Technical Reports of the Australian Museum, Online (2014) No. 24, pp. 83–88.
ISSN 1835-4211 (online)
http://dx.doi.org/10.3853/j.1835-4211.24.2014.1622

Leukemogenesis by Murine Leukemia Viruses: Lessons for Koala Retrovirus (KoRV)

Hung Fan

Department of Molecular Biology and Cancer Research Institute
University of California, Irvine Irvine, CA 92697-3905, United States of America
hyfan@uci.edu

Abstract. Murine leukemia viruses (MuLVs) are the prototypical gammaretroviruses, and they have been extensively studied with regard to how they cause disease. Leukemogenesis by two MuLVs is reviewed here: the endogenous Akv MuLV of AKR mice, and exogenous Moloney MuLV. Important features of MuLV leukemogenesis include the in vivo generation of envelope recombinants (MCFs) through recombination with endogenous MuLVs, and induction of preleukemic changes typified by splenic hyperplasia secondary to bone marrow defects. Studies of MuLV leukemogenesis help to frame virological questions about how koala retrovirus (KoRV) may induce neoplastic or other diseases in koalas.

Fan, Hung. 2014. Leukemogenesis by murine leukemia viruses: lessons for koala retrovirus (KoRV). In *The Koala and its Retroviruses: Implications for Sustainability and Survival*, ed. Geoffrey W. Pye, Rebecca N. Johnson and Alex D. Greenwood. *Technical Reports of the Australian Museum, Online* 24: 83–88.

The discovery of koala retrovirus (KoRV) in free-ranging and captive koalas *(Phascolarctos cinereus)* has been viewed with concern and interest. The primary concern is that KoRV-associated disease such as neoplasms, while yet to be conclusively proven to be KoRV caused, could increase the threats to survival of these animals. In the scientific community there is interest for several reasons: KoRV may be associated with lymphoma in koalas, it appears to be recently introduced into this species, and endogenization is an ongoing process. KoRV infection in koalas may provide an opportunity to study introduction and spread of a gammaretrovirus into a new host species and its accompanying effects. This process has happened in other species, notably mice, but in the more distant past, so some of the processes can only be deduced. At the same time, information learned from the relationship of murine gammaretroviruses and their hosts may provide lessons for understanding the potential relationships of KoRV and disease in koalas. The recent discovery of a second KoRV (KoRV-B) that may be associated with leukemogenicity (Xu *et al*., 2013) has similarities to oncogenesis in murine leukemia viruses (MuLVs). Leukemogenesis by MuLVs will be summarized here and possible implications to KoRV pathogenesis will be pointed out.

Murine leukemia viruses

MuLVs were first discovered in inbred mouse strains that had high incidences of leukemia. These studies resulted in isolation of several MuLV strains that cause leukemias of different hematopoietic lineages. For instance Moloney MuLV (M-MuLV) and Gross MuLV induce T-lymphoma, while Friend (F-MuLV) and Rauscher MuLV (R-MuLV) induce erythroleukemia and myeloid leukemia (Fan, 1997). These are the predominant MuLVs used in studies of MuLV leukemogenesis. They are prototypical retroviruses of the gammaretrovirus family.

MuLVs can be classified into types based on their envelope proteins and the kinds of cells that they infect, determined by the cell surface proteins that they bind. The leukemogenic MuLVs are mostly *ecotropic*; they infect cells of mice and rats, but they do not infect most