

**Nef variants from non-pathogenic lentiviral strains
inhibit iron uptake through an AP2-dependent
inhibition of transferrin endocytosis**

Herwig Koppensteiner, Kristin Höhne, Marcos Gondim, Francois-Xavier Gobert, Miriam Widder, Swantje Gundlach, Anke Heigele, Frank Kirchhoff, Michael Winkler, Philippe Benaroch, et al.

► **To cite this version:**

Herwig Koppensteiner, Kristin Höhne, Marcos Gondim, Francois-Xavier Gobert, Miriam Widder, et al.. Nef variants from non-pathogenic lentiviral strains inhibit iron uptake through an AP2-dependent inhibition of transferrin endocytosis. *Retrovirology*, BioMed Central, 2013, 10 (Suppl 1), pp.P42. <inserm-00868814>

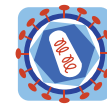
HAL Id: inserm-00868814

<https://www.hal.inserm.fr/inserm-00868814>

Submitted on 2 Oct 2013

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

Nef variants from non-pathogenic lentiviral strains inhibit iron uptake through an AP2-dependent inhibition of transferrin endocytosis

Herwig Koppensteiner^{1,2*}, Kristin Höhne^{1,2}, Marcos Vinicius Gondim¹, Francois-Xavier Gobert³, Miriam Widder², Swantje Gundlach², Anke Heigle⁴, Frank Kirchhoff⁴, Michael Winkler⁵, Philippe Benaroch³, Michael Schindler^{1,2}

From *Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts*
Cambridge, UK. 16-18 September 2013

Background

Increased cellular iron levels are associated with high mortality in HIV-1 infection. Moreover iron is an important cofactor for viral replication, raising the question of whether modulation of intracellular iron can be linked to the pathogenicity of lentiviral infections. Here, we evaluated the effect on cellular iron uptake upon expression of the accessory protein Nef from divergent lentiviruses.

Results

Surface Transferrin receptor (TfR) levels are unaffected by Nef proteins of HIV-1 and its simian precursors but elevated in cells expressing Nefs from most other primate lentiviruses due to reduced TfR internalization. The SIV Nef-mediated reduction of TfR endocytosis is dependent on an N-terminal AP2 binding motif that is not required for downmodulation of CD4, CD28, CD3 or MHCI. Importantly, SIV Nef-induced inhibition of TfR endocytosis leads to the reduction of Transferrin uptake and intracellular iron concentration and is accompanied by attenuated lentiviral replication in macrophages.

Conclusions

Thus, this new SIV Nef function might limit viral replication in myeloid cells and may contribute to the absence of disease in SIV-infected monkeys. Altogether, lentiviruses actively modulate replication by the manipulation of cellular iron, which is an important determinant for viral pathogenicity.

Authors' details

¹Institute of Virology, Helmholtz Zentrum Munich, German Research Center for Environmental Health, Munich, Germany. ²Heinrich Pette Institute, Leibniz Institute for Experimental Virology, Hamburg, Germany. ³Institut Curie, INSERM U932, Paris, France. ⁴Ulm University Medical Center, Institute of Molecular Virology, Ulm, Germany. ⁵German Primate Center, Göttingen, Germany.

Published: 19 September 2013

doi:10.1186/1742-4690-10-S1-P42

Cite this article as: Koppensteiner *et al.*: Nef variants from non-pathogenic lentiviral strains inhibit iron uptake through an AP2-dependent inhibition of transferrin endocytosis. *Retrovirology* 2013 10 (Suppl 1):P42.

Submit your next manuscript to BioMed Central and take full advantage of:

- Convenient online submission
- Thorough peer review
- No space constraints or color figure charges
- Immediate publication on acceptance
- Inclusion in PubMed, CAS, Scopus and Google Scholar
- Research which is freely available for redistribution

Submit your manuscript at
www.biomedcentral.com/submit



¹Institute of Virology, Helmholtz Zentrum Munich, German Research Center for Environmental Health, Munich, Germany
Full list of author information is available at the end of the article