Nef-specific CD45RA+ CD8+ T cells secreting MIP-1beta but not IFN-gamma are associated with nonprogressive HIV-1 infection.

ABSTRACT: Long-term survival of HIV-1 infected individuals is usually achieved by continuous administration of combination antiretroviral therapy (ART). An exception to this scenario is represented by HIV-1 infected nonprogressors (NP) which maintain relatively high circulating CD4+ T cells without clinical symptoms for several years in the absence of ART. Several lines of evidence indicate an important role of the T-cell response in the modulation of HIV-1 infection during the acute and chronic phase of the disease. We analyzed the functional and the differentiation phenotype of Nef- and Tat-specific CD8+ T cells in a cohort of HIV-1 infected NP in comparison to progressors, ART-treated seropositive individuals and individuals undergoing a single cycle of ART interruption. We observed that a distinctive feature of NP is the presence of Nef-specific CD45RA+ CD8+ T cells secreting MIP-1beta but not IFN-gamma. This population was present in 7 out of 11 NP. CD45RA+ IFN-gammaneg MIP-1beta+ CD8+ T cells were not detected in HIV-1 infected individuals under ART or withdrawing from ART and experiencing a rebounding viral replication. In addition, we detected Nef-specific CD45RA+
IFN-gamma neg MIP-1beta+ CD8+ T cells in only 1 out of 10 HIV-1 infected individuals with untreated progressive disease. The novel antigen-specific CD45RA+ IFN-gamma neg MIP-1beta+ CD8+ T cell population represents a new candidate marker of long-term natural control of HIV-1 disease progression and a relevant functional T-cell subset in the evaluation of the immune responses induced by candidate HIV-1 vaccines.