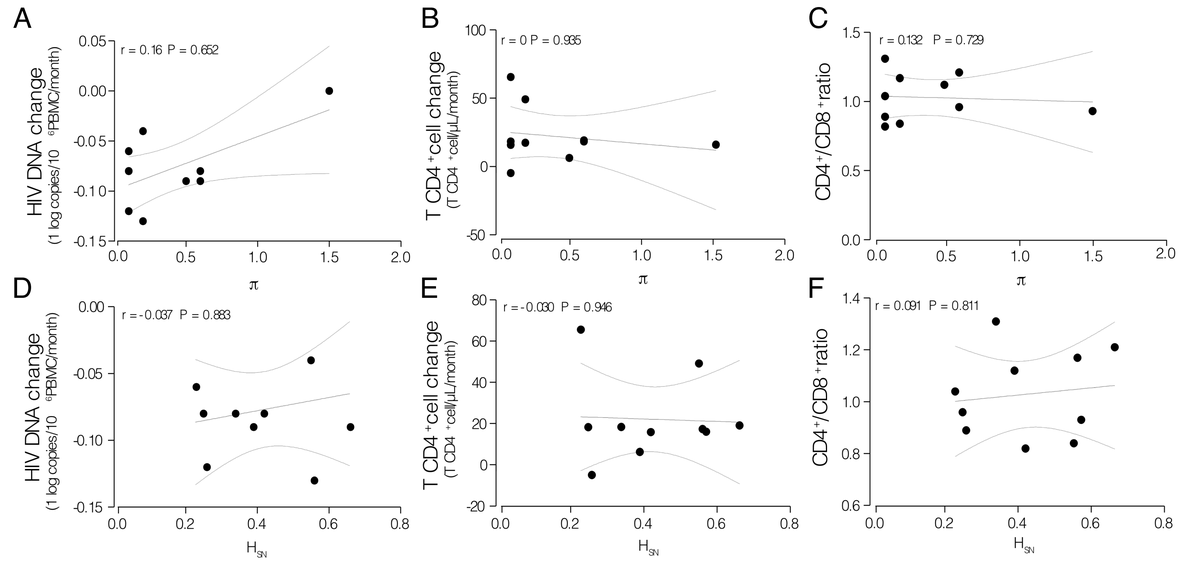


**Figure 4 - Correlations between proviral HIV-1 diversity indices and immunologic and virologic measurements**. The HIV decay in PBMC, T $CD4^+$ cell change and $CD4^+/CD8^+$ ratios in $M12_{ART}$ visit were compared with the π (A, B and C) and $H_{SN}$ (D, E and F) indices.

## CONCLUSION

- One year of cART initiated in acute phase fo HIV-1 infection was sufficient to reduce the size and complexity of proviral reservoir, and to achieve immunological restoration, independently of the HIV-1 plasmatic viral load, $CD4^+$ T cells count or HIV-1 subtype.

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Support: CAPES FAPERJ Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro CNPq Conselho Nacional de Desenvolvimento Científico e Tecnológico