



# OA031-04. Impairment of HIV-1-specific CD8+ T cell function by soluble epithelial adhesion molecules

# Citation

Streeck, H., D. Kwon, J. S. Jolin, K. Trocha, M. Chevalier, T. Caron, K. Law, et al. 2009. 0A031-04. Impairment of HIV-1-specific CD8+ T cell function by soluble epithelial adhesion molecules. Retrovirology 6(Suppl 3): 022.

# **Published Version**

doi:10.1186/1742-4690-6-S3-022

# Permanent link

http://nrs.harvard.edu/urn-3:HUL.InstRepos:4885953

# Terms of Use

This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA

# **Share Your Story**

The Harvard community has made this article openly available. Please share how this access benefits you. Submit a story.

Accessibility

# Retrovirology



Oral presentation Open Access

# OA031-04. Impairment of HIV-1-specific CD8+ T cell function by soluble epithelial adhesion molecules

H Streeck\*1, D Kwon1, JS Jolin1, K Trocha1, M Chevalier1, T Caron2, K Law2, A Pyo1, I Toth1, DE Kaufmann1, SJ Rodig2, BD Walker1 and M Altfeld1

Address: <sup>1</sup>Ragon Institute of MGH, MIT and Harvard, Charlestown, MA, USA and <sup>2</sup>Brigham and Women's Hospital, Boston, MA, USA

\* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, 6(Suppl 3):O22 doi:10.1186/1742-4690-6-S3-O22

This abstract is available from: http://www.retrovirology.com/content/6/S3/O22 © 2009 Streeck et al; licensee BioMed Central Ltd.

# **Background**

HIV-1-specific CD8+ T cell responses play an important role in the control over viral replication. Under persistent antigenic stimulation virus-specific CD8+ T cell become increasingly dysfunctional and upregulate several inhibitory molecules. The interaction and co-regulation of these molecules is largely unknown. The gastrointestinal associated lymphoid tissue (GALT) is one of the major sites of viral replication. Despite a substantial infiltration and expansion of HIV-1-specific CD8+ T cells in the GALT, viral replication appears to be more active in the GALT than in other body compartments. Here we show a distinct mechanism of inhibition of HIV-1-specific CD8+ T cells by soluble epithelial adhesion molecules with increasing viral loads in chronic HIV-1 infection.

## **Methods**

HIV-infected individuals with chronic-progressive or chronic-controlled HIV-1 infection were analyzed. The distribution of E-cadherin in intestinal tissue was determined by immunohistochemistry. Plasma levels of soluble E-cadherin were determined using ELISA. Cytokine secretion by antigen-specific CD8+ T cells in the presence or absence of recombinant soluble E-cadherin was assessed by intracellular cytokine staining and Luminex.

### Results

HIV-1 infected individuals had abnormal distribution of E-cadherin in the intestinal mucosa relative to uninfected individuals. These subjects also had significantly increased soluble E-cadherin levels in the plasma relative to HIV-negative subjects (p < 0.05). The viral load in chronic HIV-1 infection correlated strongly with E-cadherin levels in the plasma (R = 0.7; p = 0.004). HIV-1-specific CD8+ T cells in subjects with chronic-progressive HIV-1 infection showed significant elevated levels of KLRG1 expression (p < 0.05). In the presence of soluble E-cadherin, a natural ligand for KLRG1, KLRG1hi HIV-1-specific CD8+ T cells showed reduced amounts of cytokine production upon antigenic stimulation, while KLRG1lo expressing cells were not affected.

## Conclusion

Our data suggest a novel mechanism by which the disruption of the gastrointestinal epithelium leads to release of soluble E-cadherin, which specifically inhibits KLRG1hi expressing HIV-1-specific CD8+ T cells.