



Chromatin control of Tat-mediated reactivation of latent HIV-1 provirus

Guillemette Masse, Emmanuel Ségéral, Stéphane Emiliani

► To cite this version:

Guillemette Masse, Emmanuel Ségéral, Stéphane Emiliani. Chromatin control of Tat-mediated reactivation of latent HIV-1 provirus. *Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts*, Sep 2009, Montpellier, France. pp.P56, 10.1186/1742-4690-6-S2-P56 . inserm-00663600

HAL Id: inserm-00663600

<https://inserm.hal.science/inserm-00663600>

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

Chromatin control of Tat-mediated reactivation of latent HIV-1 provirus

Guillemette X Masse^{*1,2}, Emmanuel Ségéral^{1,2} and Stéphane Emiliani^{1,2}

Address: ¹Institut Cochin, Université Paris Descartes, CNRS (UMR 8104), Paris, France and ²Inserm, U567, Paris, France

* Corresponding author

from *Frontiers of Retrovirology: Complex retroviruses, retroelements and their hosts*
Montpellier, France. 21-23 September 2009

Published: 24 September 2009

Retrovirology 2009, **6**(Suppl 2):P56 doi:10.1186/1742-4690-6-S2-P56

This abstract is available from: <http://www.retrovirology.com/content/6/S2/P56>

© 2009 Masse et al; licensee BioMed Central Ltd.

Background

Human Immunodeficiency Virus (HIV-1) persists in a latent state within resting CD4⁺ T cells of infected patients treated with highly active retroviral therapy (HAART). This latent reservoir should be eliminated for the clearance of infection. In these cells, silenced replication-competent viruses are integrated into the host genome and can be reactivated by T-cell stimuli. The establishment of this post-integration form of latency is a multifactorial process leading to transcriptional repression. The cellular and molecular mechanisms underlying HIV-1 promoter reactivation from latently infected cells are still poorly understood.

Materials and methods

We used a Jurkat CD4⁺T cell model of post-integration latency (J-lat cells) to assess the role of cellular factors in controlling gene silencing and Tat-mediated reactivation of silenced HIV proviruses. Our study focused on: (1) the Tat-associated-kinase complex P-TEFb (e.g. Cyclin T1 and CDK9), stimulating progressive elongation, (2) chromatin remodeler SWI/SNF complexes (e.g. Brm and Brg-1), (3) and potential regulators of gene silencing as Heterochromatin Protein 1- γ (HP1- γ and Argonaute 1 (Ago1). Upon transient shRNA knockdowns, viral reactivation by NF κ B inducers (TNF α) and/or HDAC inhibitors (TSA) was analyzed by FACS and un-spliced and multi-spliced forms of HIV-1 transcripts were quantified by RT-qPCR.

Results

Our results showed that, as expected, P-TEFb factors inhibition impaired transcriptional reactivation of latent HIV-

1. On the contrary, Brg-1 knockdown stimulated TNF α -induced HIV-1 expression, suggesting that the SWI/SNF complex could participate to transcriptional repression in this model. Furthermore, TNF α - and TSA-induced viral mRNA transcript abundance showed a 3 to 4 fold increase upon Ago1 knockdown.

Conclusion

HIV-1 viral clearance through reactivation would imply the regulation of cellular cofactors involved in the chromatin control of the LTR. Our data suggest that establishment and reactivation of viral latency is under the control of several cellular mechanisms involving factors controlling heterochromatin formation, as well as complexes mediating RNA silencing.