Role of regulatory T cells in the pathogenesis of HIV-1 infection

Yves Lévy

Retrovirology

BioMed Central

Invited speaker presentation

Open Access

Role of regulatory T cells in the pathogenesis of HIV-1 infection

Yves Lévy

Address: INSERM, Unite U955, Universite Paris 12, Faculte de Medecine, AP-HP, Groupe Henri-Mondor Albert-Chenevier, Immunologie clinique, Creteil, F-94010 France

from Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts
Montpellier, France. 21-23 September 2009

Published: 24 September 2009

Retrovirology 2009, **6**(Suppl 2):I22 doi:10.1186/1742-4690-6-S2-I22

This abstract is available from: http://www.retrovirology.com/content/6/S2/I22

HIV-1 infection is characterized by chronic and generalized immune activation which, in combination with the progressive depletion of CD4 T cells, profoundly perturbs antigen-specific CD8 T cell responses. The population of CD4+CD25^{high} FoxP3+ regulatory T cells (Treg) suppresses antigen-specific T cell responses and controls inappropriate or exaggerated immune activation induced by pathogens, thereby influencing the outcome of various infections. Accumulating data pinpoint Treg as a key factor for the inefficiency of CD8-T-cell responses in viral persistence.

We have receently demonstrated that in the setting of a healthy immune system, Treg cells fine-tune the memory/effector cell balance and promote the accumulation of long-living memory cells in case of strong stimulation. These effects were at least in part mediated by a decreased expression of PD-L1, but not of programmed death 1 (PD-1), on CD8 T cells after activation (*Nikolova et al, Blood. 2009*).

In the setting of HIV-1 infection, we, and others, have reported an HIV-driven expansion of Treg in chronically and acutely infected patients (*Weiss et al, Blood 2004; Kared et al, AIDS 2008*). These cells suppress *in vitro* HIV-specific CD4 and CD8 effector T-cell responses. A relationship between the expansion of Treg, the level of cellular immune activation and the depletion of CD4 T cells has been shown in acutely HIV-1 infected patients.

The mechanisms by which Treg mediate their suppressive activity remain poorly understood. Treg constitutively express the ectonucleotidase CD39/ENTPD1 (Ectonucleoside triphosphate diphosphorylase-1; EC 3.6.1.5), the dominant immune system ectonucleotidase that hydrolyses extra-cellular ATP in the sites of immune activation, and generates adenosine with the help of CD73. We found a significantly increased Treg-associated expression of CD39 in HIV-1 infected patients and that the CD39-adenosinergic axis is involved in Treg-mediated inhibition of the proliferation of T cells from HIV-1 infected patients (*Nikolova et al, CROI 2008, Nikolova et al, submitted*). We show that effector CD8 T cells from untreated HIV-1 infected patients are more sensitive to adenosine analogues, as compared to HIV negative controls, due to a higher A2AR expression, the receptor of Adenosine. Finally, the expansion of the Treg CD39+ subset correlates with the level of immune activation and lower absolute CD4 T cell counts in HIV-1 infected patients.

Globally, these results suggest that the CD39/Adenosine pathway may be important to keep an adequate balance between activation and regulation of effector immune response in the setting of HIV-1 infection.