Characterization of Functional Profile of HIV-Specific CD4+ T Cells in VISCONTI Group of Patients

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Background: The mechanisms underlying the exceptional control of HIV replication and reservoirs observed in Post Treatment Controllers (PTC) remain unknown. To further understand such control we evaluated the functional profile of HIV-specific CD4+ T cells of PTCs from the prospective VISCONTI study (Virological and Immunological Sustained CONtrl after Treatment Interruption).

Methodology: Ten VISCONTI patients# defined as controlling HIV (<400cp/mL) for a median 89 [IQR:73-103] months long interruption of a median 3 [IQR:1.7-5.9] years long HAART initiated within 10 weeks post-infection. Multiparametric flow cytometry assessed HIV-specific CD4 T cells producing IFNγ, IL2, TNFα,MIP1β or expressing CD40L after stimulation by HIV-p24 peptides pool or p24 recombinant protein. Results were compared to those from 10 control fully-suppressed treated patients (pts) under at least 5 years long HAART initiated within 10 weeks post-infection. Statistics were done using Mann-Whitney tests.

Results: Relatively high frequencies of CD4+ T cells against the HIV-p24 peptide pool and recombinant protein were found and did not significantly differ between both groups with median values of: 0.125% [0.03-0.49] and 0.12% [0.02-0.68], respectively in VISCONTI pts, and 0.195% [0.01-1.16] and 0.44% [0.1-1.44] in control treated pts, though lower in the VISCONTI pts. In both groups, CD4+ T cells specific for HIV-p24 peptides produced more IL2 and MIP1β than IFN-γ while CD4+ T cells specific for the p24 recombinant protein were more polyfunctional, producing IL2, IFNγ and MIP1β and expressed CD40L. Polyfunctional CD4 T cells directed against HIV p24 pool and p24 recombinant protein can be detected in both groups. Nevertheless in both groups specific CD4+ T cells expressed 1 to 4 functions with 29%, 37% 20% and 6% vs 55%, 17%, 15% and 1% producing 1, 2, 3 or 4 functions against HIV p24 peptide pools and 51%, 26%, 12% and 3% vs 62%, 13%, 14% and 1% against the p24 recombinant protein in Visconti vs controls pts . VISCONTI pts CD4 T cells against HIV p24 peptides produced significantly at least 2 functions than control treated pts (p=0.029).

Conclusions: The major virus control observed in PTC from the VISCONTI study is associated with relatively high frequencies of multi-functional HIV-specific CD4+ T cells. The 3 years long HAART regimen introduced early after infection might have preserved those HIV-specific cells which might participate in the post-treatment control of HIV.

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