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Maria Nikolova, Matthieu Carrière, Jean-Daniel Lelievre, Maria Muhtarova, Armand Bensussan, Yves Lévy

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Oral presentation

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

M Nikolova¹, M Carriere², J Lelievre³, M Muhtarova¹, A Bensussan² and Y Lévy^{*3}

Address: ¹National Center of Infectious and Parasitic Diseases, Sofia, Bulgaria, ²INSERM, Unité U955, Créteil, France and ³Immunologie clinique, AP-HP, Groupe Henri-Mondor Albert-Chenevier; Université Paris 12, Créteil, France

* Corresponding author

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Background

Generation of CD8 T cell responses following viral infection or vaccination is indispensable for infection control. Regulatory CD4⁺ CD25⁺ 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⁺ 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⁺ patients as compared to HIV- controls (mean CD39⁺ 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⁺ 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⁺ CD8 T cells were characterized by an elevated expression of A2AR. The inhibitory effect of Treg on HIV⁺ CD8 T cell proliferation was reproduced by adenosine agonist. Finally, the percentage of Treg CD39⁺ was correlated with plasma HIV RNA values in HIV⁺ treatment-naïve 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⁺ function might be an attractive approach for enhancing CD8 T lymphocyte responses.