Retrovirology

BioMed Central

Poster presentation

Open Access

Activity of ancestral restriction factors against ancient retroviruses

Nadia Rahm*[1], Joke Snoeck[1,2], Millan Ortiz[1], Angela Ciuffi[1] and Amalio Telenti[1]

Address: [1]Institute of Microbiology and University Hospital, Lausanne, Switzerland and [2]Rega Institute for Medical Research, KU Leuven, Leuven, Belgium

* 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):P75 doi:10.1186/1742-4690-6-S2-P75

This abstract is available from: http://www.retrovirology.com/content/6/S2/P75

Analysis of TRIM5α and APOBEC3G genes suggests that these two restriction factors underwent strong positive selection throughout primate evolution. This pressure was possibly imposed by ancient exogenous retroviruses, of which endogenous retroviruses are remnants. Our study aims to assess in vitro the activity of these factors against ancient retroviruses by reconstructing their ancestral gag sequences, as well as the ancestral TRIM5α and APOBEC3G for primates.

Based on evolutionary genomics approach, we reconstructed ancestors of the two largest families of human endogenous retroviruses (HERV), namely HERV-K and HERV-H, as well as primate ancestral TRIM5α and APOBEC3G variants. The oldest TRIM5α sequence was the catarhinne TRIM5α, common ancestor of Old World monkeys and hominoids, dated from 25 million years ago (mya). From the oldest, to the youngest, ancestral TRIM5α variants showed less restriction of HIV-1 in vitro [1]. Likewise three ancestral APOBEC3Gs sequences common to hominoids (18 mya), Old World monkeys, and catarhinnes (25 mya) were reconstructed. All ancestral APOBEC3G variants inhibited efficiently HIV-1Δvif in vitro, compared to modern APOBEC3Gs. The ability of Vif proteins (HIV-1, HIV-2, SIVmac and SIVagm) to counteract their activity tallied with the residue 128 on ancestral APOBEC3Gs. Moreover we are attempting to reconstruct older ancestral sequences of both restriction factors by using prosimian orthologue sequences. An infectious one-million-years-old HERV-K_{CON} previously reconstituted was shown to be resistant to modern TRIM5α and APOBEC3G [2]. Our ancestral TRIM5α and APOBEC3G variants were inactive against HERV-K_{CON}. Besides we reconstructed chimeric HERV-K bearing ancestral capsids (up to 7 mya) that resulted in infectious viruses resistant to modern and ancestral TRIM5α. Likewise HERV-K viruses bearing ancestral nucleocapsids will be tested for ancestral and modern APOBEC3G restriction.

In silico reconstruction and structural modeling of ancestral HERV-H capsids resulted in structures homologous to that of the gammaretrovirus MLV. Thus we are attempting to construct chimeric MLV virus bearing HERV-H ancestral capsids. These chimeric ancestral HERVs will be tested for infectivity and restriction by ancestral TRIM5α. Similarly chimeric MLV viruses bearing ancestral HERV-H nucleocapsids will be reconstructed and tested for APOBEC3G restriction.

References

1. Goldschmidt V, Ciuffi A, Ortiz M, Brawand D, Muñoz M, Kaessmann H, Telenti A: **Antiretroviral activity of ancestral TRIM5alpha.** *J Virol* 2008, **82(5):**2089-96.
2. Lee YN, Bieniasz PD: **Reconstitution of an infectious human endogenous retrovirus.** *PLoS Pathog* 2007, **3(1):**e10.