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HAL Id: inserm-00924957
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Submitted on 7 Jan 2014

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The antisense protein of HTLV-2 positively modulates HIV-1 replication

Cynthia Torresilla1*, Sonia Do Carmo1, Émilie Larocque1, Estelle Douceron2, Jean-Michel Mesnard3, Renaud Mahieux2, Benoit Barbeau1

From 16th International Conference on Human Retroviruses: HTLV and Related Viruses
Montreal, Canada. 26-30 June 2013

Unlike HTLV-1, HTLV-2 does not induce leukemia and has been tentatively associated with an HTLV-1-associated myelopathy-like disorder. It has been reported that HTLV-2/HIV-1 co-infected patients progress less rapidly to AIDS than HIV-1-infected individuals. Tax2 has been suggested to mediate this protective state by inducing MIP-1α expression and blocking HIV-1 infection. As cells from HTLV-2-infected individuals mainly express Antisense Protein 2 (APH-2), our objective was to determine if this protein might also intervene in controlling HIV-1 replication in dually infected individuals. Using Jurkat cells, we first demonstrated that both APH-2 and HBZ, the HTLV-1 analogue, equally induced MIP-1α in unstimulated and stimulated Jurkat T cells. To assess if APH-2 might directly affect HIV-1 replication, a full length luciferase-expressing proviral DNA was tested in Jurkat cells. Surprisingly, upon co-transfection with an APH-2 expression vector, an increase in luciferase activity was observed, while HBZ expression rather led to reduced reporter gene expression. Western blot analyses and ELISA assay further indicated that HIV-1 p24 levels were more important in APH-2-expressing cells. To determine if APH-2 was directly modulating HIV-1 LTR activity, both NF-κB and NFAT were tested in stimulated Jurkat cells. Unexpectedly, HBZ and APH-2 inhibited NF-κB and NFAT activation, albeit at different extent. In addition, LTR activation was also inhibited by both antisense proteins although APH-2 had a more modest effect. Our results thus highlight the complex interplay between HTLV antisense transcript-encoded proteins and HIV-1 expression and further studies will be required to determine the potential impact of APH-2 in HTLV-2/HIV-1-infected individuals.

Authors’ details
1Département des sciences biologiques and Centre de recherche BioMed, Université du Québec à Montréal, Montréal (Québec) Canada. 2Oncogénèse Rétrovirale, Ligue Nationale Contre Le Cancer, CIRI, INSERM U1111-CNRS UMR5308, Université Lyon 1, Ecole Normale Supérieure de Lyon, LabEx ECOFECT, Lyon, Cedex 07, France. 3Université Montpellier 1, Centre d'études d'agents Pathogènes et Biotechnologies pour la Santé, CNRS, UMR5236, Montpellier, France.

Published: 7 January 2014

doi:10.1186/1742-4690-11-S1-P118

Cite this article as: Torresilla et al. The antisense protein of HTLV-2 positively modulates HIV-1 replication. Retrovirology 2014 11(Suppl 1): P118.