CD4+ T cells with an activated and exhausted phenotype distinguish immunodeficiency during aviremic HIV-2 infection - DTU Orbit (27/12/2018)

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OBJECTIVE: HIV-2 represents an attenuated form of HIV, where many infected individuals remain “aviremic” without antiretroviral therapy (ART). However, aviremic HIV-2 disease progression exists, and in the current study we therefore aimed to examine if specific pathological characteristics of CD4+ T cells are linked to such outcome. DESIGN: HIV-seronegative (n=25), HIV-1 (n=733), HIV-2 (n=79, of whom 26 were aviremic), and HIV-1/2 dually (HIV-D) (n=13) infected subjects were enrolled from an occupational cohort in Guinea-Bissau. METHODS:: CD4+ T cell differentiation, activation, exhaustion, senescence, and transcription factors were assessed by polychromatic flow cytometry. Multidimensional clustering bioinformatic tools were used to identify CD4+ T cell subpopulations linked to infection type and disease stage. RESULTS: HIV-2-infected individuals had early- and late-differentiated CD4+ T cell clusters with lower activation (CD38+HLA-DR+) and exhaustion (PD-1) than HIV-1 and HIV-D-infected subjects. We also noted that aviremic HIV-2-infected individuals possessed fewer CD4+ T cells with pathological signs compared to other HIV-infected groups. Still, compared to HIV-seronegatives, aviremic HIV-2-infected subjects had T-bet+ CD4+ T cells that showed elevated immune activation/exhaustion, and particularly the frequencies of PD-1+ cells were associated with suboptimal percentage of CD4+ T cells. CONCLUSIONS: Increased frequencies of CD4+ T cells with an activated/exhausted phenotype correlate with exacerbated immunodeficiency in aviremic HIV-2-infected individuals. Thus, these findings encourage studies on the introduction of ART also to individuals with aviremic HIV-2 infection.

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