FREQUENCY AND PHENOTYPE OF REGULATORY (TREG) AND TH17 T-CELLS IN THE CONTEXT OF HIV-1 INFECTION AND CONTROL IN SOUTH AFRICAN BLACK INDIVIDUALS

Bianca Da Costa Dias[1], Sharon Shalekoff[1], Shayne Loubser[1], Osman Ebrahim[2], Ziyaad Waja[3,4], Neil Martinson[3,4], Caroline T. Tiemessen[1,4]

[1]Centre for HIV and STIs, National Institute for Communicable Diseases, National Health Laboratory Service, and Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [2]School of Clinical Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa [3]Perinatal HIV Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [4]Medical Research Council Soweto Matlosana Centre for HIV/AIDS and TB Research, Johannesburg, South Africa

Email: biancad@nicd.ac.za

Background

Regulatory CD4+ T cells (Tregs) maintain immune-homeostasis by controlling tolerance to self-antigens and by limiting immune-activation during chronic infections through suppression of effector T-cell responses. CD39+ Tregs, shown to correlate positively with HIV-1 disease severity, are unique in their ability to suppress Th17 cells. Pro-inflammatory Th17 cells are involved in mucosal homeostasis and antimicrobial immune responses. Both Treg and Th17 cells are adversely affected by HIV-1 infection and disease progression. As these cells possess reciprocal roles, the balance between them (Th17:Treg ratio) is more meaningful as a marker of immune-homeostasis than the proportions of either subset alone. In this study we investigated Treg and Th17 cell subsets in the context of differential HIV-1 control in a cohort of black South African individuals.

Methods

The relative frequencies of Tregs and Th17 cells were assessed in the peripheral blood of HIV-1 uninfected healthy controls (HCs) and an HIV-1 infected cohort that included: elite controllers (ECs, viral load (VL) <20 RNA copies/ml), viraemic controllers (VCs, VL>20 but <10 000 RNA copies/ml; CD4+ counts >500 cells/µl) and progressors (VL>10 000 RNA copies/ml; CD4+ counts <500 cells/µl). Peripheral Treg cells were defined as CD25+CD127-CD4+ T-cells and were further stratified into: effector (CD39+); memory(CD45RA-) or naïve CD45RA+) and primed (CCR4+) or unprimed (CCR4-) subsets. Th17 cells were defined as CCR4+CXCR3-CCR6+CD4+ T-cells.

Results

The Treg frequency was significantly elevated in progressors when compared to HCs (p=0.0017), ECs (p=0.0028) and VCs (p=0.0035). In the HIV-1 infected cohort, the Treg proportion correlated positively with viral load (rs=0.5278, p=0.0023). Interestingly, the Treg proportions were similar between VCs and ECs despite the viral loads within the VC group displaying a very broad range.

In contrast with previous studies, no significant differences were observed between our study groups with respect to the proportion of naïve, memory, effector and primed Tregs cells,.

The proportion of Th17 cells was significantly higher in ECs compared to VCs (p=0.0376). Notably, the frequency of Th17 cells in progressors was higher than that observed in VCs and moderately higher than both HCs and ECs, but did not reach statistical significance.

Th17: Treg ratios did not differ significantly between HCs and any of the HIV-1 infected subgroups. However, Th17:Treg ratios of ECs were significantly higher compared to VCs (p=0.0355) with a strong trend to higher ratios when compared to progressors (p=0.0670).

Conclusions

Previous studies have demonstrated a positive correlation in Treg frequency and a negative correlation in Th17 frequency and Th17:Treg ratio with increasing viral load. However, our data showed that VCs have

Treg proportions comparable to HCs and ECs, while progressors had proportions of Th17 cells significantly higher than VCs. Furthermore, although the Th17:Treg ratio was higher in ECs compared to VCs and HCs, the ratio was not different between progressors, VCs and HCs. Thus, previously defined relationships between the frequencies of Treg and Th17 cells and HIV-1 disease progression may not be maintained in HIV-1 infected black South Africans and warrants further investigation.