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Defining Putative Koala Retrovirus-Associated Disease in Koalas

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Abstract. Koalas suffer from a wide range of diseases and illness, some of which are well understood, and others that are observed but have unclear aetiologies. A largely undescribed and poorly defined area in koala health is diseases presumed to be associated with koala retrovirus (KoRV) infection. Disease conditions putatively linked to KoRV infection are defined here as "putative KoRV-associated diseases" (PKAD). These include neoplasia, severe dermatological and oral conditions, life-threatening fungal and opportunistic infections, haematological disorders, chronic ill-thrift or poor body condition of undefined cause and other conditions suggestive of immune dysfunction. Multiple conditions are usually present at once and koalas invariably die despite treatment. The multifactorial nature of PKAD and the lack of clarity around KoRV's role in many conditions means that developing a standard case definition encompassing all presentations is difficult. As such, presenting conditions have been defined as dysplastic/neoplastic versus those associated with immune dysfunction (putative immune dysfunction disorders—PIDDS).

Introduction

Koala retrovirus (KoRV) is present in almost all koalas (*Phascolarctos cinereus*) throughout Australia as both endogenous (integrated into the germ line and heritable) and exogenous (replication-competent, transmissible) virus. KoRV subtypes A-M exist, with only the subtype A showing evidence of endogenization and being ubiquitous in koalas from Queensland (QLD) and New South Wales (NSW) (Quigley & Timms, 2020; Blyton, Young, *et al*., 2022). Koalas in South Australia and Victoria do not appear to have endogenous forms of KoRV; however, there is evidence of recombinant variants of KoRV (recKoRVs) across the koala's range which are thought to be largely defective, or non-replication competent (Löber *et al*., 2018; Tarlinton *et al*., 2022). Exogenous forms of KoRV have been detected across the koala's range and there is mounting evidence to suggest that viral load may be an important factor to consider when investigating links to disease in koalas (Maher *et al*., 2019; Fabijan *et al*., 2020; Quigley & Timms, 2020; Blyton, Pyne, *et al*., 2022).

Koalas suffer from a wide range of diseases and illness, some of which are well understood and others that have unclear aetiologies. Diseases presumed to be associated with KoRV infection are a largely undescribed and poorly defined area in koala health. This knowledge gap is partly due to our poor understanding of how KoRV might act as an aetiological agent, but also the need to clearly define what constitutes KoRV-associated disease. Diseases putatively linked to KoRV infection are defined here as "putative KoRV-associated diseases" (PKAD).

Putative KoRV-associated diseases comprise a suite of conditions that present in koalas similarly to those caused by other pathogenic gammaretroviruses which affect other species (e.g., feline leukaemia virus, murine leukaemia virus, gibbon ape leukaemia virus) (Hanger & Loader, 2014). Examples of such conditions include leukaemia, lymphoma, aplastic anaemia, tumours, and immunodeficiency disorders (Beatty, 2014; MacLachlan & Dubovi, 2017). Despite compelling similarities between disease presentations in koalas and other species affected with gammaretroviruses, further research is required to substantiate a causal link

Keywords: koala retrovirus, KoRV, leukaemia, myelodysplasia, ill-thrift, neoplasia, dermatitis, putative KoRV-associated disease (PKAD), immune dysfunction
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