HIV PERSISTENCE IN LYMPH NODE TISSUE AND PERIPHERAL BLOOD: THE ROLE OF IMMUNE CHECKPOINTS

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Background:
In HIV-infected individuals on antiretroviral therapy (ART), latent HIV is enriched in $CD4^+$ T-cells expressing immune checkpoints (ICs). We aimed to explore the relationship of two ICs, programmed cell death-1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), with HIV persistence, in both blood and lymph node (LN).

Methods:
HIV-infected adults on suppressive ART (plasma viral load <50 copies/mL for >3 years), underwent leukapheresis and LN biopsy (n=6). Blood and LN memory $CD4^+$ T-cells ($CD45RA^-CD3^+CD4^+$) were sorted via flow cytometry into double negative (DN; $PD\text{-}1^-CTLA\text{-}4^-$), double positive (DP; $PD\text{-}1^+CTLA\text{-}4^+$) and single positive (SP PD-1/ SP CTLA-4) populations. Cell-associated total HIV DNA, unspliced (US) HIV RNA and inducible multiply-spliced (MS) HIV RNA (tat/rev induced limiting dilution assay) were quantified in the sorted populations. An interim descriptive analysis of the cohort is described. Comparisons were made using a Wilcoxon-signed rank test.

Results:
The level of HIV DNA in memory $CD4^+$ T-cells was 1.8-fold greater in LN (median of 411 copies/million cells) compared to blood (222 copies/million cells). In blood, HIV DNA was significantly enriched in both the SP CTLA-4 (1.5-fold increase; p=0.03) and DP (1.7-fold increase; p=0.03) cells, while there was no enrichment in the SP PD-1 population compared to DN cells. In comparison, in LN, HIV DNA was enriched in all PD-1/CTLA-4 expressing populations. A trend towards increased US HIV RNA (blood and LN) was observed for all PD-1/CTLA-4 expressing populations when compared to the DN population. In blood, there were less cells containing inducible MS HIV RNA in all IC expressing populations compared to DN cells.

Conclusion:
Despite the enrichment of HIV in cells that express CTLA-4 alone or in combination with PD-1, there is less inducible MS HIV RNA in these cells, suggesting that latent HIV may be more resistant to reactivation in IC^+ cells compared to IC^- cells.