

Low Frequency of FOXP3⁺ Regulatory T cells in Peripheral Blood from HIV-1+ Elite Controllers

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Background: A subset of circulating T cells with immunosuppressive properties is the CD4⁺CD25⁺FOXP3⁺ regulatory T cells (Treg). Tregs are essential for induction and maintenance of self-tolerance and prevention of autoimmunity. However, Tregs have also been shown to suppress immune responses to human tumors, bacterial infections, and acute viral infections in animal models. This leads to one hypothesis holding that Tregs prevent chronic immune activation, hence is beneficial and another hypothesis that these cells are harmful as they suppress the antiviral immune response. To gain more information of the role of Tregs in chronic HIV-1 infection, we are in this ongoing study evaluating the Treg population in chronic HIV-1 infected patients on Highly Active Anti Retroviral Therapy (HAART patients) and HIV-1 infected Elite Controllers (EC).

Methods: PBMC from a total of 20 HIV-1 infected patients were tested, 10 HAART patients and 10 ECs. PBMCs were isolated from heparinized blood by density gradient centrifugation. To identify the Tregs, 1x10⁶ PBMCs were subjected to staining and five-color flow cytometry using following antibodies (Abs): CD3 PerCP, CD4 APC-AlexaFlour750, CD25 PE, CD127, and FOXP3 APC. Data was acquired using a LSR II flow cytometer and the results were analysed using FlowJo.

Results: Our data in this ongoing study show that Tregs (CD25⁺FOXP3⁺) constitute a smaller fraction of CD4⁺ T cells in ECs than in HAART patients with a median of 1.46% (range 1.39 – 4.07) and 3.9% (range 1.82-9.61) respectively. Furthermore, evaluating data in regards to CD25, FOXP3 and CD127low, another marker for Treg, also showed a lower frequency of Tregs in ECs compared to HAART patients with median 1.22% (range 0.07-2.70) and 3.10% (range 1.60-8.49) respectively.

Conclusion: In this study we found higher frequencies of Tregs in HAART patients than in ECs. Seen in the light of the ECs ability to control HIV-1 infection and studies showing polyfunctional CD8⁺ T cell responses in ECs, these preliminary data suggest that Tregs suppress HIV-1 specific CD8⁺ T cell responses, hence are harmful for the patient.