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Immunization with Envelope Proteins of the KoRV as a Basis for a Preventive Vaccine

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Abstract. The rapid spread of the koala retrovirus (KoRV) in Australia and in international zoos calls for effective counter measures. As is the case with the human immunodeficiency virus (HIV) epidemic, a preventive vaccine is urgently needed. Vaccines inducing neutralizing antibodies are a good way to prevent retrovirus infections. Although for HIV there is still no effective vaccine available, commercial vaccines protecting cats from disease caused by the feline leukemia virus (FeLV) already exist and have been proven effective. KoRV is a retrovirus more closely related to FeLV than to HIV. Immunizing different species (rats, goats, hamsters, guinea pigs, mice, cats) with the transmembrane (TM) and surface (SU) envelope proteins of FeLV, as well as of the porcine endogenous virus (PERV) we always obtained neutralizing antibodies. PERV is also closely related to the KoRV. Based on the immunization studies with the envelope proteins of FeLV and PERV, we cloned and expressed the corresponding envelope proteins of the KoRV and immunized goats and rats. In all cases we obtained antibodies neutralizing the KoRV. However this does not mean that neutralizing antibodies will be obtained when immunizing koalas *(Phascolarctos cinereus)* with the envelope proteins of the KoRV or immunizing pigs with the envelope proteins of PERV. Therefore, koalas should be immunized with KoRV envelope antigens to determine whether neutralizing antibodies are induced and if so, whether such antibodies are able to protect healthy animals from infection. Furthermore, whether immunization with these antigens has a therapeutic effect on animals already infected with KoRV should be investigated. If *Chlamydia* infection of koalas is an opportunistic infection made possible by KoRV-induced immunodeficiency, immunization against KoRV will also protect animals from *Chlamydia* infection.

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Infection of koalas with the KoRV, and infection of humans with HIV-1 leading to AIDS. Retroviruses have long been known to be capable of infecting new host species by transspecies transmission. Interest in this subject has been boosted by the finding that the human immunodeficiency viruses (HIV-1 and HIV-2) are the product of such a transspecies transmission (Gao 1994,1999) and by recent concerns over the potential transmission of PERVs after xenotransplantation of pig organs into humans (Denner & Tönjes, 2012). The koala retrovirus (KoRV) is the result of such a transspecies transmission which is even associated with endogenization of the virus into the germ line of the animals (Hanger *et al*., 2000; Denner & Young, 2013). The KoRV is closely related to the gibbon ape leukemia virus (GaLV), which however remained exogenous in gibbons (Hanger *et al*., 2000). Both are related to endogenous retroviruses of South Eastern Asian mice, (Martin *et al*., 1999) and bats, (Cui *et al*., 2012a,b) however the origin and the transmission routes are still unknown.

Retroviruses are known to induce tumors and immunodeficiencies and HIV is the most prominent retrovirus inducing an acquired immunodeficiency syndrome. Although HIV, a lenti(retro)virus, and the KoRV, a gammaretrovirus, are not closely related, the clinical picture of the syndrome