Decreased frequency of colon-resident memory T cells is associated with HIV-1 persistence on ART

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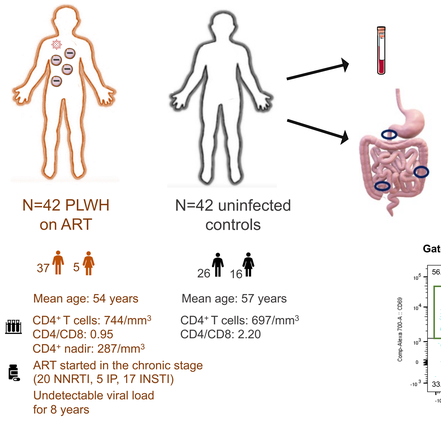
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BACKGROUND

The gut is a major target for HIV-1 replication and persistence. Tissue-resident memory (TRM) cells play a critical role in mucosal immunity, but this cell population could be compromised by HIV-1 replication in the mucosa. Their depletion may contribute to a persistent imbalance in mucosal homeostasis and the persistence of HIV-1 in the gut on ART.

METHODS

ANRS EP61 GALT study



RESULTS

CD4+ and CD8+ TRM cells were significantly depleted in the colonic mucosa of PLWH compared to uninfected controls (Fig. 1)

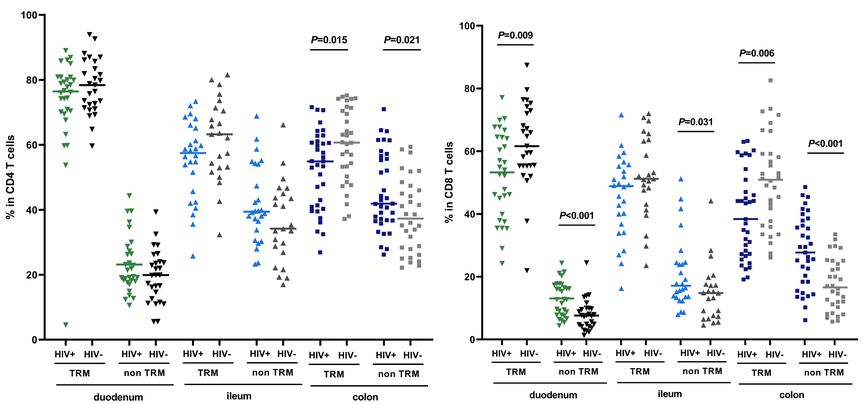
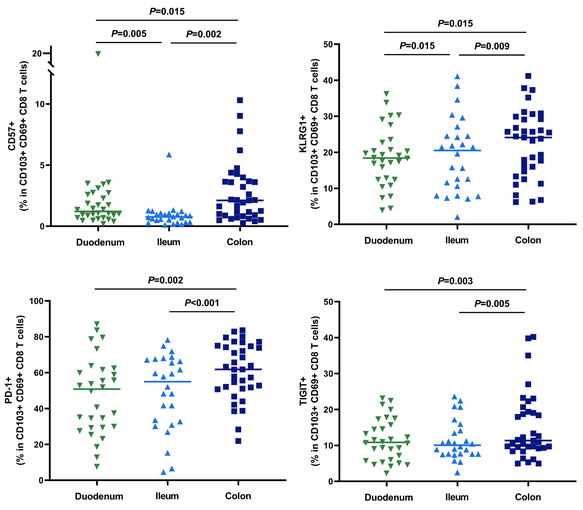


Fig. 1. Frequency of CD4+ and CD8+ TRM and non-TRM in the duodenum, ileum and colon *lamina propria* of PLWH on suppressive ART and uninfected controls, measured by flow cytometry.

TRM are depleted in the intestinal mucosa of PLWH on ART, particularly in the colonic mucosa, and this depletion is associated with HIV-1 persistence in the colon.



CD8+ TRM from the colon express higher levels of activated/exhausted markers (CD57, KLRG1, PD1 and TIGIT) than CD8+ TRM from the duodenum and the ileum of PLWH on suppressive ART (Fig. 2).

Fig. 2. FACS phenotyping of CD8+ TRM in the duodenum, ileum and colon of PLWH on ART.

Colonic mucosa non-TRM are overall more activated/exhausted than TRM in PLWH on suppressive ART (Fig. 3).

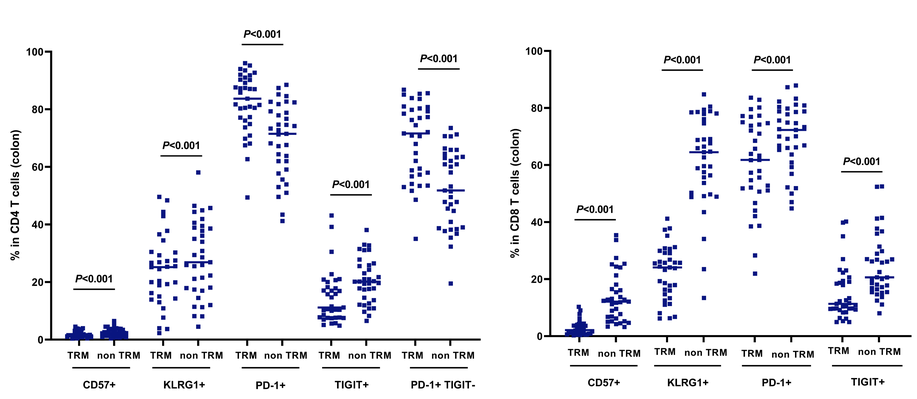


Fig. 3. Expression of activated/exhausted markers on CD4+ and CD8+ TRM and non-TRM from the colonic mucosa of PLWH on suppressive ART, measured by flow cytometry.

CD4+ and CD8+ TRM cell frequencies were negatively associated with total HIV-1 DNA and residual HIV-1 RNA, while non-TRM cells were associated with higher quasispecies genetic complexity (Fig. 4).

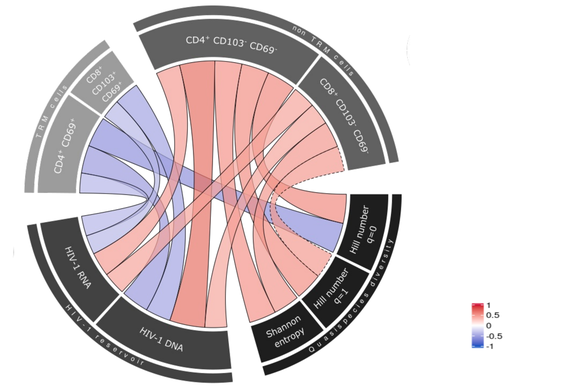


Fig. 4. Associations between TRM and non-TRM and HIV-1 reservoir in the colon of PLWH on ART.

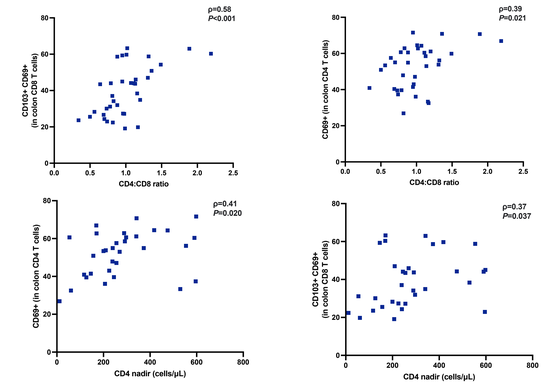


Fig. 5. Associations between colon TRM and CD4 T cell nadir and the CD4:CD8 ratio in PLWH on ART.

CONCLUSIONS

The frequencies of CD4+ and CD8+ TRM cells remained reduced in PLWH on ART, particularly in the colon. Irreversible damage to these cell populations may have occurred prior to ART initiation. The loss of these cells may promote HIV-1 persistence in the colon.

ADDITIONAL KEY INFORMATION

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