Retrovirology

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Changes of biological properties and pathogenesis of CAEV chimeras expressing Nef and Vpx/Vpr accessory proteins in infected goats

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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):P22 doi:10.1186/1742-4690-6-S2-P22

This abstract is available from: http://www.retrovirology.com/content/6/S2/P22

Background

Caprine Arthritis Encephalitis Virus (CAEV) is a goat lentivirus closely related to HIV that is naturally attenuated with only a minor proportion of infected goats that develop inflammatory diseases, in absence of progression in AIDS. In contrast, to HIV CAEV does not infect productively the CD4+ T cells and has a simpler genome organization. Indeed, CAEV lacks 3 out of 6 regulatory/accessory genes found in HIV. We thought that CAEV/goat is an excellent model to study the functions and the implication of primate lentiviral accessory proteins in the biology and the pathogenesis of lentiviruses.

Materials and methods

We generated CAEV chimeras by inserting *nef* or *vpx/vpr* or both coding sequences in the genome of CAEV [1,2]. All chimeras replicated productively and expressed their transgenes in infected target cells. Interestingly, all 3 chimeras showed increased cytopathicity in target cells, while no modification of the virus titer was observed. We used the chimeric virus that expresses both Nef and Vpx/Vpr in parallel with the parental CAEV to conduct experimental infection of newborn kids and to examine them for 6 months.

Results

Interstingly, animals infected with the chimeric virus exibited a more persistent viral replication in peripheral blood cells than those infected with CAEV. Longitudinal counts of white blood cells combined with phenotypic examinations of these cells showed persistent decrease in the proportion of circulating T cells in the chimera-infected goats compared with those infected with CAEV. Examination of viral dissemination in tissues of sacrificed animals at 6 months PI showed no difference in target tissues except that virus was isolated CNS of goats infected with the chimera but not with CAEV. Interestingly, all animals infected with the chimera but none with CAEV developed typical interstitial pneumonia in their lungs. In addition we found increased expression of MCP-1 and IP-10 chemoattractant chemokines in the inflamed lungs of chimera-compared with CAEV-infected animals.

Conclusion

Altogether these data clearly associate the addition/insertion of *nef* and *vpx/vpr* transgenes in CAEV genome, with increased virulence of the virus.

Acknowledgements

This work was supported by the NIH Cobre, K-IMBRE grants and by INRA animal Health Department.

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