The Koala and its Retroviruses:
Implications for Sustainability and Survival

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Establishing Priorities for Research on the Epidemiology of Koala Retrovirus (KoRV) in Koalas *(Phascolarctos cinereus)*

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Abstract. This manuscript summarizes the break-out session held on the epidemiology of disease expression of koala retrovirus (KoRV) in koalas *(Phascolarctos cinereus)* at the *Koala Conservation Workshop: The koala and its retroviruses: implications for sustainability and survival* held at San Diego Zoo, April 17–18, 2013. The goals of this break-out session were to develop and prioritize specific research goals related to KoRV epidemiology, to identify actions, and to determine the responsible parties and timelines. Identified areas for epidemiologic research include studies in both wild and captive populations. For wild populations, baseline estimates of incidence and prevalence that account for potential biases in surveillance are needed. Landscape-level studies that determine whether KoRV contributes to the decline or stability of wild populations are also a priority. Captive populations with high-quality health data and management records can provide opportunities to identify factors associated with disease expression. These populations may also be pivotal in understanding the clinical importance of different KoRV subtypes.

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Relevant to any epidemiologic study are the two important questions: What do we already know and what are the current gaps in knowledge?

What do we know? There are koala populations with low KoRV prevalence and with no disease expression. The Kangaroo Island population is a good example of lower KoRV prevalence with little disease expression (Simmons *et al.*, 2012). There are also populations with high KoRV prevalence with little disease expression (e.g., St. Bees Island) (Tarlinton *et al.*, 2006; Bill Ellis, pers. comm. 2014). There appears to be a difference in prevalence and disease expression between populations of northern koalas versus southern koalas (Simmons *et al.*, 2012). There also appears to be similar prevalence of KoRV with widely differing prevalence of disease expression between southeastern and central Queensland koala populations (Simmons *et al.*, 2013; Amber Gillett and Sean FitzGibbon pers. comm. 2013). One challenge in Australia is that there have only been a few studies where sampling and testing was limited and opportunistic.

Gaps in knowledge. Currently the important gaps in knowledge are: Does KoRV causes disease in koalas and if so, is it associated with declines? What diseases (e.g., neoplasia) are caused by KoRV in koalas? Are there environmental, social, or other triggers for disease expression? What role do the exogenous and endogenous variants of KoRV play in causing disease? Does KoRV viral load increase with age?

Major epidemiologic questions for wild and captive populations:

Wild populations

1 *What is the baseline prevalence of KoRV and KoRV-associated disease in wild populations? What are the demographic and geographic characteristics of affected populations?*

What data do we need?

1.1 Baseline data: prevalence of KoRV and prevalence of associated disease across widespread geographic areas or across a few intensely-studied populations. Note that intensely studied populations may provide better information on KoRV-associated disease.

1.2 Data on demographics for individuals within the population.

Important considerations

1.3 Surveillance bias: Biases in prevalence estimates can result from surveillance sources that are a non-randomized subsets of the koala population. For example, it is unknown whether differences in prevalence observed across koala populations reflect true differences in prevalence of wild populations or differences in workups of koalas in hospitals, which are often used as disease surveillance sources due to the ease of data attainment (Amber Gillett, pers. comm.). Sources of information should be recorded, appropriate controls identified, and analyses and conclusions should take these potential biases into consideration.

1.4 Standardization of mortality data: veterinary pathologists should be involved to help establish consistency in post-mortem disease surveillance methodology (e.g., collecting the same sets of tissues) and diagnoses.

1.5 Data are needed on disease negative and, if possible, KoRV negative animals.

2 *What is the incidence of KoRV infection and disease in wild populations and is it changing over time?*

What data do we need?

2.1 Capture-recapture studies to measure KoRV and disease status in populations where some animals remain infection-free (e.g. Kangaroo Island).

2.1.1 To estimate incidence of KoRV infection, the study population should be groups with some KoRV-free koalas. The KoRV-free koalas should be followed forward through time to determine the rate of new infections. Baseline data on disease prevalence in the source population should be documented at the time of the study.

2.1.2 To estimate incidence of KoRV-related disease, the study population should be KoRV-positive; individuals with confirmed KoRV infection should be followed forward through time to determine the rate of disease outcomes. KoRV-negative animals should also be followed for the same disease outcomes to estimate rate differences by infection status. Consideration should be given to differences in disease rates across different KoRV subtypes.

2.1.3 These studies could ultimately help estimate the rate of spread in a population and contribute to eventual development of infectious disease models.

2.2 Multi-year prospective disease monitoring could help to determine if disease incidence is increasing.

2.3 Data to collect would include blood samples for KoRV status and virus subtyping, age, sex, source population, and reason for sampling (e.g., specific research project, animal injured and brought to hospital, etc.). Additional health and demographic data can be collected. Location of sampling and GPS coordinates if applicable would also be ideal information to obtain.

Important considerations:

2.4 If the rate of spread is expected to be low, then alternative study designs should be considered in consultation with epidemiologists.

2.5 Longitudinal studies currently in progress, where blood samples are being collected and stored, may help answer these questions.

3 *Is KoRV infection and associated disease a factor contributing to koala declines or is it a factor in maintaining stable population?*

What data do we need?

3.1 Landscape-level data on site-specific population declines

3.2 Landscape-level data on KoRV status and disease prevalence at the same locations

3.3 Other landscape-level factors that may contribute to declines, i.e., potential confounders such as habitat destruction, dog density estimates, roads, etc.

Important considerations:

3.4 A large epidemiology study of this magnitude will be challenging.

3.5 Partnering with biologists already studying wild populations is important for more expedited research.

Captive populations

1 *Is KoRV-B more of a risk to captive populations than KoRV-A? Do we need to be more concerned about KoRV-B (Xu et al., 2013)?*

What data do we need?

1.1 Proportional mortality study of death rates among koalas with varying KoRV subtypes.

1.1.1 Needs to be done at an Australian facility where both variants have been observed.

1.1.2 Complete post-mortem disease surveillance with diagnoses for all animals at risk (not just animals where lesions are present).

1.1.3 Need samples for determining KoRV status. Test for presence/absence of all known strains.

1.1.4 A prospective survey would be ideal. The KoRV status of koalas would be determined (negative, KoRV-A only, KoRV-B only, both KoRV-A & B, other variants) and then koalas would be followed prospectively to determine incidence of KoRV-related disease in the different groups.

1.1.5 If banked data are available, a retrospective study could be used to expedite research.

2 *Are there demographic or management factors that contribute to individual susceptibility related to KoRV-related disease and how does viral load modify disease susceptibility?*

What data do we need?

2.1 Need to determine which factors are most important to focus on.

2.1.1 Ideally, they would be characteristics that could be modified through management (e.g., harem size) or monitored (e.g., age group).

What risk factors are we interested in?

2.2 Age class (e.g., does disease only affect post-reproductive, geriatric animals and is there a relationship between age and viral load?).

2.3 Harem size.

2.4 Genetic relatedness.

2.5 Importation of new animals (e.g., introduction of variants of KoRV).

2.6 Which koalas are housed together with changes captured over time.

2.7 Medical history.

What data do we need?

2.8 Electronic management, medical, and necropsy records.

2.9 KoRV status, subtype, and measures of viral load.

3 *Is the pattern of cyclical expression of KoRV-related disease observed at San Diego Zoo real? Are other factors (e.g., aging, importation) related to the observed pattern?*

What data do we need?

3.1 Electronic management, medical, and necropsy records.

Ideas for working together to tackle these research questions:

- Dr Amber Gillett, Australia Zoo Wildlife Hospital will look into sample banking in Australian facilities.
- Carmel Witte can help design and consult on epidemiology studies.
- San Diego Zoo has banked samples and archived data that may address some of the basic epidemiology questions. Medical data and management data are currently not in electronic form and so person-time is needed to more thoroughly investigate.

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