Skewed distribution of HIV-2 reservoir with limited input of central memory T-cells

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BACKGROUND AND OBJECTIVES

HIV-2 is a Lentivirus responsible for a less pathological infection than the infections caused by HIV-1, and characterized by a slower clinical progression, a prolonged maintenance of peripheral CD4 lymphocytes, a lower rate of CD4 T-cell depletion and a lower risk of the development of AIDS defining events. However, HIV-2, like HIV-1, is integrated but inactive in infected cells, which is considered to be a potential long-term reservoir of the virus in vivo at least in the CD4+ cells. The objectives were:

- To analyse the latent and inducible blood reservoir of HIV-2, the immune activation in the different sub-populations of peripheral CD4 cells from uninfected patients of the HIV-2-defining CD4+ cohort.
- To compare in the same patients the correlations between the reservoir results and the immunological characteristics of immune activation, and with other factors (such as lymphoid sampling, age, HIV-2 CD4 T-cell reservoir and HLA which are also determined) possibly on an ANRS research center.

The aim of this study was to evaluate the correlation and activation of the HIV-2 reservoir of patients already included in the ALT-EC (Assay of Long-Term engineered Monocytes CD4+ cells from uninfected subjects).

SUBJECTS AND METHODS

Patients: The patients characteristics are reported in Table 1. The study is performed on at least 14 samples from patients infected with HIV-1 of the cohort ANRS-CO5, including 11 Copenhagen (T3 Long-Term Follow-up) and 3 progressors.

Methods: The whole reservoir is studied in sorted CD4+ subsets from CD4-depleted cells as follows. The cells have been thawed and depleted from CD8 cells. Sorting CD4+ cells is performed on the FACS-Aria II system placed in a 4°C, to preserve the same population for the CD4+ [CD4+ (CD8-) and CD4+ (CD8+)], CD4+ (CD107d+) cells.

- **Total reservoir:** CD4+ (CD107d+) + CD4+ (CD8-) + CD4+ (CD8+).
- **Cellular reservoir:** CD4+ (CD107d+) + CD4+ (CD8-)
- **Peripheral reservoir:** CD4+ (CD8-)

Each sample contributes to the pool of infected CD3 T cells that are responsible for the transmission of HIV to CD4+ T cells and CD8+ T cells. HIV-2 is transmitted via mucosal transmission or sexual transmission, mainly in HIV-2 infected patients.

CONCLUSIONS

Overall, these HIV-2-infected patients had low circulating HIV-2 reservoirs that were quantifiable only in 5 of the 14 patients tested, mainly distributed in TCM. HIV-2 DNA was undetectable in most of the CD4 subsets tested. Statistically significant differences were observed in the circulating reservoir of TCM cells in the TMT and TCT patients, as compared to TCM and TEM, respectively.

We determined the relationship between TMT and TCM T-cell counts, TMT and total PBMC HIV-2 DNA levels, TCM T-cell counts and TCM HIV-2 DNA levels in the ALT-EC cohort. The analysis showed that the number of TCM cells was significantly correlated with the presence of HIV-2 DNA in PBMC, with a Pearson correlation coefficient of 0.51 (p = 0.04). This suggests that the presence of TCM cells is a marker of HIV-2 infection.