HAL
archives-ouvertes.fr

The reciprocal antagonistic interplay between HIV-1 Tat and SIN3A specifies the epigenetic switch between de-repression versus maintenance of HIV-1 gene silencing

Anurag Kulkarni, Estelle Villemaine, Ann Mccartin, Elena Woods, Celine Marban, Virginie Gautier

▶ **To cite this version:**

Anurag Kulkarni, Estelle Villemaine, Ann Mccartin, Elena Woods, Celine Marban, et al.. The reciprocal antagonistic interplay between HIV-1 Tat and SIN3A specifies the epigenetic switch between de-repression versus maintenance of HIV-1 gene silencing. Retrovirology, BioMed Central, 2013, 10 (Suppl 1), pp.O12. <inserm-00868801>

HAL Id: inserm-00868801
http://www.hal.inserm.fr/inserm-00868801

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.

RETROVIROLOGY

ORAL PRESENTATION Open Access

The reciprocal antagonistic interplay between HIV-1 Tat and SIN3A specifies the epigenetic switch between de-repression versus maintenance of HIV-1 gene silencing

Anurag Kulkarni[1*], Estelle Villemaine[1], Ann Marie McCartin[1], Elena Woods[1], Celine Marban[2], Virginie Gautier[1]

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

Background

Post-integration latency is a critical barrier to achieving a complete cure for HIV. Epigenetic micro-environment alterations at the integrated HIV-1 LTR, coupled with modulations of the HIV-1 Tat feedback circuit, influence the onset and maintenance of latency. In this context, we have previously identified the epigenetic core pressor SIN3/HDAC complex as part of the *in-vitro* HIV-1 Tat nuclear interactome. Here we delineate the dynamics of their antagonistic functional relationship in the control of HIV-1 latency.

Methods

Well-studied T-cellular models of HIV-1 latency viz. J-LAT A1 & A72, with latent integrated LTR-Tat-IRES-GFP-LTR and LTR-GFP-LTR cassettes respectively, and ACH-2, with latent full-length integrated HIV-1 provirus in their genome, were employed. We used ChIP-qPCR to study protein occupancy at the HIV-1 LTR; and RT-qPCR and p24 ELISA/GFP FACS to concurrently monitor the reactivation of HIV-1 gene expression. SIN3A knock-down was performed with shRNA targeting sin3a or non-target control using Amaxa nucleofection, and was validated by WB and RT-PCR analysis. Immunofluorescence microscopy was performed in Hela cells co-transfected with Tat and Sin3a.

Results

The latent HIV-1 LTR displays a constitutive enrichment of the SIN3/HDAC complex.

ChIP-qPCR revealed that the SIN3/HDAC key components SIN3A, SAP18, Sap3O and HDAC-1 were enriched in ACH-2, J-LAT A1 and A72 cells. Importantly, a key event in HIV-1 reactivation from latency is the displacement of the SIN3/HDAC complex from the HIV-1 LTR, as TNFα (NF-KB activator), 5-AZA (DNA methylation inhibitor) or SAHA (HDAC inhibitor) treatments disrupted SIN3/HDAC association with the HIV-1 LTR in latently infected cells.

SIN3A is critical for the maintenance of HIV-1 post-integration latency. SIN3A depletion in J-LAT A1 and A72 resulted in HIV-1 reactivation from latency, which was associated with the depletion of SIN3A and concurrent recruitment of POLII and/or HIV-1 Tat, at the HIV-1 LTR. Next we combined SIN3A knock-down with various reactivation treatments and observed that SIN3A depletion potentiated proviral reactivation by TNFα, PMA/ionomycin (Protein Kinase C activator), 5-AZA and SAHA in J-LAT A1 cells. Thus when associated with the HIV-1 LTR, SIN3A participates in the silencing of the provirus.

Authors' details
[1]UCD-Centre for Research in Infectious Diseases (CRID), School of Medicine and Medical Science, University College Dublin, Dublin, Ireland. [2]INSERM U1121, Faculté de Chirurgie Dentaire, Université de Strasbourg, Strasbourg, France.

Published: 19 September 2013

doi:10.1186/1742-4690-10-S1-O12
Cite this article as: Kulkarni *et al.*: The reciprocal antagonistic interplay between HIV-1 Tat and SIN3A specifies the epigenetic switch between de-repression versus maintenance of HIV-1 gene silencing. *Retrovirology* 2013 **10**(Suppl 1):O12.

[1]UCD-Centre for Research in Infectious Diseases (CRID), School of Medicine and Medical Science, University College Dublin, Dublin, Ireland
Full list of author information is available at the end of the article

BioMed Central

© 2013 Kulkarni et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.