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The role of cytotoxic T cells

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Introduction

The development of anti-HIV T cell-based vaccines is a current major objective in the strategy to halt AIDS pandemic. For this purpose the understanding of the mechanisms underlying effective HIV-specific CD8+ T cell responses is of great importance. One of the most appealing models for such efficient responses is found today in HIV controllers (HICs), rare individuals able to control HIV infection to undetectable levels for more than ten years in the absence of therapy.

Results and discussion

Despite very low levels of antigen in blood, most HICs have high frequencies of HIV-specific CD8+ T cells that preferentially target the viral Gag protein. Studies of CD8+ T cell responses in HICs have revealed important characteristics of functional HIV-specific CD8+ T cells in HIV infection. Contrary to cells from viremic individuals, HIV-specific CD8+ T cells from HICs can, upon stimulation with their cognate antigen, proliferate and generate a multifunctional response. This could be related to a peculiar (HLA-DR+CD38-) activation phenotype of these cells and to constitutive telomerase activity that protects them against senescence. Our lab has recently shown that CD8+ T cells from most HICs are endowed with a striking capacity to suppress HIV infection ex vivo through a cytotoxic mechanism, a property that is likely to be relevant in vivo. This is likely related to a higher capacity of HIV-specific CD8+ T cells from HICs to upregulate perforin and granzyme. Extending this observation, we have found that HIV-suppressive capacity of CD8+ T-cells is strongly correlated to the frequency of HIV-specific CD8+ T-cells in HIV controllers (but not in viremic individuals), and in particular to the frequency of Gag-specific CD8+ T-cells. Actually, the depletion of Gag-specific CD8+ T-cells but not other specificities abrogates HIV suppression, suggesting that not all the cells in HICs have the same anti-HIV potential.

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