School of BioSciences

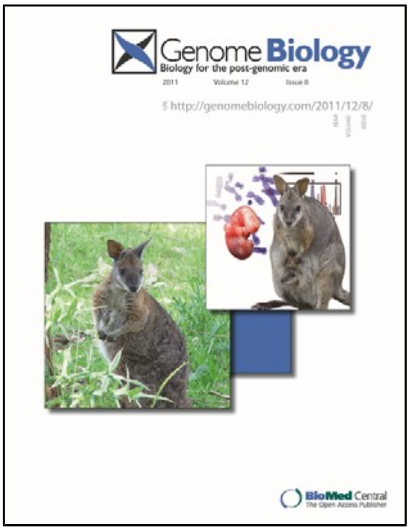
Reproduction and Development

Renfree & Shaw & Pask Laboratories

Research Projects Available for 2015

Laboratory Heads	**Research Fellows**
Professor Marilyn Renfree email: m.renfree@unimelb.edu.au Professor Geoff Shaw email: g.shaw@unimelb.edu.au Associate Professor Andrew Pask email: a.pask@unimelb.edu.au	Dr Stephen Frankenberg Dr Danielle Hickford Dr Brandon Menzies Dr Hongshi Yu

Our research covers a wide range of questions in reproductive and developmental biology, using physiological, endocrine, molecular, genetic and comparative genomic techniques. We have a strong research output including over 90 publications in the last 5 years, with papers in leading journals such as *Nature*, *Nature Genetics*, *PLoS One*, *PLoS Biology* and *PNAS*. We have recently published the genome of the tammar wallaby in Genome Biology that underpins all the studies outlined below and are currently assembling an improved genome coverage.



The Reproduction and Development laboratories are well equipped and students gain training in a broad range of relevant, cutting edge techniques in molecular biology, endocrinology, physiology and anatomy that will enhance future career prospects. We can take excellent Honours, Masters and PhD students.

Graduate prospects and employment

Our laboratory is well connected and internationally highly regarded, so our graduates have excellent prospects for personally and professionally rewarding careers. All our past postgraduates have established outstanding careers in academia, research, medicine, veterinary science and industry. For example, Rebecca Spindler (PhD 1997, Embryonic diapause) worked at the Smithsonian Institute developing embryo culture systems for rare and endangered species including pandas and jaguars, then headed the Reproductive Department at Toronto Zoo in Canada and is now head of reproduction and conservation at Tooronga Zoo, Sydney. Deanne Whitworth (PhD 1996; sexual differentiation) worked on hyaenas in California, then went to the MD Anderson Cancer Research Center in Houston, Texas and is now a lecturer in the University of Queensland. Doug Coveney continued his PhD interest in gonadal differentiation with a postdoctoral position in the Capel lab at

Rebecca Spindler

1997 PhD Embryonic diapause (supervised by Marilyn Renfree & David Gardner).

1997-2004 Research Fellow Smithsonian Institute, USA, developing embryo culture protocols for endangered species including pandas and jaguars.

2004-2007 Toronto Zoo, Canada, head of reproduction

2007- Taronga Zoo, Sydney: Head, Research & Conservation

Duke University, North Carolina before returning to Australia. He is now product manager at Leica Microsystems. Eleanor Ager (PhD 2007, Genomic imprinting) is now a research fellow in the Department of Surgery at the Austin Hospital working on cancer. Deidre Mattiske (PhD 2002, control of ovarian follicle development) undertook a postdoctoral fellowship in the Hogan Lab at Duke University, and is currently a Research Fellow at the Murdoch Childrens Research Institute. Gratiana Wijayanti (PhD 2004, Germ cell origins and migration) is a lecturer in Indonesia. Brandon Menzies (PhD 2008, Growth and development) was awarded a prestigious Alexander von Humboldt Fellowship at the Institute for Zoo and Wild Animal Research in Berlin and is now a Centenary Fellow of the University of Melbourne; Damien Paris (PhD 2004, sperm biology and artificial insemination) held a Marie Curie Fellowship in Glasgow, then went to Utrecht in Netherlands and is now a lecturer at James Cook University. Nanette Schneider (PhD 2008, Olfaction and the vomeronasal organ) took a post-doc in the German Institute of Human Nutrition Potsdam-Rehbrücke in Berlin and then as a research fellow in Dijon France.

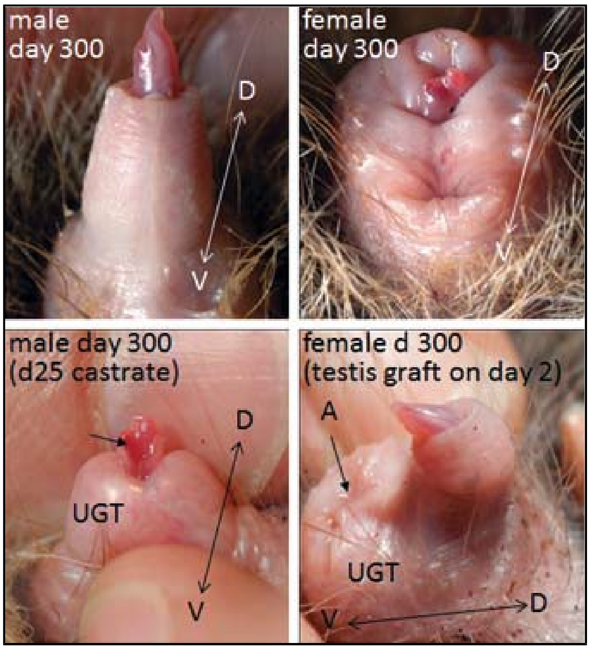
Marsupials are a valuable model for many questions because of some unique aspects of their biology, and differences and similarities between marsupials and other mammals have been very informative. For example, developmental stages that are essentially embryonic are easily accessible for investigation because much of development occurs whilst they are in the pouch, and much can be learned from the similarities and differences in timing of developmental events. Marsupials have proven to be important biomedical models. However, we also use other model species, from mice to elephants as applicable to a particular research question. Our research is supported by grants from the National Health and Medical Research Council as well as from the Australian Research Council. The techniques used range from molecular and developmental biology to endocrinology and reproductive physiology, and include immunohistochemistry, *in situ* hybridization, quantitative PCR, bioinformatics, cell and organ culture and field studies.

Research areas with projects include (but are not limited to):

Bioinformatics

All projects on offer in our group require some bioinformatics analyses. If you have a specific interest in bioinformatics we could design a project that fits in with currently funded projects.

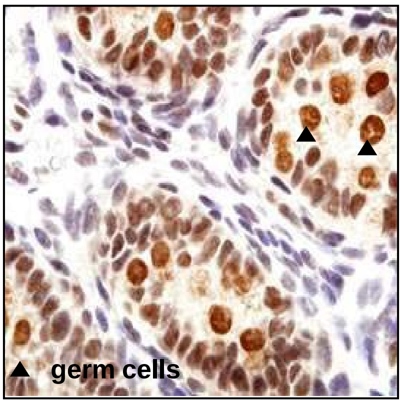
Molecular and endocrine control of hypospadias



Disorders of sexual differentiation (DSDs) are amongst the most common birth defects (1 in 4,000) births but malformations of the phallus are the most common and overt signs of impaired male differentiation. Hypospadias, the ectopic opening of the urethra, affects 1 in every 125 live male births in Victoria. The frequency of hypospadias is increasing internationally and in Australia.

Endocrine disruptors with oestrogenic activity in the environment may contribute to this increase. Hypospadias is caused when the urethral folds fail to close normally during fetal development and its severity depends on the location of the urethral opening. Despite its extraordinary prevalence, the only real option for affected boys at present is surgical intervention at 6-24 months of age. In most mammals, penile development is hard to investigate experimentally as it occurs in the fetus. We are capitalising on marsupials in which sexual differentiation, including penile development, occurs post-natally and mutant mice. Our ongoing research has already generated new paradigms with the discovery that some sex differences have a sex-specific genetic origin independent of gonadal hormones. We recently discovered an alternative pathway for androgen biosynthesis, the first new steroid hormone pathway described in the last 50 years. This pathway has now been demonstrated in mice and humans and has been translated into medical practise in a new Endocrine Society (USA) *Clinical Guideline*. The overall goal of this project is to provide new data on the interactions of the hormones, genes and morphogens essential for penile patterning and growth, using a unique model of controlled endocrine disruption to induce hypospadias.

Male germ cell development



Development of the male germ line before the onset of spermatogenesis has been well characterised in mice and to a lesser extent humans but little is known about this process in marsupials. Characterisation of this process in marsupials will provide the basic information which will allow us to isolate and purify specific stages of marsupial germ cell development. This ability would enable us to perform transcriptome and proteomic analyses to characterise events occurring during this process and would also have implications for conservation efforts as well as the isolation of potential spermatogonial stem cells. This project would use immunohistochemistry and bioinformatics of our gonad transcriptome to find proteins that characterise pre-spermatogenesis development of the male germ line.

Hormonal control of reproduction in the swamp wallaby, *Wallabia bicolor*

The breeding biology of the swamp wallaby appears to include a unique strategy, superfetation. Superfetation is the ability to gestate two or more conceptuses at different stages of development in order to optimse reproductive output. To date, only one species, the European brown hare, has been shown conclusively to have superfetation. Therefore, the identification of this phenomenon in a separate class of mammals would provide key insights into its evolution and function. Swamp wallabies are a common, solitary species in Victoria and eastern Australia that have previously been difficult to study intensively in captivity. They are the only macropodid to have an oestrous cycle shorter than their pregnancy length. Since marsupiala have two separate uteri, it is thought that females ovulate and mate before birth to conceive a new embryo which develops adjacent to the incumbent almost full term fetus. We have a small group of swamp wallabies on our breeding colony. Female swamp wallabies will be caught regularly and monitored for the presence of new pouch young and sampled for blood through pregnancy. The plasma will be analysed by radioimmunoassays to characterise hormonal profiles of progesterone and oestradiol measured to detect pre-partum oestrus.

If you are interested in research that is not covered on the list above, please come and see us. Which projects we are able to support from 2015 onwards will depend on success of grant applications that we currently have under consideration with the National Health and Medical Research Council, and the Australian Research Council. Funding announcements for these will probably not be made until November.

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