Monocytes/macrophages contribute only marginally to the gut reservoir of HIV-1 on ART

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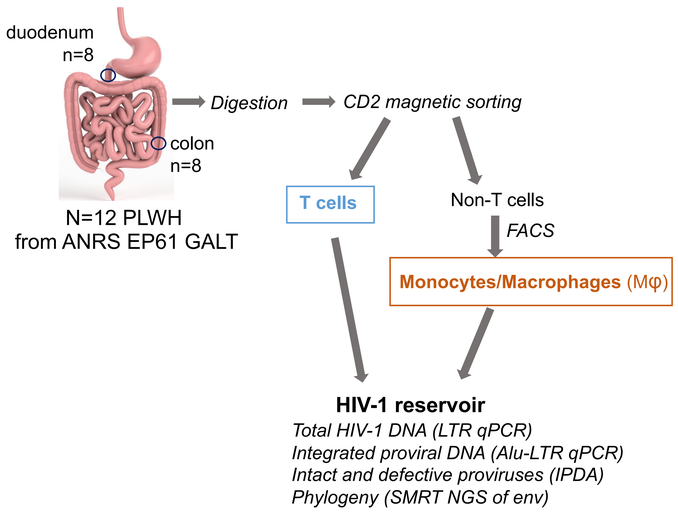
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BACKGROUND

Current antiretroviral treatments (ART) are unable to cure HIV-1 infection due to the persistence of latently infected cells. The gut mucosa contains numerous target cells, and high levels of HIV-1 DNA persist in this compartment under ART. CD4$^+$ T cells are the best characterized reservoir of HIV-1. However, macrophages are abundant long-lived cells in the gut, but their involvement in HIV-1 persistence on ART remains controversial.

METHODS



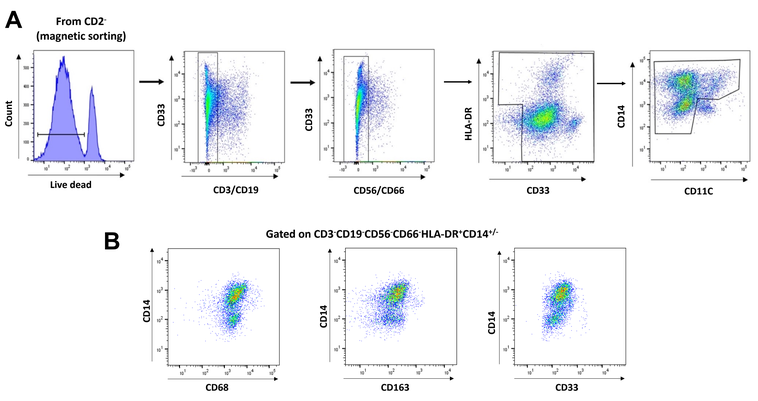


Fig. 1 Sorting strategy of intestinal Mφ from an intestinal mucosal biopsy (A), and verification of the phenotype of sorted Mφ (B)

Monocytes/macrophages from the intestinal mucosa of both the duodenum and colon of PLWH on suppressive ART contain 300-fold less HIV-1 DNA than T cells. We found compartmentalization of HIV-1 sequences between monocytes/macrophages and T cells of the duodenum and colon in some subjects.

RESULTS

Total HIV-1 DNA levels in intestinal T cells (median 3,398 copies/10^6 CD4$^+$ T cells) were significantly higher than those in Mφ (median 12 copies/10^6 Mφ) (P<0.001) (Fig 1). Unintegrated HIV-1 DNA was detected in one-third of the T cell and Mφ-positive samples. Using the IPDA, we detected intact HIV-1 proviruses in 4/16 of the T cell samples but only in 1/6 of the Mφ samples (Fig 2). Phylogenetic analyses of viral quasispecies revealed viral compartmentalization between intestinal T cells and Mφ in 2/3 of subjects analyzed (Fig 3).

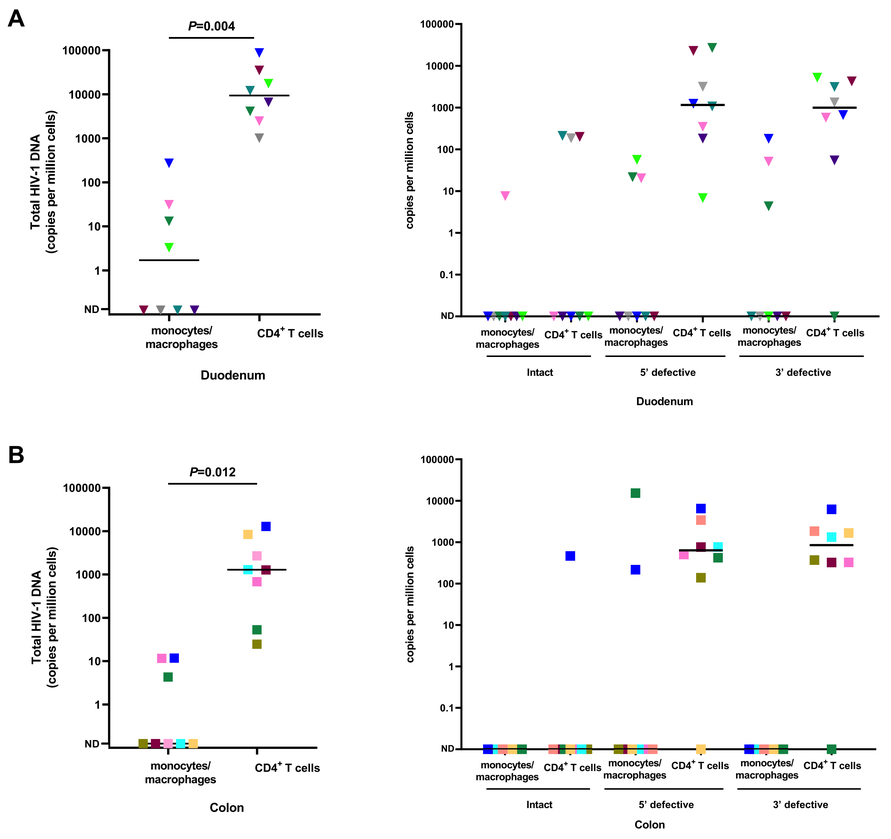


Fig. 2. Levels of total HIV-1 DNA, intact and defective HIV-1 proviruses in Mφ and CD4$^+$ T cells sorted from the duodenum (A) and the colon (B) of 12 PLWH.
Each color corresponds to a sample from the same PLWH. ND: not detected.

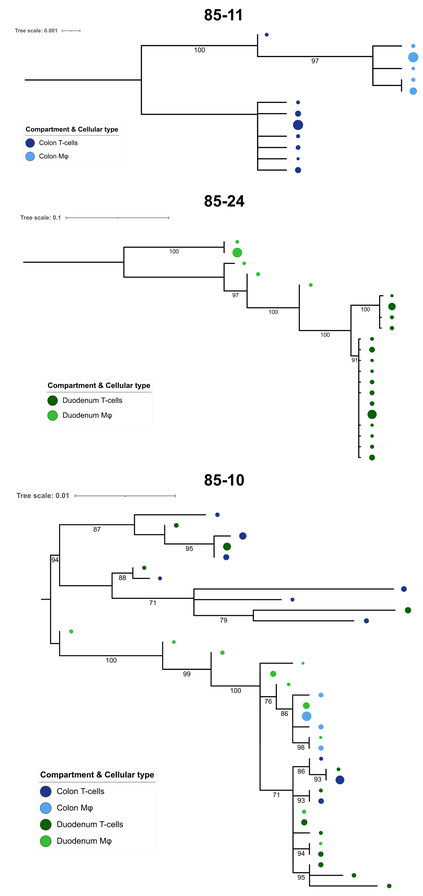


Fig. 3. Phylogenetic trees of HIV-1 *env* sequences from three PLWH on ART. The size of the disks is proportional to the number of reads for each sequence.

CONCLUSIONS

Monocytes/macrophages from the intestinal mucosa of both the duodenum and colon of PLWH on suppressive ART can contain HIV-1 DNA, even intact or unintegrated, but at much lower levels (300-fold lower) than those found in T cells. In addition, our results showed that in some cases compartmentalization of HIV-1 sequences can be found between monocytes/macrophages and T cells on ART.

ADDITIONAL KEY INFORMATION

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