Retrovirology

BioMed Central

Poster presentation

HIV-1 infection induces retrotransposition of LINE-1 elements

R Brad Jones*[1], Keith E Garrison[2], Haihan Song[1], Anton Buzdin[3], Naveed Anwar[1], Duncan A Meiklejohn[4], Lishomwa C Ndhlovu[2], Douglas F Nixon[2] and Mario A Ostrowski[1,5]

Address: [1]Department of Immunology, University of Toronto, Toronto, ON Canada, M5S 1A8, [2]Division of Experimental Medicine, UCSF, San Franscico, CA, USA, 94110, [3]Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, Moscow, Russia, [4]Gladstone Inst. of Virology and Immmunology UCSF, San Francisco, CA, USA, 94143 and [5]Li Ka Shing Institute, St. Michael's Hospital, Toronto, Canada, M5B 1W8

* 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):P43 doi:10.1186/1742-4690-6-S2-P43

This abstract is available from: http://www.retrovirology.com/content/6/S2/P43

Background

Intact LINE-1 (L1) elements are the only non-LTR retrotransposons encoded by the human genome known to be capable of autonomous replication. Retrotransposition of these elements is controlled by host-factors, including members of the APOBEC3 family of proteins. HIV-1 encodes the accessory protein Vif, which induces the proteasomal degradation of APOBECs 3F/3G. We hypothesized that this would result in the induction of L1 retrotransposition events in HIV-1-infected cells.

Materials and methods

DNA copy numbers of L1PA family L1 elements were quantified over *in vitro* HIV-1 infection time-courses by qPCR. High molecular weight genomic DNA was isolated from these samples by electrophoresis and subjected to L1 quantitation. Cells from infections were stained for HIV-1-Gag, and sorted by FACS. DNA copy numbers of L1 elements in Gag+ and Gag- fractions were quantified. Using targeted genome differences analysis (TGDA) we queried HIV-1-infected cells for *de novo* genomic L1 Insertions. An eGFP-reporter retrotransposition assay was used to study the effect of HIV-1 and HIV-1-ΔVif infection of Jurkat cells on L1 retrotransposition frequency.

Results

L1 element DNA increased over time in both total and high-molecular weight DNA from HIV-1-infected cells, consistently reaching 2-3 fold above baseline within 144 hours. By absolute quantitation this was determined to represent the generation of tens of thousands of novel L1 sequences per cell. By sorting Gag+ from Gag- cells we confirmed that this increase was primarily restricted to HIV-1 infected cells. Using TGDA we identified *de novo* LINE-1 insertions in HIV-1 infected primary CD4+ T cells. These sequences displayed the hallmarks of L1 retrotransposition events including long poly(A) tracts at the insertional junction, and were absent in DNA from autologous uninfected cells. The eGFP reporter retrotransposition assay showed an increased L1 retrotransposition frequency in HIV-1 infected Jurkat cells as compared to uninfected controls. Infection with HIV-1 ΔVif resulted in L1 retrotransposition frequences which were substantially less than that observed with wild-type virus, but still elevated as compared to uninfected controls (36.0 +/- 1.2% eGFP+ for wild-type infection, versus 18.4 +/- 0.5% for HIV-1 ΔVif, and 6.3 +/- 0.7%, $p < 0.0001$ for either comparison).

Conclusion

HIV-1 infection induced high frequencies of L1 retrotransposition in primary CD4+ T cells. This induction was partially dependent upon HIV-1-Vif. However, the observed enhancement of retrotransposition by Vif-deleted virus suggests the involvement of additional mechanisms. Our findings demonstrate the largely unexplored potential for interactions between exogenous retroviruses, such as HIV-1, and endogenous retrotransposable elements.