T cell activation positively correlates with cell-associated HIV-DNA level in PBMCs in viremic patients with acute or chronic HIV-1 infection

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Objective: To evaluate the relationship between levels of T-cell activation and HIV-DNA in PBMCs in viremic patients with acute or with chronic HIV infection before and after antiretroviral treatment (ART) interruption (TI).

Methods: Patients with chronic infection (CHI) included in a substudy of the ANRS 116 SALTO trial, a multicenter study of TI that enrolled patients who started ART with CD4 count >350 /mL and VL < 50,000 copies/ml and exhibiting at TI (baseline) CD4 counts >450/mL and VL < 400 copies/ml were selected for the study and monitored at BL and M12 of TI. Patients diagnosed with primary HIV infection (PHI) were also investigated before introduction of cART. CD4 and CD8 T cell activation were analyzed in relation with HIV-DNA level in PBMCs using Spearman tests.

Results: In ART-treated CHI patients (n=25), at baseline, median (IQR) level of HIV-DNA was 2.56 log copies/10^6PBMCs (2.00; 2.93) while at 12 months of TI, median (IQR) HIV-RNA and HIV-DNA levels were 4.25 (3.69; 4.57) and 3.13 (2.67; 3.49), respectively. At baseline, there was no relationship between HIV-DNA levels and T-cell activation, whether assessed by expression of HLA-DR and/or CD38 on CD4 CD8 T cells. In contrast, at M12 of TI, HIV-DNA levels strongly correlated with the proportion of CD8 and CD4 T cells expressing CD38 ($r=0.77$, $p< 10^{-3}$ and $r= 0.72$, $p< 10^{-3}$, respectively). In untreated PHI patients (n=22), plasma HIV-RNA and HIV-DNA levels were 5.7 (4.8; 6.1) and 3.7 (3.0; 4.0), respectively. Again, HIV-DNA levels correlated with the proportion of CD8 expressing Ki-67 ($r= 071$; $p< 10^{-3}$), CD38 ($r= 0.64$, $p=0.001$) and co-expressing HLA-DR and CD38 ($r= 0.47$; $p=0.034$). Moreover, HIV-DNA levels also correlated with the proportion of HLA-DR+CD4 T cells ($r= 0.53$; $p= 0.013$) and Ki67+CD4 T cells ($r= 0.61$; $p= 0.003$).

Conclusions: Levels of T-cell activation positively correlate with HIV-DNA levels in viremic patients with acute or chronic infection. The lack of association between HIV-DNA levels and T-cell activation in ART-treated patients suggests that the residual immune activation is not directly dependent on the size of the latent HIV reservoir at least in early ART-treated patients.