



HAL
open science

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

Yves Lévy

► **To cite this version:**

Yves Lévy. Role of regulatory T cells in the pathogenesis of HIV-1 infection. *Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts*, Sep 2009, Montpellier, France. pp.I22, 10.1186/1742-4690-6-S2-I22 . inserm-00668487

HAL Id: inserm-00668487

<https://inserm.hal.science/inserm-00668487>

Submitted on 9 Feb 2012

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

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>

© 2009 Lévy; licensee BioMed Central Ltd.

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 recently 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.