RECTAL CCR6+ CD4+ T-CELLS ARE AN IMPORTANT RESERVOR IN HIV-INFECTED INDIVIDUALS ON ART

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Background:
In HIV-infected individuals on antiretroviral therapy (ART), HIV integrated DNA is enriched in blood central memory CD4+ T-cells expressing CCR6 and CXCR3. As these chemokine receptors (CKR) enable homing of CD4+ T-cells to tissue, we examined if expression of CKR or their chemokine ligands were associated with HIV persistence in rectal and lymph node (LN) tissue in individuals on suppressive ART.

Methods:
Blood (n=48), rectal (n=19) and inguinal LN (n=8) biopsies were collected from individuals on suppressive ART ≥3 years. HIV integrated DNA (intDNA) and unspliced RNA (US-RNA) were quantified by PCR in total CD4+ T-cells sorted from each site. CKR expression was measured via flow cytometry. Chemokine mRNA in tissue was measured by RT-qPCR. Relationships between HIV persistence and CKR or chemokine expression were assessed via negative binomial regression.

Results:
In CD4+ T-cells from rectum, HIV intDNA and US-RNA was 3.9- and 4.6-fold higher than blood respectively (both $p<0.0001$), and intDNA was 2.4-fold higher than LN ($p=0.014$). CCR6+CXCR3+CD4+ T-cells were more frequent in rectum versus blood or LN (69.8%, 21.6% and 12.4% respectively, Kruskall Wallis $p<0.0001$). CCL20 (ligand for CCR6) was also 12.7-fold higher in rectum versus LN.

In rectum, HIV intDNA and US-RNA positively associated with the frequency CCR6+CXCR3-CD4+ T-cells ($p=0.025$ and $p=0.030$ respectively) but inversely associated with the frequency of CCR6+CXCR3+CD4+ T-cells ($p=0.028$ and $p=0.027$ respectively). Overall, the median contribution of infected CCR6+CXCR3+ T-cells was 78% of the total HIV burden in rectum. Different associations were observed for CD4+ T-cells in LN.

Conclusion:
Rectal tissue from individuals on ART has high CCR6+CXCR3+CD4+ T-cells, high CCL20 expression and positive association between HIV persistence and CCR6+CXCR3-CD4+ T-cell frequency. CCR6+CXCR3+CD4+ T-cells are a major

component of the HIV reservoir in rectum. Interventions blocking CCR6-CCL20 should be explored as a strategy to reduce HIV persistence in rectal tissue on ART.

Disclosure of Interest Statement:
SRL and JLA perform collaborative research with Merck and Infinity Pharmaceuticals that is unrelated to this study.