The Frequency of Occurrence and Nature of Recombinant Feline Leukemia Viruses in the Induction of Multicentric Lymphoma by Infection of the Domestic Cat with FeLV-945

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Feline leukemia viruses (FeLV) are naturally transmitted retroviruses and common pathogens of the domestic cat population that frequently cause proliferative, degenerative and malignant disorders. During infection in the domestic cat, viruses with a novel envelope gene arise by recombination between endogenous FeLV-related elements inherited in the cat genome and the corresponding gene from the exogenous infecting species. These recombinant viruses (FeLV-B) are of uncertain disease association, but have been linked to the induction of thymic lymphoma. FeLV-945 is a unique, natural FeLV variant identified in our laboratory as predominant in a cohort of naturally infected animals in a geographic cluster. FeLV-945 contains unique sequence motifs in the regulatory elements of the long terminal repeat and in the envelope gene, both of which contribute to a distinct disease spectrum characterized by multicentric lymphoma of B-cell origin. Preliminary evidence indicated that the generation of recombinant viruses is relatively infrequent in FeLV-945 infection, thus altering the accepted model for FeLV-induced disease. To assess the role of FeLV-B recombinants in the induction of multicentric lymphoma and other non-T-cell disease, the frequency of occurrence and nature of FeLV-B was examined in diseased tissues from a large collection of FeLV-infected animals. Twenty-two naturally infected animals were examined, representing the geographic and temporal cohort from which FeLV-945 was originally identified. Twenty-two experimentally infected animals were examined from several previous studies in which neonatal cats were inoculated with prototype FeLV-A/61E, with chimeric viruses in which the unique LTR and/or SU gene of FeLV-945 were substituted into FeLV-A/61E, or with the myc-oncogene containing LC-FeLV isolate. Diseased tissues were examined by Southern blot and PCR amplification to detect the presence of FeLV-B. Further analysis was performed to establish the recombination junctions and infectivity of FeLV-B in diseased tissues. The results confirm the frequent association of FeLV-B with thymic lymphoma but showed infrequent generation, low levels and lack of infectivity of FeLV-B in non-T-cell diseases including multicentric lymphoma. The findings indicate that the generation of recombinant FeLV-B is unlikely to play a significant role in the induction of these diseases, thus altering the accepted model for FeLV-mediated pathogenesis.

This work was supported by grant R01-CA083823 from the National Cancer Institute (NIH) to L.S.L.