

PEI2

T-cell immunity in testicular tissue of ART-treated HIV-infected subjects: results from the Orchid study

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Background: HIV persistence in anatomical reservoirs is a major hurdle in HIV eradication. Testis represent a neglected but nonetheless important viral anatomical reservoir as it constitutes an immune privileged site. We assessed T-cell distribution in testis versus blood in HIV-infected individuals receiving suppressive ART.

Methods: Testicular tissue and blood samples were collected from virally suppressed individuals (n=6) on ART for at least 6 months prior to surgery and uninfected controls (n=10) who underwent elective orchiectomy for gender reassignment. T-cells were purified using CD3 microbeads from freshly isolated testicular interstitial cell suspensions. T-cell subsets, CCR5 and ectonucleotidases (CD39 and CD73) expression, T-cell activation, and frequency of regulatory T-cells (Tregs) were assessed using multicolor flow cytometry.

Results: Lower proportions of CD4 T-cells among total T cells were found in testis versus blood, in both HIV- and HIV+ subjects (37±9.5% vs. 80±9.4% and 29.2±7.4% vs. 73±11.5%; p< 0.001). A decrease in naïve and an increase in effector-memory T-cell subsets were observed in testis compared to PBMCs in both groups (p< 0.001). Importantly, up to 77 fold increases in the CCR5 expression on testicular CD4 and CD8 T-cells were observed when compared to blood (CD4 HIV-: p< 0.0001, CD4 HIV+: p=0.003, CD8 HIV-: p=0.0005, CD8 HIV+: p=ns). Increased T-cell immune activation (CD38/HLA-DR co-expression) in testis was observed in HIV+ individuals. A higher expression of immunosuppressive CD39+ Tregs was found in testis of both HIV- and HIV+ subjects compared to blood (64±22% vs. 37±27%, p=0.002 and 62.9±11.5%, vs. 42.6±10%, p< 0.001). A massive increase in the proportion of testicular CD73+ memory CD8 T-cells in HIV- and HIV+ subjects versus blood was also observed (24.6±13.2 vs. 77.4±4% and 13.8±4 vs. 67.6±14.6%, p< 0.001).

Conclusions: For the first time, our results indicate an increase in the proportion of effector memory T-cells, CCR5 expression on T-cells and higher expression of ectonucleotidases in testicular tissue when compared to blood regardless of HIV status. However, virally suppressed subjects on ART had elevated levels of testicular T-cell immune activation when compared to HIV- controls. Collectively, these findings demonstrate the contribution of distinctive T-cell distribution in testicular tissue as anatomical reservoirs for HIV persistence.