Prevention and Treatment of Koala Retrovirus (KoRV) Infection: Lessons from Studies of AIDS Viruses in Nonhuman Primate Models

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Abstract. The presence of multiple retroviruses in koalas (*Phascolarctos cinereus*), including viruses with exogenous infectious forms that may be associated with malignant disease manifestations, poses challenges for both management of captive populations and species preservation in the wild. The development of antiretroviral medications (ARV) for the treatment of human immunodeficiency virus (HIV) infection is one of the triumphs of modern medicine, and many of these drugs have relatively broad antiretroviral activity, suggesting they might be active against koala retroviruses (KoRVs). However, accumulating experience with the use of these medications in non-human primate (NHP) models of HIV infection and acquired immune deficiency syndrome (AIDS) points out several caveats and provides guidance in attempting to use anti-HIV drugs in the treatment of retroviral infection in nonhuman species. This manuscript reviews that experience from the perspective of potential use of ARVs for prevention and treatment of KoRV infection.

The koala (*Phascolarctos cinereus*) represents a fascinating instance of retrovirus/host species interactions, with geographically high prevalence of an endogenizing retrovirus, provisionally designated koala retrovirus-A (KoRV-A), that is also found in exogenous, pathogenic forms, along with a more recently described distinct exogenous related virus, provisionally designated KoRV-B, that utilizes a different cellular receptor and is associated with malignant hematologic manifestations (Ávila-Arcos et al., 2013; Canfield et al., 1988; Hanger et al., 2000; Oliveira et al., 2007; Shojima et al., 2013; Simmons et al., 2012; Stoye, 2006; Tarlinton et al., 2005, 2006, 2008). These viruses represent a management problem for captive populations, and a challenge for species preservation in the wild. The development of antiretroviral drugs for the treatment of HIV infection has dramatically improved both survival and quality of life for HIV infected individuals, and the relatively broad antiretroviral activity of many of these drugs suggest they may also be active against retroviruses affecting non-human species, such as KoRVs (Oliveira et al., 2007). However accumulating experience with the use of anti-HIV drugs in NHP models highlights important considerations and potential limitations to such use that may help inform efforts to use anti-HIV drugs for the treatment of KoRV infection in koalas (Del Prete & Lifson, 2013). Factors to consider include potency against the target virus (compared to HIV), drug delivery, pharmacokinetics, toxicity and sustainability of treatment. Perhaps the most important consideration is the relationship between the mechanism(s) of action and targets of the drugs considered in relation to the underlying pathogenesis of the disease process of concern.