Retrovirology

BioMed Central

Poster presentation

P20-21 LB. Gene-to-gene differences in evolutionary rate between HIV-1 and natural SIV from sooty mangabeys: implications for vaccine tests in non-human primates

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from AIDS Vaccine 2009
Paris, France. 19-22 October 2009

Published: 22 October 2009

Retrovirology 2009, **6**(Suppl 3):P425 doi:10.1186/1742-4690-6-S3-P425

This abstract is available from: http://www.retrovirology.com/content/6/S3/P425

Background

The most useful model system for HIV vaccines is SIV infection of non-human primates (typically rhesus macaques). The pathogenic SIV strains in common use were derived from macaques infected in captivity by viruses originally from sooty mangabeys. In the course of developing new viral stocks and vaccine antigens for challenge studies, we investigated the mode of evolution in natural SIV isolates from sooty mangabeys, comparing it to that of HIV-1 isolates from the global pandemic.

Methods

We assembled a diverse SIV set comprising sooty mangabey SIV (SIV_{smm}) whole-genome sequences from published and unpublished sources, including novel sequences; all sequences were either directly isolated or minimally passaged. Diversity-matched HIV-1 data sets were constructed for HIV-1 M-group sequences for four vaccine candidate genes, Gag, Pol, Env, and Nef. We constructed phylogenetic trees, and calculated substitution rate ratios to infer selective pressure upon the two different viruses in the two different primate hosts.

Results

The ratios of synonymous to non-synonymous substitutions (D_n/D_s) for Gag, Pol, Env, and Nef) were 1.4 to 2.0 times higher for HIV-1 than for the SIV_{smm}. The greatest disparities were observed in HIV-1 Gag and Pol. In both these genes, SIV_{smm} and HIV-1 have similar numbers of amino-acid changes, but SIV_{smm} has a higher number of synonymous substitutions. In constrast, non-synonymous substitutions are elevated in HIV-1 Env relative to SIV_{smm}, and HIV-1 Nef has a higher rate of both synonymous and non-synonymous substitutions.

Conclusion

HIV-1 in humans is under stronger diversifying selection in general than is SIV_{smm} in sooty mangabeys. This disparity is strikingly pronounced in Env, possibly due to greater immune pressure in humans this has implications for studying the impact of vaccine-elicited immune responses on pathogenesis and protection, and the relevance of macaque vaccine studies to humans.