

**OA031-02. Regulatory T cells inhibit CD8 T cell proliferation in HIV-1 infection through CD39/adenosine pathway**

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► **To cite this version:**

Maria Nikolova, Matthieu Carrière, Jean-Daniel Lelievre, Maria Muhtarova, Armand Bensussan, et al.. OA031-02. Regulatory T cells inhibit CD8 T cell proliferation in HIV-1 infection through CD39/adenosine pathway. Anna Laura Ross. AIDS Vaccine 2009, Oct 2009, Paris, France. BioMed Central, 6 (Suppl 3), pp.O20, 2009, Retrovirology. <10.1186/1742-4690-6-S3-O20>. <inserm-00663922>

**HAL Id: inserm-00663922**

**<http://www.hal.inserm.fr/inserm-00663922>**

Submitted on 27 Jan 2012

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## OA03 I-02. Regulatory T cells inhibit CD8 T cell proliferation in HIV-1 infection through CD39/adenosine pathway

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from AIDS Vaccine 2009  
Paris, France. 19–22 October 2009

Published: 22 October 2009

Retrovirology 2009, 6(Suppl 3):O20 doi:10.1186/1742-4690-6-S3-O20

This abstract is available from: <http://www.retrovirology.com/content/6/S3/O20>

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### Background

Generation of CD8 T cell responses following viral infection or vaccination is indispensable for infection control. Regulatory CD4<sup>+</sup> CD25<sup>+</sup> T cells (Treg) are a key factor for the inefficiency of CD8 responses in viral persistence. The mechanisms of this suppression are not elucidated. Treg constitutively express the ectonucleotidase CD39, that generates immunosuppressive adenosine in the sites of immune activation.

### Methods

HIV<sup>+</sup> patients either treated or not with antivirals (CD4 >350 cells/mkl, n = 47) were studied in parallel with HIV- controls (n = 25). CD8 and Treg cells were purified by magnetic beads separation. Anti-CD3 stimulated CD8 T cell proliferation was assessed on CFSE-stained CD8 T cells cultured in the presence of either: i) Treg preincubated with anti-CD39 blocking mAb or isotype control; ii) adenosine analogue CGS 21680. Expression of the adenosine A2A receptor (A2AR) was quantified by RT-PCR.

### Results

Treg – associated CD39 expression was significantly increased in HIV<sup>+</sup> patients as compared to HIV- controls (mean CD39<sup>+</sup> Treg %2.1 vs. 0.98 and mean CD39 MFI 1011 vs. 606, P < 0.01 for both). In the presence of Treg, proliferation of HIV<sup>+</sup> CD8 T cells was significantly inhibited (mean inhibition 56% vs. 22.5% for HIV- controls; P < 0.01), while the inhibition decreased to an average of

12.3% (P < 0.01) in the presence of anti-CD39 blocking mAb. HIV<sup>+</sup> CD8 T cells were characterized by an elevated expression of A2AR. The inhibitory effect of Treg on HIV<sup>+</sup> CD8 T cell proliferation was reproduced by adenosine agonist. Finally, the percentage of Treg CD39<sup>+</sup> was correlated with plasma HIV RNA values in HIV<sup>+</sup> treatment-naive patients and inversely with CD4 AC.

### Conclusion

Treg CD39-adenosinergic axis is involved in the progression of chronic HIV-1 infection and Treg-mediated inhibition of CD8 T cell proliferation. Modulation of Treg CD39<sup>+</sup> function might be an attractive approach for enhancing CD8 T lymphocyte responses.