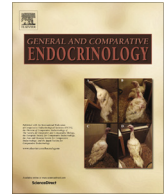




Contents lists available at ScienceDirect

# General and Comparative Endocrinology

journal homepage: [www.elsevier.com/locate/ygcen](http://www.elsevier.com/locate/ygcen)

## Immune-endocrine interactions in marsupials and monotremes



E. Peel, K. Belov\*

Faculty of Veterinary Science, University of Sydney, Sydney, Australia

### ARTICLE INFO

#### Article history:

Received 15 February 2016

Revised 27 November 2016

Accepted 24 January 2017

Available online 27 January 2017

#### Keywords:

Marsupial

Monotreme

Thymus involution

Tasmanian devil

DFTD

### ABSTRACT

Interactions between the immune and endocrine systems are not well studied in marsupials and monotremes. One exception to this is the phenomenon of semelparity, which is well covered in the literature as this is an unusual reproductive strategy amongst mammals and is only observed in some dasyurid and didelphid marsupials. Thymus involution provides a direct link between the endocrine and immune systems and warrants further study in marsupials and monotremes. The thymus is a primary immune tissue which is essential for overall immune function. Whilst the organ is large in juvenile animals, it begins to involute around puberty due to the suppressive effects of sex steroids. Thymus involution has a significant effect on the immune system, as it signals the onset of immune aging and decline in function. The output of naïve T lymphocytes by the thymus decreases, increasing susceptibility of aged individuals to infection and cancers. Understanding the links between the immune and endocrine system in marsupials and monotremes may shed light on diseases such as devil facial tumour disease (DFTD) which threatens the future of the Tasmanian devil. We hypothesise that changes in sex hormones around puberty may drive changes in the immune system, such as thymus involution, which may make devils more susceptible to DFTD as they age. In addition, the Schwann cell origin of DFTD may enable tumours to respond to sex hormones, as occurs in similar cancers in humans.

Crown Copyright © 2017 Published by Elsevier Inc. All rights reserved.

### 1. Introduction

The interaction of the immune and endocrine systems is well studied in eutherian mammals. However, our understanding of immune-endocrine interactions in marsupials and monotremes is limited. Monotremes are classed as prototherian mammals, and lie basal to therian mammals in the phylogenetic tree. Therian mammals are further divided into eutherian mammals such as humans and mice, and marsupials. In this paper we review the current literature of immune-endocrine interactions in marsupials and monotremes, drawing information from our current knowledge of this interaction in eutherian mammals, and then provide an example of why increasing our understanding of this field is important for conservation of our unique fauna.

### 2. Marsupial and monotreme endocrine system

The three major endocrine axes identified in eutherian mammals are also present in marsupials and monotremes;

hypothalamic-pituitary-adrenal (HPA) axis (McDonald et al., 1988; Than and McDonald, 1973; Weiss and McDonald, 1967), hypothalamic-pituitary-gonadal (HPG) axis (Busby et al., 2014; Farmer et al., 1981; Warren et al., 2008) and the renin-angiotensin-aldosterone system (RAAS) (Johnston et al., 1967; Reid, 1971). Marsupial and monotreme endocrine glands are generally anatomically and functionally similar to eutherians. An exception is the brushtail possum (*Trichosurus vulpecula*) adrenal gland, which is unusual amongst mammals in that sexually mature females have an additional zone of cells within the cortex that enlarges during pregnancy and secretes corticosteroids (Bourne, 1949; Weiss and Ford, 1984). The adrenal gland of Monotremes is similar to reptiles (Bourne, 1949; Chester Jones, 1957). As in eutherian mammals, the major glucocorticoid varies in marsupials and monotremes (Oddie et al., 1976). Generally, marsupials and monotremes have a low dose response to endogenous and exogenous adrenocorticotropic hormone (ACTH) compared to eutherians (Bradley and Stoddart, 1990; Johnston et al., 1967; Martin and McDonald, 1986; McDonald and Bradshaw, 1977; McDonald et al., 1988; Than and McDonald, 1973; Weiss and McDonald, 1967; Weiss and Richards, 1971), especially the echidna, *Tachyglossus aculeatus* (Sernia and McDonald, 1977; Weiss et al., 1979). As a result, adrenal hormones are secreted in lower concentrations

\* Corresponding author at: R.M.C Gunn Building, Faculty of Veterinary Science, University of Sydney, Regimental Dr, Camperdown, N.S.W 2006, Australia.

E-mail addresses: [emma.peel@sydney.edu.au](mailto:emma.peel@sydney.edu.au) (E. Peel), [kathy.belov@sydney.edu.au](mailto:kathy.belov@sydney.edu.au) (K. Belov).

when compared to eutherian species. The functional significance of this remains unknown.

### 3. Immune-endocrine interactions in marsupials and monotremes

Direct interactions between endocrine and immune systems are not well studied in marsupials and monotremes, especially the influence of sex steroids on immune mechanisms and cells. However, given the similarities in endocrine and immune systems across the three mammalian lineages, sex steroids are thought to have similar effects to those in eutherians. Immune-endocrine interactions are well studied in eutherian mammals, especially humans and mice. A direct link between the endocrine and immune systems is evidenced by the expression of hormone receptors within immune cells and tissues (Baschant and Tuckermann, 2010; Pennell et al., 2012). The involvement of sex steroids and glucocorticoids in immune cell development, differentiation and function is well known in eutherian mammals (Baschant and Tuckermann, 2010; Pennell et al., 2012). One mechanism of action is via intracellular receptors which act as transcriptional regulators. Glucocorticoid and sex steroid receptors located within the cytoplasm of immune cells such as lymphocytes and antigen presenting cells respond to ligand binding by translocating to the nucleus. The ligand bound complex then binds to hormone response elements in gene promoter regions, thereby controlling transcription of downstream genes (Baschant and Tuckermann, 2010; Pennell et al., 2012).

There are multiple types of CD4+ helper T lymphocytes, two of which secrete cytokines that direct the immune system towards a cell mediated response (Th1) or humoral response (Th2). The balance between Th1 and 2 responses is essential for immune regulation and is significantly influenced by sex steroids. However, this interaction is dependent upon many factors including hormone concentration and immune cell type. Oestrogen promotes Th2 responses by inducing release of cytokines that increase proliferation of B cells, which in turn increase antibody production (Bouman et al., 2005; Grimaldi et al., 2005). However, this response is concentration dependent as at low levels oestrogen promotes Th1 proliferation (Pennell 2012). On the other hand, androgens promote Th1 responses and decrease antibody production (Bouman et al., 2005; Pennell et al., 2012). Hormones also influence immune cell development. Oestrogens decrease B cell lymphopoiesis in the bone marrow (Ackermann, 2006) and the number of developing T cells in the thymus (Pennell et al., 2012). Similarly, glucocorticoids also decrease the number of B cells (Baschant and Tuckermann, 2010; Cupps et al., 1985), as well as induce apoptosis of T lymphocytes and suppress activation of antigen presenting cells (Baschant and Tuckermann, 2010).

Unlike eutherian mammals, little is known of the interaction between endocrine and immune systems in marsupials and monotremes. Most of the literature in this field relates to male semelparity, as this is an unusual life history trait for mammals. Semelparity is a reproductive strategy where individuals survive for only a single breeding period. This reproductive strategy is rare in mammals, and only seen in some species of dasyurid and didelphid marsupials (Boonstra, 2005; Cockburn, 1992; Naylor et al., 2008). These species experience complete male mortality following a single, intense breeding period (Boonstra, 2005; Naylor et al., 2008). Mortality is due to the effects of high circulating levels of free cortisol, relative to the non-breeding season, arising from an androgen-dependent decrease in corticosteroid binding globulin, impaired negative feedback mechanisms and aggressive social interactions (Bradley, 1990; Bradley et al., 1980; McDonald et al., 1981; McDonald et al., 1986). The high concentrations of free cortisol

suppress the immune system, causing an increase in parasitic and bacterial infections and severe ulceration of the upper gastro-intestinal tract leading to haemorrhage and death (Naylor et al., 2008). Females usually do not survive past the weaning of their juveniles but some can survive and breed a second time (Naylor et al., 2008).

### 4. Thymus involution

Thymus involution is one aspect of endocrine-immune interactions which has largely been overlooked, but warrants further attention as it provides direct links between the endocrine and immune system and has significant effects on immune competence, especially in old age. The thymus is the primary immune tissue responsible for the development and maturation of T lymphocytes. From early T cell progenitors within the thymus, thymocytes undergo T cell receptor rearrangement, positive and negative selection to become naïve T lymphocytes which are exported to the periphery (Fink, 2012; Manley et al., 2011). The thymus in marsupials and monotremes is functionally and anatomically similar to eutherians (Haynes, 2001; Yadav, 1973). Numerous histological and anatomical studies of marsupial and monotreme lymphoid tissues were conducted in the early 1900's. However, few examined the thymus in detail, observed involution or discussed functional changes associated with involution. The thymus is the first lymphoid organ to mature and is largest in juvenile animals but regresses with age (Baker et al., 1999). The mature thymus is anatomically similar to eutherians and is characterised by a defined cortex and medulla, and presence of Hassall's corpuscles (Diener and Ealey, 1965; Haynes, 2001; Yadav, 1973).

Thymus number and anatomical position differs between mammalian species (Wong et al., 2011). Eutherians such as humans and sheep only have a thoracic thymus (Haynes et al., 2000; Jordan, 1976). Similarly, monotremes (Haynes, 2001; Mackenzie and Owen, 1919) and polyprotodont marsupials such as the Tasmanian devil (*Sarcophilus harrisii*) and gray short-tailed opossum (*Monodelphis domestica*) have a single thoracic thymus (Yadav, 1973). Diprotodont marsupials such as macropods and the common wombat (*Vombatus ursinus*) have a cervical and thoracic thymus (Yadav, 1973), similar to laboratory mice (Dooley et al., 2006). The cervical thymus is anatomically and functionally similar to the thoracic thymus, however is larger and develops first (Yadav, 1973). Both thymuses are involved in lymphocyte development, as thymectomy before day 20 results in lymphocyte depletion and delays antibody response by 4 months (Stanley et al., 1972). This is supported by gene expression profiles of cervical thymic tissue, indicating an involvement in T cell lineage commitment and development (Wong et al., 2011).

Thymus involution is one of the most significant effects of aging on the immune system and signals the onset of immunosenescence (Castelo-Branco and Soveral, 2014). Involution in eutherian species is well characterised, with numerous studies determining timing and extent of involution, as well as changes in tissue architecture and cell populations (Rezzani et al., 2014). Information on the structural and functional changes associated with involution in marsupials and monotremes is lacking and must be inferred from morphological and histological observations. As for eutherians, the onset of involution in marsupials and monotremes is marked by infiltration of fat into the perivascular space. In some species, adipocytes constitute up to 35% of thymic tissue by 21 months of age (Hubbard et al., 1991). Adipocyte infiltration has been recorded in numerous marsupials including the brushtail possum (Johnstone, 1898), gray short-tailed opossum (Hubbard et al., 1991), stripe-faced dunnart (*Sminthopsis macroura*) (Old et al., 2003a) and red necked wallaby (*Macropus rufigriseus*)

Download English Version:

<https://daneshyari.com/en/article/5587823>

Download Persian Version:

<https://daneshyari.com/article/5587823>

[Daneshyari.com](https://daneshyari.com)