

**P16-23. Antigen processing influences HIV-specific
cytotoxic T lymphocyte immunodominance**

Stefan Tenzer, Edmund Wee, Anne Burgevin, Guillaume Stewart-Jones, Lone Friis, Kasper Lamberth, Chih-Hao Chang, Mikkel Harndahl, Mirjana Weimershaus, Jan Gerstoft, et al.

► **To cite this version:**

Stefan Tenzer, Edmund Wee, Anne Burgevin, Guillaume Stewart-Jones, Lone Friis, et al.. P16-23. Antigen processing influences HIV-specific cytotoxic T lymphocyte immunodominance. AIDS Vaccine 2009, Oct 2009, paris, France. pp.P252, 10.1186/1742-4690-6-S3-P252 . inserm-00663574

HAL Id: inserm-00663574

<https://www.hal.inserm.fr/inserm-00663574>

Submitted on 27 Jan 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.

Poster presentation

Open Access

PI6-23. Antigen processing influences HIV-specific cytotoxic T lymphocyte immunodominance

S Tenzer¹, E Wee⁶, A Burgevin², G Stewart-Jones⁶, L Friis⁶, K Lamberth³, C Chang⁶, M Harndahl³, M Weimershaus², J Gerstoft⁴, N Akkad², P Klenerman⁶, L Fugger⁶, EY Jones⁶, AJ McMichael⁶, S Buus³, H Schild¹, P van Endert² and AK Iversen^{*5,6}

Address: ¹University of Mainz, Mainz, Germany, ²INSERM, Unité 580, Université Paris-Descartes, Paris, France, ³University of Copenhagen, Copenhagen, Denmark, ⁴Rigshospitalet, The National University Hospital, Copenhagen, Denmark, ⁵Oxford University, Oxford, UK and ⁶Wellcome Trust Centre for Human Genetics, Oxford University, Oxford, UK

* Corresponding author

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

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P252 doi:10.1186/1742-4690-6-S3-P252

This abstract is available from: <http://www.retrovirology.com/content/6/S3/P252>

© 2009 Tenzer et al; licensee BioMed Central Ltd.

Background

Cytotoxic T cells (CTL) play a key role in limiting human immunodeficiency virus (HIV)-1 replication. However, although the cellular immune response in HIV-infected individuals can potentially target multiple virus epitopes, the same few are repeatedly recognized. Here we investigated the factors determining observed CTL response hierarchies in Gag p17 and p24.

Methods

We used constitutive and immuno-proteasomal digestion assays, transporter associated with antigen processing (TAP) binding assays, endoplasmic reticulum aminopeptidase (ERAAP) trimming assays, HLA binding assays, T cell cloning and ELISpot assays to evaluate the contribution of each of these factors to final epitope presentation and recognition. Key findings were further examined using structural analyses.

Results

We show that CTL-immunodominance in regions of HIV-1 p17- and p24-Gag correlates with epitope abundance, which is influenced strongly by proteasomal digestion profiles, TAP-affinity and ERAAP-mediated trimming, and moderately by HLA affinity. Structural and functional

analyses demonstrate that proteasomal cleavage-preferences modulate the number and length of epitope-containing peptides, thereby affecting T cell response avidity and clonality. Cleavage patterns were affected by both flanking and intra-epitope CTL-escape mutations.

Conclusion

Our analyses show that antigen processing shape CTL-response hierarchies, that viral evolution modify cleavage patterns, and suggest strategies for in vitro vaccine optimization.