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Stéphane Hua, Camille Lecuroux, Asier Saez-Cirion, Gianfranco Pancino, Isabelle Girault, et al.. The potential role of HIV-specific CD38-/HLA-DR+ CD8+ T cells in viral suppressive activity and cytotoxicity in HIV controllers. BMC Infectious Diseases, BioMed Central, 2014, 14 (Suppl 2), pp.P64. <inserm-00995736>

**HAL Id: inserm-00995736**

**<http://www.hal.inserm.fr/inserm-00995736>**

Submitted on 23 May 2014

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POSTER PRESENTATION

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# The potential role of HIV-specific CD38-/HLA-DR+ CD8+ T cells in viral suppressive activity and cytotoxicity in HIV controllers

Stéphane Hua<sup>\*</sup>, Camille Lecuroux, Asier Saez-Cirion, Gianfranco Pancino, Isabelle Girault, Martine Sinet, Olivier Lambotte, Alain Venet

From Abstracts from International Symposium HIV and Emerging Infectious Diseases 2014  
Marseille, France. 21-23 May 2013

## Introduction

In HIV-1 infection, some rare patients called HIV controllers (HICs) are capable to spontaneously control viral replication in vivo. Interestingly, HICs exhibit higher frequency of a particular activated phenotype CD38-HLA-DR+ HIV-specific CD8+ T cells. The aim of this study was to characterize this profile and evaluate its role in HICs.

## Materials and methods

To investigate the functionality of the CD38-HLA-DR+ profile, we compared it with the classically activated phenotype CD38+HLA-DR+ by evaluating several qualitative parameters: (1) activation measured by CD69, CD25, CD71, CD40 and Ki67 expression, (2) memory parameters measured by proliferation capacity, CD127 and Bcl-2 expression, cytokine production measured by IL-2 production and (3) cytotoxic activity. We also determined the mechanism responsible for this particular profile.

## Results

CD38-HLA-DR+ cells exhibited a more resting profile than CD38+HLA-DR+ cells marked by a lower expression of several activation markers. Although they presented similar ex vivo profile especially concerning survival, IL-2 production, CD38-HLA-DR+ cells displayed significantly higher HIV-specific cytotoxic capacity after in vitro culture compared to CD38+HLA-DR+ cells (13% [7%-23%] vs. 7% [3%-11%],  $p=0.02$ ). Furthermore only the frequency of CD38-HLA-DR+ HIV-specific CD8+ T cells correlated with the capacity of CD8+ T cells to inhibit viral replication ex vivo ( $r=0.32$ ,  $p<0.0001$ ). Moreover, the CD38-HLA-DR+

profile was preferentially displayed after activation by low doses of antigen. These results are in line with the enhanced expression of this profile in patients which exhibit high functional sensitivity ( $r=0.41$ ,  $p=0.01$ ).

## Conclusions

Collectively, these data highlight the cytotoxic role of CD38-HLA-DR+ expressing HIV-specific CD8+ T cells in HICs and we provide insights into the mechanism of its induction. Induction of this type of protective cell subset could be an important goal in vaccine strategies.

Published: 23 May 2014

doi:10.1186/1471-2334-14-S2-P64

**Cite this article as:** Hua et al.: The potential role of HIV-specific CD38-/HLA-DR+ CD8+ T cells in viral suppressive activity and cytotoxicity in HIV controllers. *BMC Infectious Diseases* 2014 **14**(Suppl 2):P64.

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