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Oral presentation

OA031-01. HIV-1 infection is characterized by early loss of CD161+ Th17 cells and gradual decline in regulatory T cells

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Background

CD4 cell depletion is central to HIV pathogenesis. However, CD4 cells present diverse lineages and the relative impact of HIV on Th17 and regulatory T cell (Treg) subsets remains unclear. CD161+ CD4 cells are a recently identified, gut-homing population with Th17 precursor potential. The balance between pro-inflammatory Th17 cells and immunoregulatory Tregs may be critical in HIV pathogenesis. This study addressed changes in CD161+, Th17 and Treg subsets during untreated HIV infection.

Methods

Peripheral blood mononuclear cells (PBMC) were isolated from 77 untreated HIV-infected and 36 HIV-uninfected subjects and stained with fluorochrome-conjugated monoclonal antibodies to characterize CD161+ CD4 cells; Th17 cells (expression of CCR6 and elaboration of IL-17A after PMA/ionomycin stimulation); Tregs (CD4+CD25hiFoxP3+ cells); and CD8 activation (CD38+/HLA-DR+ cells). *In vitro* infectability of CD161+ and Th17 cells was assessed by incubating activated healthy donor CD4 cells with HIV Bal for 5 days and co-staining for CD161/IL-17A and intracellular p24.

Results

Peripheral blood Th17 cells were depleted 10-fold in HIV-infected, compared to HIV-uninfected, subjects ($P < 0.0001$) across a range of disease stages, accompanied by a significant reduction of CD161+ T cells ($P = 0.024$). Both Th17 cells and CD161+ CD4 cells were highly targeted by HIV *in vitro*. The preferential and early loss of Th17 cells contrasted with a gradual decline in absolute Treg numbers during HIV disease progression in untreated subjects followed longitudinally ($R = 0.71$, $P = 0.003$). Loss of Tregs was associated with increased immune activation ($R = -0.33$, $P = 0.03$).

Conclusion

HIV-infected subjects showed preferential loss of Th17 and CD161+ CD4 subsets, which were both highly targeted by HIV *in vitro*. Loss of CD161+ cells, which are Th17 cell precursors, may limit Th17 reconstitution. A gradual decline in Tregs during disease progression was associated with increased immune activation. Loss of both Th17 and Treg subsets may enhance disease progression through impaired mucosal defences, and increase in immune activation.