

Effect of Thymic Output on the Homeostasis of the HIV Reservoir

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Conflict of interest disclosure

The authors have no conflict to declare.

Introduction

The main mechanism of HIV persistence in suppressed individuals is the **survival and proliferation** of latently infected CD4+ T cells. The activity of the thymus, a key player in the **homeostasis of the T cell compartment**, is known to decrease with age.

Hypothesis and objectives

We hypothesized that the **age-associated thymic involution could contribute to the persistence of HIV reservoir** in older people.

Our objectives are to assess:

- ➡ The size of HIV reservoir in older infected individuals
- ➡ The relationships between the generation of new non-infected naive T cells, immune phenotype and markers of HIV persistence

Methodology

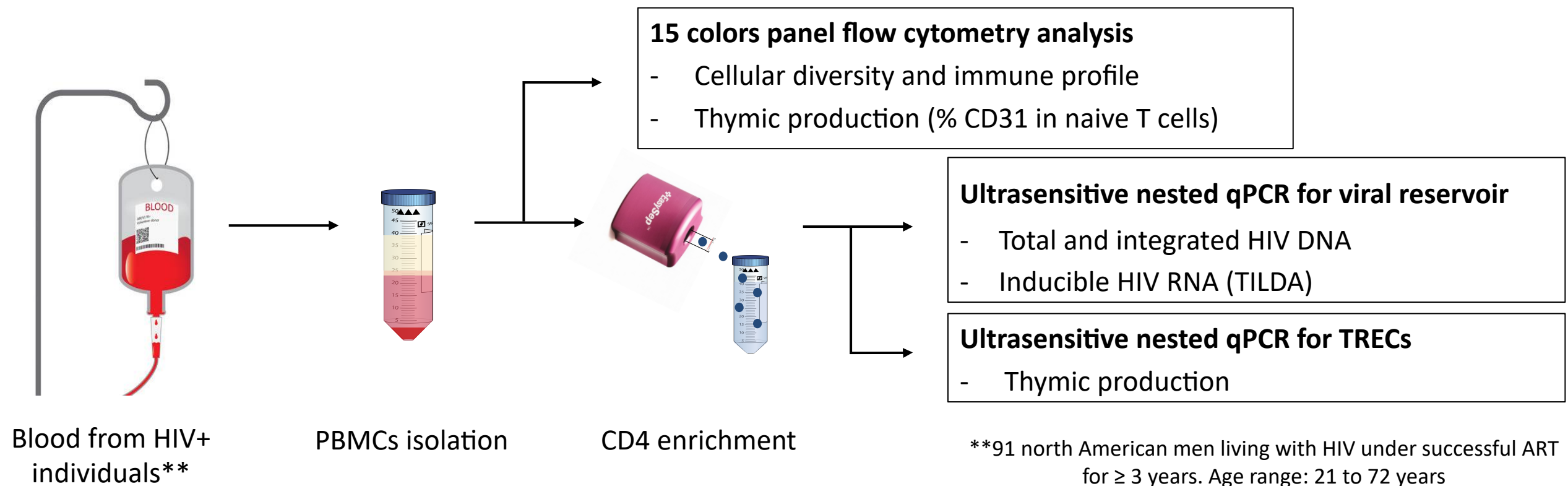
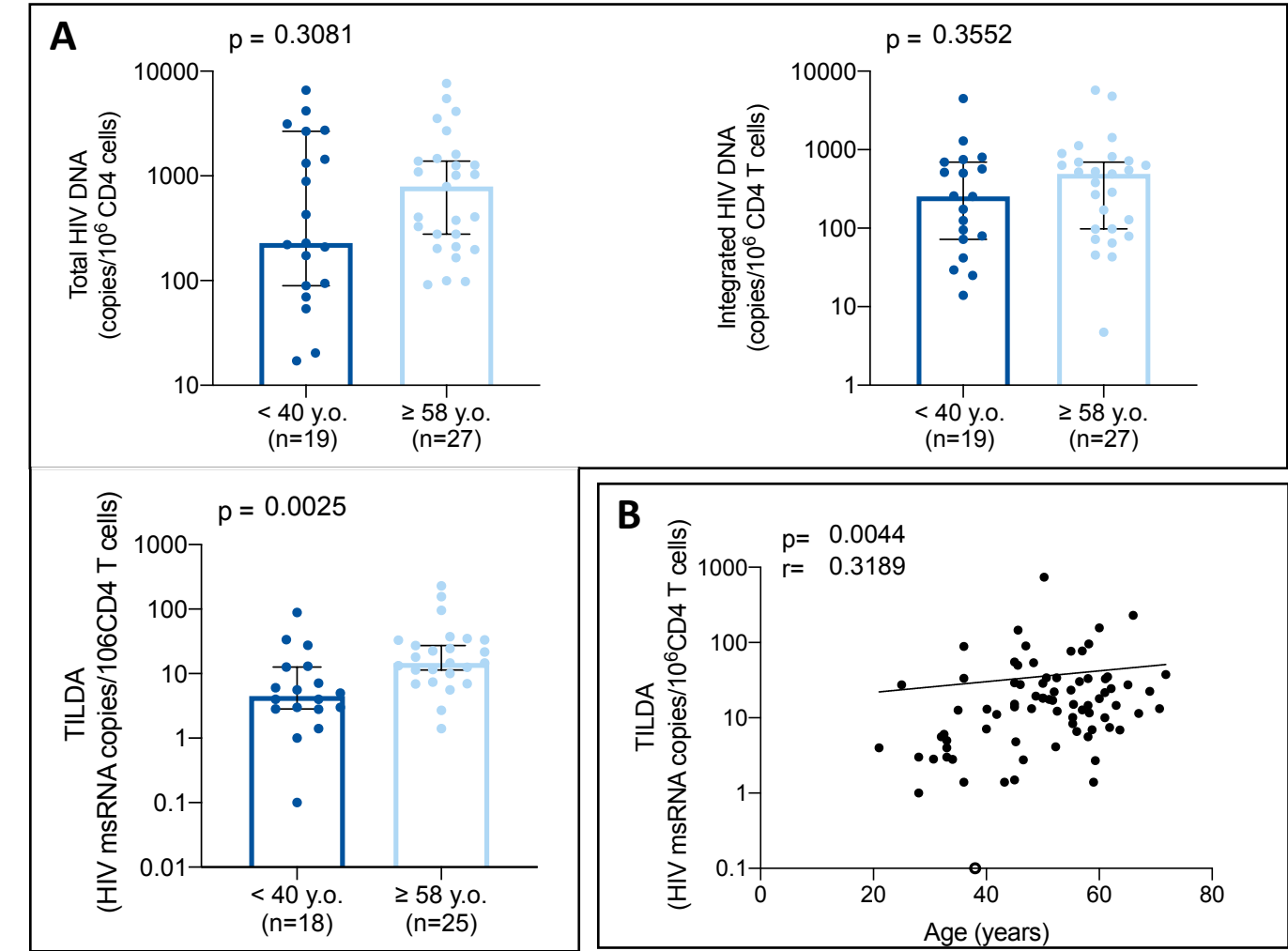
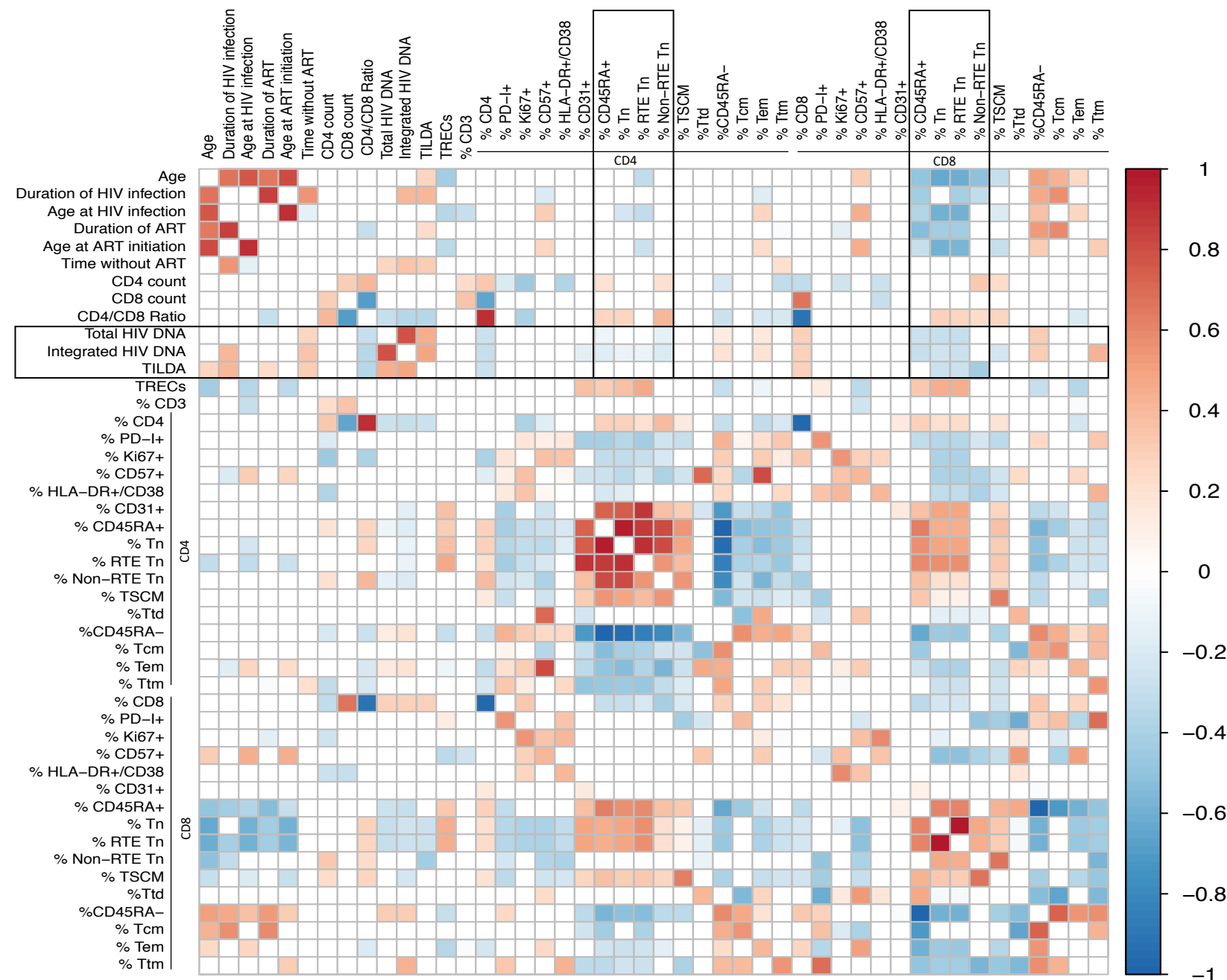


Figure I. Impact of aging on markers of HIV persistence (n=78)



- ➡ Inducible HIV RNA (TILDA), but not integrated nor total HIV DNA, is larger in individuals ≥ 58 y.o. when compared to their younger counterparts (A).
- ➡ The age of the participants is positively associated with TILDA measures (B).

Figure II. Correlation matrix for age related factors and HIV persistence markers (n=91)



- ➡ Several markers of HIV persistence are negatively associated with the frequency of RTE in both the CD4 and CD8 compartments
- ➡ A main confounding factor in our study is the duration of HIV infection, which is associated with age and both TILDA and integrated HIV DNA measures.

Figure III. Impact of age on markers of thymic output (n=82)

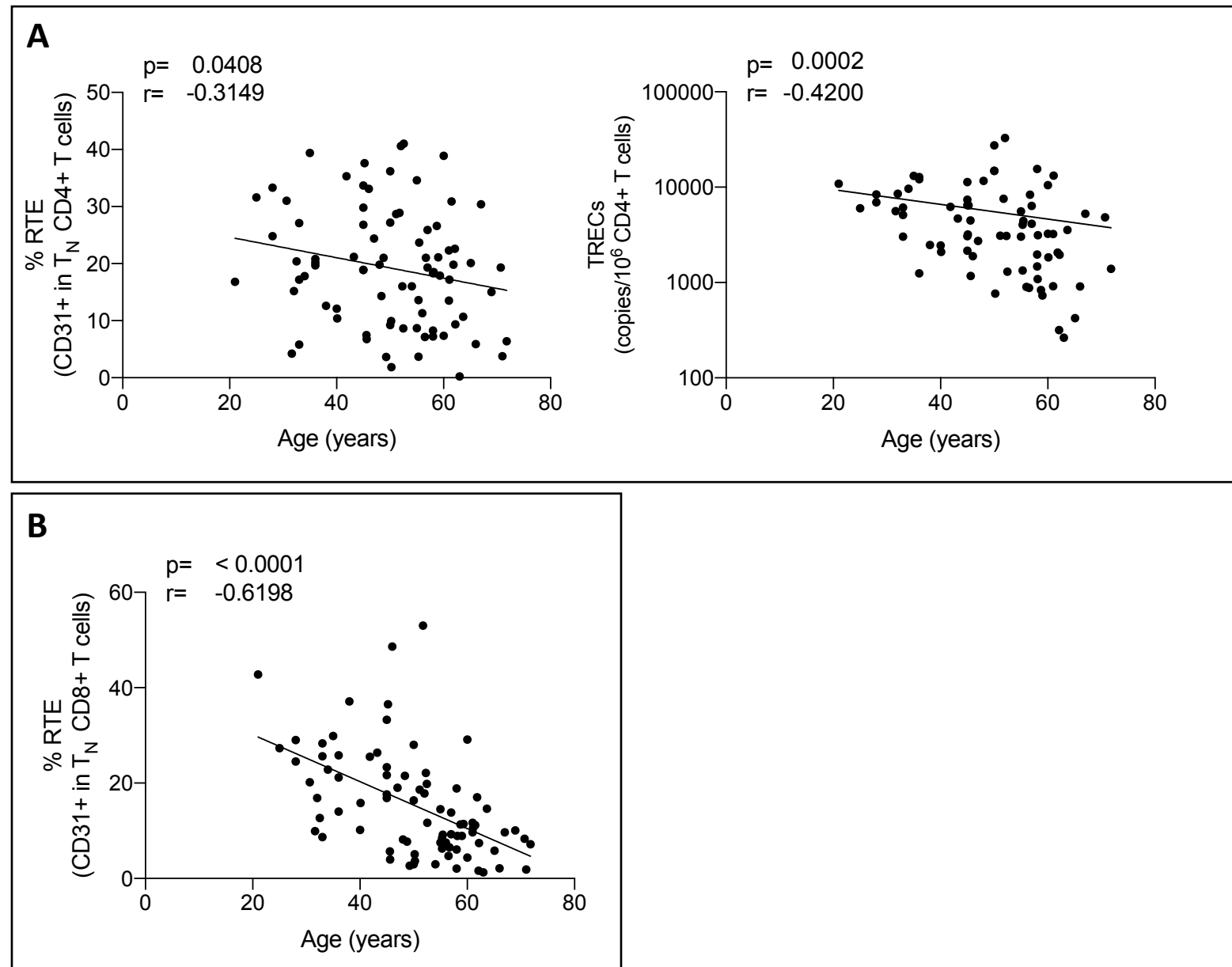
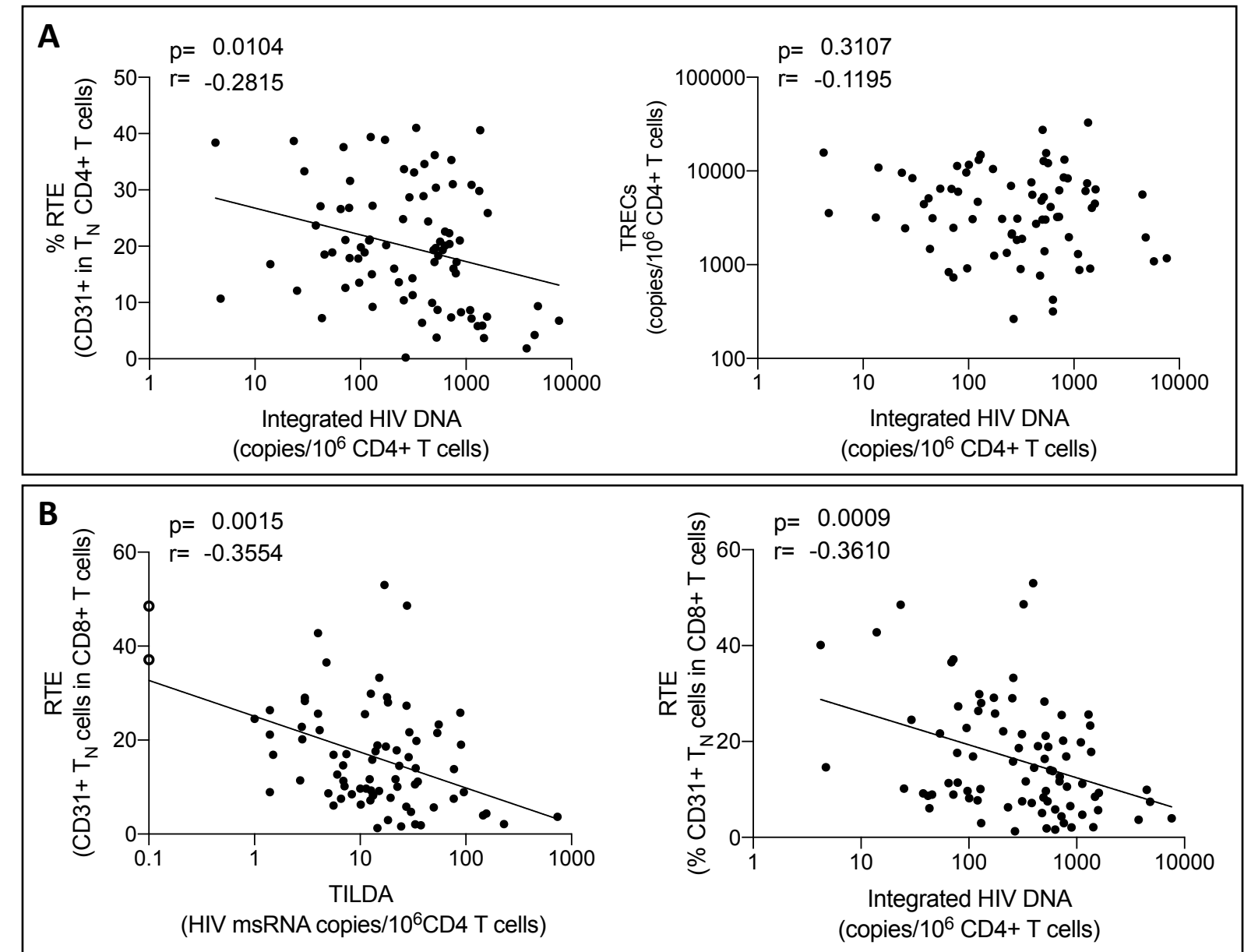


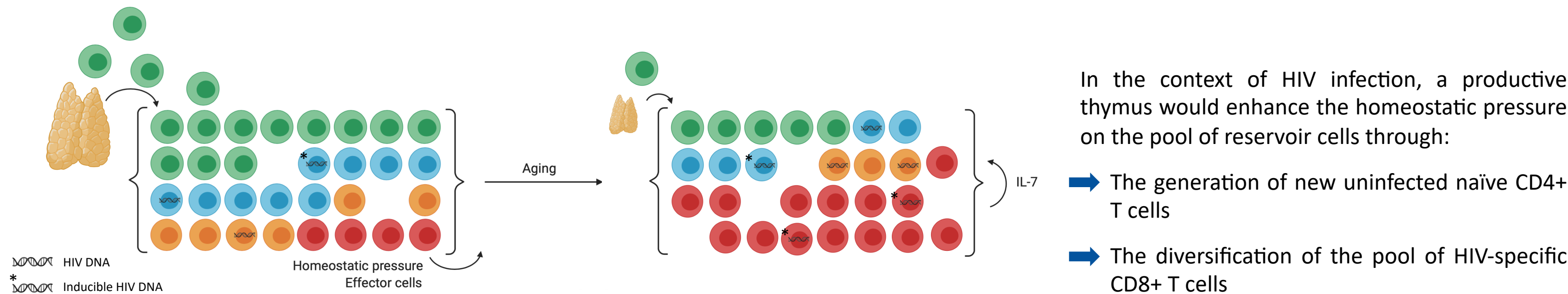
Figure IV. Impact of thymic output on HIV persistence markers (n=82)



- ➡ Thymic output of CD4+ T cells measured by 2 approaches (CD31 expression in naives and TRECS) correlates with age (A).
- ➡ Thymic output of CD8+ T cells measured by CD31 expression in naïve cells strongly correlates with age (B).

- ➡ The frequency of recent thymic emigrants (RTEs) in the CD4 compartment, measured by CD31 expression in naïve cells, is negatively associated with the levels of integrated HIV DNA. However, there is no association between TRECs levels and integrated HIV DNA (A).
- ➡ The frequency of recent thymic emigrants (RTEs) in the CD8 compartment is negatively associated with TILDA measures and levels of integrated HIV DNA (B).

Figure V. Model of the proposed dynamics



Discussion

- ➔ A better understanding of the mechanism of HIV persistence, particularly in the context of aging, is essential to achieve a cure for HIV.
- ➔ Our results suggest that thymic output exerts a pressure on the HIV reservoir and that thymic involution may contribute to a larger inducible reservoir in older individuals.
- ➔ Our results suggest that restoring the thymic function in people living with HIV may accelerate the decay of the HIV reservoir during ART. We are currently testing this hypothesis in a clinical trial.

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