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Robust HIV-specific T-cells in post-treatment controllers from the VISCONTI cohort

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Background: Post-Treatment-Controllers (PTCs) represent models of functional HIV remission with an exceptional HIV control years after interruption of an early-initiated antiretroviral therapy. The enrichment in the HLA-B35 allele, associated with symptomatic primary-infection and poor prognosis, instead of the protective HLA alleles reported in Elite Controllers (ECs) questions the role mechanism of this HIV control and the role of anti-HIV T cell responses, particularly those driven by HLA-B35. We therefore compared the PTCs HIV-specific CD4 and CD8 T cells to those from continuously early-treated patients (CETs) and ECs.

Methods: We included 12 PTCs from the VISCONTI study*, half HLA-B35+, 10 CETs under a cART initiated within 10 weeks post-infection and 8 ECs from the ANRS-Co15 cohort. Multiparametric flow-cytometry assessed HIV-specific IFNg, IL2, TNFα, MIP1β or CD40L producing CD4 and CD8 T cell stimulated with HIV-p24 protein and peptides. The cell-associated HIV-DNA was measured in PBMCs and naïve and memory sorted resting CD4 T cell subsets.

Results: High frequencies of HIV-p24 specific CD4+ cellswere observed in PTCs and did not differ from the ECs or CETs ones. A third of these PTCs HIV-p24 specific CD4 cells were highly polyfunctional producing 2, 3 and 4 functions, similarly to from CETs and ECs. HLA-B35 did not influence these results. In contrast frequencies of PTCs CD8+ cells producing against HIV-p24 peptides IFNg (p=0.015) or MIP1b (p=0.001) were lower than ECs but equivalent to CETs ones, without differences in poly-functionality between the 3 groups. Among the functions tested here-in there were 20-fold less IFN-g producing HLA-B35+ CD8 T cells than HLA-B35- ones (0.006% versus 0.130%, p=0.041) against HIV-p24 peptides.

Conclusions: The model of HIV remission represented by VISCONTI PTCs is characterized by robust polyfunctional HIV-specific CD4+ T cells similar to those from Elite Controllers and from continuously early-treated patients, independently from the HLA-B35 allele which negatively impacts IFN-g producing CD8 T cells. These results illustrate differences between ECs and PTCs linked to HLA background and suggest early initiation of treatment allows maintenance of robust HIV-p24 specific CD4 T cells in PTCs.