The Preservation of Thymic activity and the naïve T cell Compartment is a Hallmark of HIV-2 and early treated HIV-1 Individuals

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Background

Antiretroviral therapy (ART) markedly improved disease prognosis, however ART-treated subjects maintain some degree of immune activation eventually associated with comorbidities. Importantly, HIV-2 infected individuals also feature significant immune activation, despite a relatively benign course and low to undetectable plasma viral load even in the absence of ART. To better understand the mechanisms underlying persistent immune activation, we investigated the correlation profile of immune parameters in circulating lymphocyte subsets of HIV-1 and HIV-2 infected individuals under effective ART. We specifically asked which parameters would allow the segregation of: 1) HIV-2 from HIV-1 infection; and 2) HIV-1 individuals who started ART during acute infection (early ART) and those who started during the chronic stage (late ART).

Aim

We investigated the correlation profile of high-dimensional immune parameters in the main circulating lymphocyte subsets of cohorts of HIV-1 and HIV-2 treated infected individuals, with effective ART as attested by undetectable plasma viral load, to better understand the mechanisms underlying chronic immune activation.

Conclusions

Remarkably, there was an overlap of the immune profile of early treated HIV-1 infected and seronegative cohorts, emphasizing the relevance of early ART.

B cell clusters mainly contribute to the segregation of HIV-2 infected individuals, which may be related to the impact of the prolonged HIV-2 disease in the secondary lymphoid organs.

Regarding B T cell clusters these were the main segregators of HIV-1 infected patients treated early versus later. Strikingly, the CD31+ naïve CD4+ T cell cluster, which includes the recently produced T cell in the thymus (recent thymic emigrants, RTEs), distinguishes the three HIV infected cohorts, indicating that HIV-2 and early treated HIV-1 patients better preserve naïve CD4+ T cell homeostasis. Since all individuals had undetectable viremia and comparable levels of immune-activation parameters, it is likely that HIV-2 infection and early HIV-1 treatment are associated with a better preserved thymic activity and/or proliferative capacity and survival of naïve CD4 T cells. This is observed despite HIV-2 individuals being older.

Identifying underlying mechanisms may help counteracting deleterious effects of the persistent inflammation in patients under ART.

Patients and Methods

To profile chronic immune activation, we enrolled patients who started ART while seroconverting (early ART, n=12), late ART HIV-1 infected individuals (n=11), HIV-2 infected individuals (n=9) along with seronegative individuals (n=11). We stained 5 million circulating leucocytes in whole blood, with a panel of combined 18 markers allowing the discrimination of cell differentiation stages and levels of activation of CD4+ and CD8+ and naïve T cells, NK and B cells by spectral flow cytometry. For a clear and comprehensive visualization of these populations and their respective phenotypes, we applied dimension reduction and clustering algorithms. We then generated corregograms and PCA analysis to uncover patterns of immune activation, integrating all main lymphocyte subsets and correlate the resulting profile with clinical parameters.

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