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Reproduction, Fertility and Development

Recent advances in reproductive research in Australia and New Zealand: highlights from the Annual Meeting of the Society for Reproductive Biology, 2022

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ABSTRACT

In 2022, the Society for Reproductive Biology came together in Christchurch New Zealand (NZ), for its first face-to-face meeting since the global COVID-19 pandemic. The meeting showcased recent advancements in reproductive research across a diverse range of themes relevant to human health and fertility, exotic species conservation, and agricultural breeding practices. Here, we highlight the key advances presented across the main themes of the meeting, including advances in addressing opportunities and challenges in reproductive health related to First Nations people in Australia and NZ; increasing conservation success of exotic species, including ethical management of invasive species; improvements in our understanding of developmental biology, specifically seminal fluid signalling, ovarian development and effects of environmental impacts such as endocrine-disrupting chemicals; and leveraging scientific breakthroughs in reproductive engineering to drive solutions for fertility, including in assisted reproductive technologies in humans and agricultural industries, and for regenerative medicine.

Keywords: agricultural breeding practices, assisted reproductive technologies, conservation, developmental biology, exotic species, First Nations reproductive health, Indigenous reproductive health, infertility, invasive species, preeclampsia, reproductive engineering, seminal fluid signalling, Society for Reproductive Biology.

Introduction

The Society for Reproductive Biology (SRB) aims to support and promote basic and applied research across all aspects of reproduction and fertility, with the ultimate goals of improving human health, reproductive outcomes, and reproductive control, improving agricultural productivity, and aiding in conservation biology. Due to the COVID-19 global pandemic, the 2022 Annual Meeting of the SRB held in Christchurch, New Zealand, was the first in-person meeting since 2019. The meeting brought together fundamental, clinical, and agricultural researchers and professionals in the field of reproductive biology from Australia, New Zealand, and around the world, and featured a diverse program that allowed attendees to connect, exchange ideas, foster new collaborations, and engage with the cutting-edge reproductive research. The highlight of this meeting were the interdisciplinary symposia sessions which are summarised in this review and showcased recent advancements in reproductive research across four key themes: reproductive health in First Nations people; exotic species conservation; developmental biology; and fundamental and applied reproductive engineering.

Indigenous reproductive health forum

Speakers: Jade Le Grice, Maree Toombs, Cameron D. Young, and Kirsty Pringle

For the first time, the SRB held an 'Indigenous Reproductive Health Forum' to showcase research conducted across Australia and New Zealand improving the health outcomes of

First Nations peoples. This forum highlighted the benefits of including First Nations peoples in study conception and design and in implementation of research findings within the community, in addition to the importance of cultural sensitivity. Across the diverse topics presented, a single takeaway message emerged: consult First Nations peoples about the research that impacts them, and let the research be guided by the community and their needs.

Indigenous Aboriginal and Torres Strait Islander (First Nations) Australians have high rates of health issues, including chronic diseases and reduced life expectancy, compared to migrant and settler populations (Nolan-Isles *et al.* 2021). They also experience high rates of common mental health disorders such as depression (Farah Nasir *et al.* 2021), trauma, and post-traumatic stress disorder (Nasir *et al.* 2021). Despite this, there is still a lack of access to health services in First Nations communities in Australia. Professor Maree Toombs' (University of Queensland) research aims to improve access to primary healthcare, particularly mental health services, for First Nations peoples. Her work situates Indigenous peoples at the centre of their own care, illustrating the power of asking the community for their input in regard to what they need. The Mobile Outreach Boomerang (MOB) van run by First Nations healthcare workers, provides primary healthcare to rural First Nations communities. The uptake of this service by the community was so impactful that additional funding from the New South Wales (NSW) government was secured to establish a fixed clinic. Through this healthcare service, the community voiced a need for a suicide intervention program that acted in real time and without judgement (Farah Nasir *et al.* 2021). Professor Toombs developed the Indigenous-Applied Suicide Intervention Skills Training program (I-ASIST), a suicide intervention model provided in partnership with Livingworks Australia (Farah Nasir *et al.* 2021). This program has trained over 10 000 people in 90 communities, giving the community a set of critical skills in mental healthcare to support their loved ones when they most need it. These projects demonstrate the positive outcomes of embracing collaborative partnerships with First Nations communities.

Associate Professor Kirsty Pringle's (University of Newcastle) work in rural NSW also centres around addressing disparities in health outcomes in First Nations communities, with a focus on developing positive and sustainable interventions to improve health outcomes for First Nations mothers and babies. The Gomeroi-Gaaynggal study ran for 10 years in Tamworth (2009–2019), successfully recruiting more than 400 mothers carrying First Nations babies. A critical part of the study design was the development of the Gomeroi-Gaaynggal Advisory Committee to consult on research direction and approval for dissemination of research findings to the broader research community. The study ran alongside an Arts Health program overseen by an Aboriginal Elder and artist in residence, all of which was embedded in the local Gomeroi community to build capacity beyond the lifespan of the study. One key finding was that while the majority of mothers (86%) initiate breastfeeding, the median duration was just 1.4 months (Ashman *et al.* 2016). Rapid discontinuation of breastfeeding is corroborated by additional studies in the field, representative of other First Nations communities across Australia (Craig *et al.* 2011; Brown *et al.* 2019). Working with the Gomeroi community, Associate Professor Pringle and her team are now moving toward building capacity in the community to mentor mothers and encourage longer periods of breastfeeding. By partnering with the Local Aboriginal Land Council and Aboriginal Medical Service, this next phase of the Gomeroi-Gaaynggal study will further improve outcomes for First Nations mothers and babies for better long-term health. Lastly, Associate Professor Pringle highlighted the importance of providing adequate context for the findings of her studies, ensuring there is a distinction from the ongoing impacts of colonisation, and the importance of First Nations healthcare workers in communities to bridge barriers in access to care.

Dr Jade Le Grice (University of Auckland) is working to identify the major challenges of equitable access to public and private fertility services and equitable care outcomes for Māori and Pacific peoples in New Zealand. The ability to contribute to the next generation of *whānau* (extended family group) is culturally significant for many Māori and Pacific peoples (Rarere 2022). However, members of these communities often face barriers when trying to access fertility services (Righarts *et al.* 2021). Dr Le Grice's research has highlighted the cultural and structural barriers such as the use of body mass index as a determinant for access to fertility treatment. This often acts as an exclusion measure that disproportionally impacts Māori and Pacific peoples' access to publicly funded fertility care (Parker and Le Grice 2022; Shaw and Fehoko 2023). Supported by Fertility New Zealand and the University of Auckland, she is currently focussing on the first-hand experiences of Māori and Pacific peoples with infertility in accessing fertility services, and their health outcomes. This has involved community-driven conversations in six Hui (Māori assembly) focus groups (19 Māori and Pacific participants) and findings thus far have highlighted the need to harness First Nations knowledge to provide holistic pathways for care and healing to support Māori and Pacific people experiencing infertility.

Finally, Cameron Young (University of Otago) highlighted the importance of understanding cultural sensitives when designing research projects, particularly in sexual and reproductive health. Indeed, approaching conversations that include topics like sexuality and reproduction in a Pacific community is very complex. These topics are considered *tapu* (sacred, forbidden) and can influence health behaviour, often due to discomfort or to avoid shame. Mr Young is exploring the views of Pacific youth on sexuality and reproduction (Young *et al.* 2022). A project of this nature requires discrete care to minimise harm. To address this, he has revitalised the Fonofale Pacific health model that is traditionally centred

around the Pacific concepts of family and culture (Pulotu-Endemann 1995). The inclusion of *tapu* and *noa* (ordinary, normal) recognises the complexity of Pacific people's health and the holistic approach needed to address prominent health issues (Young *et al.* 2022). Using the analogy of a three-layered cake, he described three important considerations for designing research projects that involve Pacific peoples; these principles can be applied to the design of all relevant research projects. Firstly, an acknowledgement of your worldview and how this may differ from the worldview of Pacific peoples. Secondly, identifying the aspirations of the project and matching these to the aspirations of the Pacific communities. Finally, adopting research methodologies that reflect the community. The Kakala and Talanoa methods are excellent examples of Pacific methodologies that inherently centre the aspirations of Pacific peoples in the research project. By collating these key messages, Mr Young provided a framework for researchers to design culturally sensitive research projects that tackle a variety of scientific questions.

The forum concluded with a panel discussion centred around the intricacies of research projects involving First Nations communities, including data governance. All panel members stressed the importance of communicating summaries of the research and sharing data with the community. Overall, this research demonstrated benefits to health outcomes when First Nations peoples are empowered to engage with and guide the trajectory of health research within their communities.

Exotic species

Speakers: Simon Clulow, Isabel Castro, Stephen Frankenberg, and Donna Bond

Invasive species have a significant, destructive impact on the unique flora and fauna of both Australia and New Zealand. This, together with difficulties that arise from trying to protect typically understudied species, often render conservation efforts ineffective. In this session, four prominent scientists discussed ways to increase conservation success, including ethical management of invasive species and improving understanding of the reproductive biology of vulnerable native species. Challenges and recent advances in the conservation of amphibians, reptiles, and the New Zealand kiwi, as well as novel strides towards control of invasive pest species by gene drive technology and long read methylation sequencing were highlighted in the symposium.

Over 50% of amphibian and 20% of reptilian species are endangered, requiring intervention to preserve genetic diversity and prevent extinction (Bower *et al.* 2017). The unique modes of fertilisation (internal, external, or parthenogenesis) and reproductive strategies (i.e. oviparity vs viviparity vs both) in these extremely diverse taxa pose many challenges for the development of assisted reproductive technologies (ART). These include some species having large, yolky eggs which remain difficult to cryopreserve (Diwan *et al.* 2020), unique sperm storage capacities (Sever 2002), and extra-genomic control of sex differentiation (i.e. incubation temperature) (Nakamura 2009). Dr Simon Clulow (University of Canberra) described recent advances in both amphibian and reptile ART and the current state of genome resource banks for species conservation (Clulow and Clulow 2016; Bolton *et al.* 2022; Clulow *et al.* 2022). He highlighted that the utility of amphibian cryobank technology is stalled by our inability to successfully cryopreserve and subsequently thaw the large, yolky eggs or embryos of this taxa (Diwan *et al.* 2020). Currently, conventional cryoprotectants are only able to preserve amphibian spermatozoa and must later be combined with fresh eggs to generate sexually mature offspring (Upton *et al.* 2018, 2021), thus presenting a problem when a mature female of an endangered/extinct species is unavailable. Encouragingly, some success has been achieved in fish and coral egg and embryo cryopreservation, which are of similar sizes and yolk content to amphibians, by using conductive gold nano rods and ultra-rapid laser warming (Jin *et al.* 2014; Khosla *et al.* 2017). Although these technologies are still in their relative infancy, it is now proposed that they could be used to get around the egg and embryo freezing block in amphibian species (Clulow *et al.* 2022). Altogether, Dr Clulow showed that significant research is still required in this field to establish successful genomic bioresources for the conservation of these animals.

Another example of harnessing unique reproductive traits of animals for conservation efforts is demonstrated with the New Zealand kiwi. Current management systems, which all have varying degrees of success (Robertson *et al.* 2011), include predator control, kiwi translocation (movement of individuals from areas where they face extinction to protected areas), and projects such as 'Operation Nest Egg', wherein eggs and young chicks are cared for in captivity or predator-free habitats until they are large enough to survive in areas with predators (Colbourne *et al.* 2005). Professor Isabel Castro (Massey University) investigates kiwi breeding behaviours and explores how this knowledge might improve conservation efforts. Professor Castro determined that the brown kiwi has a mating system that includes monogamy and polygamy. Polygamy has genetic advantages over monogamy because it has the potential to alleviate inbreeding depression and encourages higher rates of gene flow. In fact, in a study population, individuals breeding together were more genetically dissimilar to each other than random birds selected from the population (Undin *et al.* 2021). Therefore, incorporation of polygamous strategies into current conservation programs may improve the genetic stability of kiwi populations and more closely mimic natural breeding strategies. Additionally, Professor Castro's team discovered that egg incubation, which is primarily carried out by the male, may also be a major driver of kiwi mate selection and reproductive success. Interestingly, the 80-day process of

egg incubation alters the hormonal profiles of the parental kiwis, which may have significant impacts on conservation strategies when eggs are translocated and the incubation process is disrupted (Jensen *et al.* 2019). Wild kiwi pairs divorce rates were found to be positively correlated to low male attentiveness at the nest (Ramos-Pallares, in preparation). In this regard, Operation Nest Egg, which sequesters eggs from wild nests into captivity for hatching may unintentionally identify the incubating males as undesirable mates in subsequent breeding rounds and indirectly remove their genetics from the population (Colbourne 2002). Ultimately, increased understanding of the reproductive biology of this remarkable avian species will increase the conservation program success.

Conservation strategies not only rely on enhancing breeding, but also on reducing the predation of vulnerable species. The unique Australian fauna and flora face major threats from invasive pests such as feral cats, rodents, rabbits, and foxes, all of which are responsible for costly biodiversity and agricultural production losses. To address this pressing issue, Dr Stephen Frankenberg and his team (University of Melbourne) are exploring 'gene drive' technology as a novel tool to manage invasive pest populations. Gene drive is a phenomenon when an allele is inherited by the offspring more than 50% of the time (Bier 2022). Dr Frankenberg hypothesised that by targeting genes that regulate female fertility (e.g. aromatase and progesterone receptor), suppression gene drives are a more effective and humane strategy to reduce/eradicate invasive species populations, particularly when compared to existing control methods which include baiting, trapping, and shooting. This work used a zebrafish model to optimise the design and subsequent efficiency of gene drive propagation through a population. Dr Frankenburg and his team are now developing pipelines to generate gene drive constructs which target non-model vertebrates including the European carp, cane toad, fox, and rabbit. This work is a perfect example of how exploiting and combining knowledge of both reproductive biology and genetic engineering could make a tremendous contribution to the conservation of our vulnerable fauna.

Another excellent example of this comes from the work of Dr Donna Bond (University of Otago). Dr Bond uses the invasive New Zealand Brushtail Possum (*Trichosurus vulpecula*) as a model to shed essential light on the reproductive strategies of these unique animals for two purposes. She aims to further efforts of possum pest control in New Zealand, which is currently a multimillion-dollar industry, and aid in conservation efforts for other Australian mainland marsupial species that are endangered. To address this, Dr Bond conducted nuclear and mitochondrial DNA analysis together with long-read methylation sequencing and identified allele/parent-specific methylation expression, not yet seen in other species. This novel insight challenges the expectation that marsupial imprinting is restricted to orthologues of mammalian imprinted genes such as in humans and mice and highlights the need for more species diversity in our analyses. These findings demonstrate that a 'one-size fits all' model does not always work across species, even closely related ones, and as such, may explain why conservation/eradication efforts remain ineffectual into the 21st century.

The intricacies of reproductive processes/strategies in exotic animal species including amphibians, reptiles, marsupials, and niche avian species (e.g. kiwi) have traditionally been understudied such that our understanding remains virtually unchanged since their initial discoveries. This has hindered conservation efforts and now presents a challenge as the list of species classified as vulnerable, endangered, or functionally extinct continues to grow annually according to the International Union for the Conservation of Nature's Red List of Threatened Species. Fortunately, these recent research efforts are improving the fundamental understanding surrounding these unique species and are directly contributing to the protection, and where appropriate eradication, of species worldwide.

Developmental biology

Speakers: Casey Spiller, John Schjenken, Timothy Hore, and Dagmar Wilhelm

This session explored recent updates in developmental biology, encompassing novel associations between endocrine-disrupting chemicals and retinoic acid (RA) signalling, the interplay between seminal fluid and the establishment of healthy pregnancies, the development of the androgen epigenetic clock and recent advances in ovarian development and function. A key theme of this session was the effects of environmental exposures, both exogenous and endogenous, on the homeostasis of the developing and adult gonads.

It is well established that the presence of RA, a derivative of vitamin A, is critical for the specification of mammalian gonads. Specifically, during fetal development, germ cells in the embryonic ovary initiate meiosis in response to the presence of RA, whereas those in the testis do not as they are shielded from this molecule (Endo *et al.* 2019). This 'shielding' occurs by virtue of an RA metabolising cytochrome P450 enzyme CYP26B1, a protein which is essential for testis development (MacLean *et al.* 2007). In situations where RA signalling is disrupted, gonadogenesis may also be disrupted, such that an 'ovary/testis hybrid' is produced akin to an intersex-like condition or congenital disorders of sex development (Bowles *et al.* 2018; Kam Draskau *et al.* 2022). Considering this, Dr Cassy Spiller (University of Queensland) is investigating the impact of RA signalling disruption by ectopic mechanisms. Specifically, her interest lies in how environmental exposures (i.e. endocrine-disrupting chemicals) might disrupt RA balance. Dr Spiller is exploring how common medicinal and agricultural antifungals (i.e. azoles), which are known to cross the placenta and have been found in embryos and fetal blood

(Pilmis *et al.* 2015), affect early testicular development. These data will have profound implications for drug prescription during pregnancy as well as informing policy regarding safe exposure levels of known and suspected environmental endocrine-disrupting chemicals.

Associate Professor Dagmar Wilhelm (University of Melbourne) also discussed the importance of early ovarian development and how perturbations may significantly affect adult fertility (Smith *et al.* 2014). Dr Wilhelm has devoted her career to detailing the molecular events that drive sex determination, ovarian development, and disease. In a recent landmark publication, Dr Wilhelm and her collaborators detailed how the gonadal sexual fate determined during embryonic development, must be actively maintained in adulthood to prevent female-to-male sex reversal (Rossitto *et al.* 2022). Using a mouse model, they showed how in the ovary, estrogen receptors and Forkhead Box L2 (FOXL2) are responsible for protecting the ovarian granulosa cells from 'transdifferentiation' into Sertoli cells (Rossitto *et al.* 2022). Specifically, they show that recruitment of Tripartite Motif-Containing 28 (TRIM28) on chromatin in the proximity of FOXL2 acts to maintain the ovarian pathway and to repress testicular-specific genes preventing sex reversal of the mouse ovary after birth. Moreover, they show the role of TRIM28 in ovarian maintenance directly depends on E3-SUMO ligase activity which regulates the sex-specific SUMOylation profile of ovarian-specific genes. Altogether, these data indicate that TRIM28 is an important player in ovarian physiology and might therefore have a potential role in genetic diseases causing reproductive disorders. For instance, environmental factors, such as drugs or chemicals explored by Dr Spiller, interfered with the SUMO-E3-ligase activity of TRIM28, causing perturbed ovarian function and fertility. Understanding the underlying molecular regulation of gonadogenesis is thus highly relevant from a clinical perspective, as congenital disorders of sex development are not uncommon (Wilhelm *et al.* 2013).

In addition to exploring how environmental factors affect gametogenesis, this session also explored how they affect the establishment of a healthy pregnancy. Dr John Schjenken (University of Newcastle) highlighted the potential impact paternal environment stressors may have on seminal vesicle secretion and function. Seminal plasma is an acellular fluid mixture produced by the male accessory glands, particularly the seminal vesicles, in most mammalian species. Emerging evidence demonstrates that seminal plasma contributes to optimal fetal development and long-term offspring health (Bromfield *et al.* 2014; Watkins *et al.* 2018). The positive impact of signalling factors carried within seminal plasma, such as the transforming growth factor beta (TGFB) superfamily and cluster of differentiation 38 (CD38), on maternal immune tolerance is well-documented (Kim *et al.* 2015; Yang *et al.* 2021). What remains less known is the impact of paternal environment stressors on seminal vesicle quality and function. Dr Schjenken and his colleagues address this question using a variety of paternal environmental exposure models. In a paternal obesity model, Dr Schjenken showed a reduction in the expression of all three TGFB isoforms in seminal vesicle fluid from obese males (Schjenken *et al.* 2021). This observation likely explains the impairment of maternal immune tolerance (Schjenken *et al.* 2021) and the reduced implantation (Mitchell *et al.* 2011) rate previously reported in females mated with obese animals. Through proteome comparisons, Dr Schjenken and his colleagues also showed that seminal vesicle secretory functions are altered following acute acrylamide exposure, with more than 300 dysregulated proteins identified including serine protease inhibitors and seminal vesicle secretory proteins (Skerrett-Byrne *et al.* 2021). Collectively, these studies provide strong evidence that seminal vesicles respond to environmental exposures in a manner that may impact fertility, fetal development, and long-term offspring health, and thus further investigation into the underlying biology is warranted.

Epigenetic modifications are also key developmental regulatory pathways (Skinner 2011). For instance, measuring DNA methylation is a precise way of estimating the chronological age of an individual. In most mammals, this epigenetic clock is accelerated in males compared to females (Lemaître *et al.* 2020). Associate Professor Timothy Hore (University of Otago) and his team recently reported the first epigenetic clock for domesticated sheep, and found that the epigenetic clock and ageing are decelerated in castrated male sheep compared to intact sheep (Sugrue *et al.* 2021). They also identified regions in the genome that become hypomethylated with age in intact male sheep, including muskelin 1 (*MKLN1*), Ewing tumour-associated antigen 1 (*ETAA1*), and LIM domain transcription factor (*LMO4*). The methylation status of these regions in females and castrated males remain unchanged and are comparable over time, indicating these loci are sensitive to androgens (Sugrue *et al.* 2021). Similar reduction in methylation is also evident in male mice over time but in a tissue-specific manner depending on local androgen receptor expression (Sugrue *et al.* 2021), suggesting androgen-dependent DNA hypomethylation with age may exist in a wide range of mammalian species. Given the increased prevalence of androgen disorders such as polycystic ovarian syndrome (Yang *et al.* 2022), the findings from Associate Professor Hore and his group may lead to a tool that can measure androgen exposure and may have implications for reproductive disease diagnosis.

In summary, this session highlighted recent discoveries in developmental biology and, in particular, the significant impact environmental exposures have on fertility and development. Thus, further understanding of the interplay between developmental biology and environmental chemical exposure is crucial to lead to novel preventative and therapeutic interventions to improve fertility, health, and wellbeing in future generations.

Fundamental and applied reproductive engineering

Speakers: Diane Rebourcet, Zaramasina L. Clark, Cheow Yuen Tan, Lana McClements, Mark A. Baker, Zamira Gibb, and Shayanti Mukherjee

The 2022 SRB meeting had a strong focus on the ways fundamental science is being used to engineer creative solutions to safeguard and improve reproductive health in humans and other species. Across two symposia, 'Fundamental Reproductive Engineering' and 'Applied Reproductive Engineering', researchers highlighted how the application of foundational knowledge, and the engineering of novel techniques and tools, provides the capability to study the reproductive organs in greater detail, has the potential to revolutionise clinical practice and improve outcomes for reproductive health, and to improve reproductive efficiency in the context of agricultural and racing industries.

Steroid hormones play an important role in male reproduction and overall health. Alterations in steroid production or activity can lead to compromised sexual health, infertility, cardiovascular disease, and metabolic disorders (Gooren 2010; Rebourcet *et al.* 2014). The financial burden and unknown long-term efficacy of conventional hormone replacement therapies necessitates the development of safer and more efficient therapies, using new technologies. Dr Diane Rebourcet (University of Newcastle) and colleagues have developed a technology to target testicular cells in adult mice to provide a novel approach to regulating steroid production. Using a *Hsd17b3* knockout mouse model that displays altered androgen production (Lawrence *et al.* 2022), Dr Rebourcet validated the effectiveness of lentiviral and adeno-associated virus 9 (AAV9)-mediated gene therapy in restoring classical androgen production. However, steroid production relies upon a pulsatile regulation from the hypothalamus–pituitary axis; therefore, to refine such approaches Dr Rebourcet has combined the fields of optogenetics and endocrinology. Optogenetics was initially developed as a tool to control neuronal activity by using specific wavelengths of light to manipulate and regulate gene transcription in a spatio-temporal manner (Emiliani *et al.* 2022). Extending on these studies, Dr Rebourcet is developing optogenetic tools to finely manipulate steroidogenic production in the mouse testis. She has transfected Leydig cell lines to overexpress a light-sensitive steroidogenic acute regulatory protein and finely control steroid production by using short bursts of light *in vitro*. These tools offer new possibilities for the development of therapeutic treatments to support endogenous androgen production and male health.

The gonadotrophic follicle-stimulating hormone (FSH) is routinely administered to women to improve the number of mature oocytes available for retrieval ahead of *in vitro* fertilisation (IVF) or embryo transfer. However, the dose of FSH is patient-dependent and high doses of FSH have been correlated with a decrease in live birth rate following IVF (Baker *et al.* 2015; Clark *et al.* 2021). Dr Zaramasina Clark (Michigan State University; Te Herenga Waka-Victoria University of Wellington) used the low ovarian reserve heifer model to better understand how high doses of FSH affect the cell types within the ovary. Heifers given an excessive (210IU Folltropin-V) dose of FSH showed high heterogeneity in the phenotypes of their cumulus-oocyte complexes (COCs). While a quarter of the COCs remained compact similar to the control lower (70 IU) FSH dose group, the remaining COCs showed variable levels of abnormality and premature development. RNA sequencing from high-dose FSH follicles identified progressive changes in oocytes, cumulus, and granulosa cell transcripts with increased levels of COC abnormality. Abnormal COCs predominantly displayed changes in pathways associated with follicular organisation, angiogenesis, and immune responses, but showed few changes in luteinisation pathways (Clark *et al.* 2022). Combined, these results suggest that the follicular microenvironment is disrupted, primarily due to the dysregulated differentiation of cumulus cells. This work defines how excessive FSH stimulation affects the follicular microenvironment, providing strong rationale to standardise FSH doses within an effective range in the clinic.

Intracytoplasmic sperm injection (ICSI) and vitrification are important ART routinely performed in clinical IVF. However, both procedures are technically challenging, requiring manual handling of oocytes by highly skilled embryologists and adherence to stringent time frames. The stress induced by these processes may lead to poor clinical outcomes (Shen *et al.* 2003; Tiegs and Scott 2020). Dr Tiffany Tan and colleagues (University of Adelaide) hypothesised that minimisation of oocyte handling will simplify both procedures and in turn, improve IVF outcomes. To address this, they designed and fabricated a micro-device to minimise oocyte handling during ICSI and vitrification. The device was fabricated by two-photon polymerisation and consists of two parts: the oocytes are held in the 'pod' and multiple pods can dock into a holding 'garage'. This design circumvents the need for a holding pipette, thus minimising the manual handling of mouse oocytes during ICSI. Additionally, this pod and garage system minimises the volume of cryoprotectant needed at vitrification, as the oocyte is held within the device when moving across solutions with increasing concentrations of cryoprotectant. Importantly, compared to standard procedures, this device showed no differences in viability, developmental competency, or metabolism for oocytes and embryos in a mouse model. While future clinical trials are still needed, these data show this device has excellent potential to simplify the clinical procedures performed during ICSI and vitrification, and thus to provide patients with consistent outcomes for fertility treatment.

Preeclampsia is a multifactorial hypertensive disorder that affects 4–6% of all pregnancies (Chappell *et al.* 2021). In preeclampsia, the extravillous trophoblasts of the placenta

fail to remodel the uterine blood vessels to sufficiently meet the energy demands of the growing fetus (McNally *et al.* 2017). Preeclampsia is challenging to examine and model, due to the lack of access to the placental tissue during pregnancy and the fact that the vast majority of other mammalian species do not spontaneously develop preeclampsia (Varas Enriquez *et al.* 2018). Associate Professor Lana McClements and her team (University of Technology Sydney) are developing new *in vitro* models of the placenta to decipher the mechanisms of preeclampsia and to test or validate potential treatment strategies. The first *in vitro* model prints a three-dimensional (3D) biofunctional hydrogel matrix containing a first trimester trophoblast cell line, which allows the differentiation of multiple subtypes of trophoblasts with different functions within the placental organoid. Next, Associate Professor McClements presented the 'placenta-on-a-chip' model, which combines first trimester trophoblast cells (ACH-3Ps) with human umbilical vein endothelial cells (HUVECs) within collagen in a microfluidic device. The trophoblast cells migrate towards the HUVECs in the middle channel of the device, forming a vascularised 3D placental model (Ghorbanpour *et al.* 2023). Combined, these models emulate the early placenta, allowing the differentiation of placental cell types, migration of trophoblast cells, and interactions with blood vessels. These functions make these models useful tools to understand placental biology and the molecular mechanisms of preeclampsia.

Male factor infertility affects a staggering 5–7% of men in the Western world, accounting for 50% of couples seeking ART (Kumar and Singh 2015). While ART procedures including IVF and ICSI have had widespread global success in helping sub- and infertile couples achieve pregnancy, these technologies are only able to treat the symptoms of infertility. The underlying causes, which may be propagated in future generations, remain a mystery in many cases. Associate Professor Mark Baker and his team (University of Newcastle) are focused on understanding the mechanisms of male factor infertility by using proteomic approaches. They have shown that the nuclear retention of specific proteins is common in poor quality sperm, and of note, despite the widely held dogma that male infertility is heterogenous in causality, they have shown across multiple donors that poor quality sperm are often characterised by nuclear retention of the same proteins (Netherton *et al.* 2020*a*). Proteomic elucidation of the transient effects of this nuclear protein retention has provided novel insight into the fundamental biology underpinning male reproductive health (Netherton *et al.* 2020*b*). The unbiased screening capacity of 'omics' approaches offer great potential for biomarker discovery research with translational potential for diagnosis and treatment of male infertility.

Proteomics are also utilised by Dr Zamira Gibb and her research team at the University of Newcastle to improve the breeding efficiency of agricultural stock and elite thoroughbred racehorses. Such racehorses have no ART alternatives to natural mating, making it imperative to maximise pregnancy rates each breeding season, where stallions are required to mate up to 200 mares over 12 weeks. Thus, a simple and accurate method of determining pregnancy probability from a single mating event is of great value to the industry. Proteomic analyses have revealed that horse spermatozoa utilise a different ATP production and energy avenue to humans (Gibb *et al.* 2014; Griffin *et al.* 2022) and such knowledge has led to the development of the Equility device which uses dismount semen samples to predict pregnancy outcome in the field (Clulow and Gibb 2022) and guided development of sperm storage media for use at ambient temperatures (Aitken *et al.* 2014). The Equility device provides a fluorescent reading proportional to mitochondrial oxidative phosphorylation, making this technology pivotal in breeder decision-making to remate pairs prior to the end of the breeding season where necessary.

Regenerative medicine is another area to benefit from the application of foundational reproductive biology. Technological advances in treating common conditions in obstetrics and gynaecology were discussed by Dr Shayanti Mukherjee (Hudson Institute of Medical Research) who emphasised the importance of understanding the practicality of technical devices and integrating this into the design process. Astonishingly, pelvic organ prolapse affects up to 50% of women following childbirth, yet lacks any effective treatment (Nygaard *et al.* 2008). Surgical intervention in the past has involved repair using a mesh implant; however, transvaginal mesh usage has been linked to severe surgical complications (Dällenbach 2015) and has been the subject of much controversy (Dyer 2016). Biomedical engineering has great potential for improving the success of pelvic reconstructive surgery; Dr Mukerjee's team have made several advances in facilitating tissue repair with new nano-fabricated mesh materials (Paul *et al.* 2020) and endometrial stem cells (Mukherjee *et al.* 2020) to improve mesh integration into pelvic tissues. The combination of effective communication with key stakeholders and integration with pre-clinical models was highlighted as integral to successful translational research.

Collectively, these two symposia were a fitting reminder that bench-side breakthroughs can provide the groundwork for translational outcomes and for powerful new research tools. In particular, they illustrated the many ways in which practical application of advances in reproductive biology can benefit our society. Further, these sessions highlighted that engineering an effective product for translation requires a strong understanding of the target consumer, their needs and the unique challenges they face, and how the technology will be used. Efforts to address challenges in the areas of reproductive medicine, agriculture, and conservation will not only bring commercial rewards, but result in meaningful improvements to our understanding of reproductive biology.

Conclusion

The 2022 SRB Meeting provided Australian and New Zealand reproductive biologists the first opportunity since the global pandemic to connect in person to disseminate recent advances in reproductive research. In particular, the 2022 meeting had a strong focus on the unique context of reproductive research in these countries. This included a focus on improving reproductive health outcomes of First Nations peoples, with researchers consistently demonstrating the importance and benefits of ensuring that research is guided by First Nations communities, their needs, and specific cultural sensitives, in terms of study conception and design, data governance, and in implementation of research findings. Novel advancements in the effort to increase conservation of native exotic species in Australia and New Zealand were also presented, including the use of genetic engineering strategies to manage invasive species, and recent improvements in the understanding of reproduction in vulnerable native species including amphibians, reptiles, and the New Zealand kiwi. Of relevance more broadly, research on fundamental aspects of developmental biology called attention to the significant impact both endogenous and exogeneous environmental exposures have on the homeostasis of the developing and adult gonads. Finally, research presented on fundamental and applied reproductive engineering demonstrated the creative and innovative ways foundational knowledge can be used to provide the groundwork for new transitional approaches in clinical and agricultural settings and the development of powerful new research tools. Collectively, the 2022 SRB Meeting provided important insights on the key challenges, but also the vast opportunities, that reproductive research has in making meaningful improvements to human health and fertility, agricultural breeding, and conservation practices, and highlighted the importance of a diverse and interdisciplinary reproductive research community, that is thoroughly engaged with key industry, government, and community stakeholders.

References

Aitken RJ, Lambourne S, Gibb Z (2014) The John Hughes memorial lecture: aspects of sperm physiology – oxidative stress and the functionality of stallion spermatozoa. *Journal of Equine Veterinary Science* **34**(1), 17–27. doi:10.1016/j.jevs.2013.10.120

Ashman AM, Collins CE, Weatherall LJ, Keogh L, Brown LJ, Rollo ME, Smith R, Rae KM (2016) Dietary intakes and anthropometric measures of Indigenous Australian women and their infants in the Gomeroi gaaynggal cohort. *Journal of Developmental Origins of Health and Disease* **7**(5), 481–497. doi:10.1017/S2040174416000325

Baker VL, Brown MB, Luke B, Smith GW, Ireland JJ (2015) Gonadotropin dose is negatively correlated with live birth rate: analysis of more than 650,000 assisted reproductive technology cycles. *Fertility and Sterility* **104**(5), 1145–1152.E5. doi:10.1016/j.fertnstert.2015.07.1151

Bier E (2022) Gene drives gaining speed. *Nature Reviews Genetics* **23**(1), 5–22. doi:10.1038/s41576-021-00386-0

Bolton RL, Mooney A, Pettit MT, Bolton AE, Morgan L, Drake GJ, Appeltant R, Walker SL, Gillis JD, Hvilsom C (2022) Resurrecting biodiversity: advanced assisted reproductive technologies and biobanking. *Reproduction and Fertility* **3**(3), R121–R146. doi:10.1530/RAF-22-0005

Bower DS, Lips KR, Schwarzkopf L, Georges A, Clulow S (2017) Amphibians on the brink. *Science* **357**(6350), 454–455. doi:10.1126/science.aao0500

Bowles J, Feng C-W, Ineson J, Miles K, Spiller CM, Harley VR, Sinclair AH, Koopman P (2018) Retinoic acid antagonizes testis development in mice. *Cell Reports* **24**(5), 1330–1341. doi:10.1016/j.celrep.2018.06.111

Bromfield JJ, Schjenken JE, Chin PY, Care AS, Jasper MJ, Robertson SA (2014) Maternal tract factors contribute to paternal seminal fluid impact on metabolic phenotype in offspring. *Proceedings of the National Academy of Sciences of the United States of America* **111**(6), 2200–2205. doi:10.1073/pnas.1305609111

Brown S, Stuart-Butler D, Leane C, Glover K, Mitchell A, Deverix J, Francis T, Ah Kit J, Weetra D, Gartland D, Yelland J (2019) Initiation and duration of breastfeeding of Aboriginal infants in South Australia. *Women and Birth* **32**(3), e315–e322. doi:10.1016/j.wombi.2018.07.009

Chappell LC, Cluver CA, Kingdom J, Tong S (2021) Pre-eclampsia. *The Lancet* **398**(10297), 341–354. doi:10.1016/S0140-6736(20)32335-7

Clark ZL, Thakur M, Leach RE, Ireland JJ (2021) FSH dose is negatively correlated with number of oocytes retrieved: analysis of a data set with ~650,000 ART cycles that previously identified an inverse relationship between FSH dose and live birth rate. *Journal of Assisted Reproduction and Genetics* **38**(7), 1787–1797. doi:10.1007/s10815-021-02179-0

Clark ZL, Ruebel ML, Schall PZ, Karl KR, Ireland JJ, Latham KE (2022) Follicular hyperstimulation dysgenesis: new explanation for adverse effects of excessive FSH in ovarian stimulation. *Endocrinology* **163**(9), bqac100. doi:10.1210/endocr/bqac100

Clulow J, Clulow S (2016) Cryopreservation and other assisted reproductive technologies for the conservation of threatened amphibians and reptiles: bringing the ARTs up to speed. *Reproduction, Fertility and Development* **28**(8), 1116–1132. doi:10.1071/RD15466

Clulow J, Gibb Z (2022) Liquid storage of stallion spermatozoa – past, present and future. *Animal Reproduction Science* **247**, 107088. doi:10.1016/j.anireprosci.2022.107088

Clulow S, Clulow J, Marcec-Greaves R, Della Togna G, Calatayud NE (2022) Common goals, different stages: the state of the ARTs for reptile and amphibian conservation. *Reproduction, Fertility and Development* **34**(5), i–ix. doi:10.1071/RDv34n5_FO

Colbourne R (2002) Incubation behaviour and egg physiology of kiwi (*Apteryx* spp.) in natural habitats. *New Zealand Journal of Ecology* **26**(2), 129–138.

Colbourne R, Bassett S, Billing T, McCormick H, McLennan J, Nelson A, Robertson H (2005) The development of operation nest egg as a tool in the conservation management. Science for Conservation.

Craig PL, Knight J, Comino E, Webster V, Pulver LJ, Harris E (2011) Initiation and duration of breastfeeding in an Aboriginal community in South Western Sydney. *Journal of Human Lactation* **27**(3), 250–261. doi:10.1177/0890334411402998

Dällenbach P (2015) To mesh or not to mesh: a review of pelvic organ reconstructive surgery. *International Journal of Women's Health* **7**, 331–343. doi:10.2147/IJWH.S71236

Diwan AD, Harke SN, Gopalkrishna, Panche AN (2020) Cryobanking of fish and shellfish egg, embryos and larvae: an overview. *Frontiers in Marine Science* **7**, 251. doi:10.3389/fmars.2020.00251

Dyer O (2016) Johnson and Johnson faces lawsuit over vaginal mesh devices. *The BMJ* **353**, i3045. doi:10.1136/bmj.i3045

Emiliani V, Entcheva E, Hedrich R, Hegemann P, Konrad KR, Lüscher C, Mahn M, Pan Z-H, Sims RR, Vierock J, Yizhar O (2022) Optogenetics for light control of biological systems. *Nature Reviews Methods Primers* **2**(1), 55. doi:10.1038/s43586-022-00136-4

Endo T, Mikedis MM, Nicholls PK, Page DC, de Rooij DG (2019) Retinoic acid and germ cell development in the ovary and testis. *Biomolecules* **9**(12), 775. doi:10.3390/biom9120775

Farah Nasir B, Brennan-Olsen S, Gill NS, Beccaria G, Kisely S, Hides L, Kondalsamy-Chennakesavan S, Nicholson G, Toombs M (2021) A community-led design for an indigenous model of mental health care for indigenous people with depressive disorders. *Australian and New Zealand Journal of Public Health* **45**(4), 330–337. doi:10.1111/1753-6405.13115

Ghorbanpour SM, Richards C, Pienaar D, Sesperez K, Aboulkheyr Es. H, Nikolic VN, Karadzov Orlic N, Mikovic Z, Stefanovic M, Cakic Z, Alqudah A, Cole L, Gorrie C, McGrath K, Kavurma MM, Ebrahimi Warkiani M, McClements L (2023) A placenta-on-a-chip model to determine the regulation of FKBPL and galectin-3 in preeclampsia. *Cellular and Molecular Life Sciences* **80**, 44. doi:10.1007/s00018-022-04648-w

Gibb Z, Lambourne SR, Aitken RJ (2014) The paradoxical relationship between stallion fertility and oxidative stress. *Biology of Reproduction* **91**(3), 77. doi:10.1095/biolreprod.114.118539

Gooren LJ (2010) Androgens and male aging: current evidence of safety and efficacy. *Asian Journal of Andrology* **12**(2), 136–151. doi:10.1038/aja.2010.4

Griffin RA, Swegen A, Baker MA, Ogle RA, Smith N, Aitken RJ, Skerrett-Byrne DA, Fair S, Gibb Z (2022) Proteomic analysis of spermatozoa reveals caseins play a pivotal role in preventing short-term periods of subfertility in stallions. *Biology of Reproduction* **106**(4), 741–755. doi:10.1093/biolre/ioab225

Jensen T, Jamieson SE, Castro I, Gartrell B, Cockrem JF, Durrant B (2019) Serum prolactin and testosterone levels in captive and wild brown kiwi (*Apteryx mantelli*) during the prebreeding, breeding, and incubation periods. *Zoo Biology* **38**(3), 316–320. doi:10.1002/zoo.21484

Jin B, Kleinhans FW, Mazur P (2014) Survivals of mouse oocytes approach 100% after vitrification in 3-fold diluted media and ultra-rapid warming by an IR laser pulse. *Cryobiology* **68**(3), 419–430. doi:10.1016/j.cryobiol.2014.03.005

Kam Draskau M, Ravn Ballegaard A-S, Ramhøj L, Bowles J, Svingen T, Spiller CM (2022) AOP key event relationship report: linking decreased retinoic acid levels with disrupted meiosis in developing oocytes. *Current Research in Toxicology* **3**, 100069. doi:10.1016/j.crtox.2022.100069

Khosla K, Wang Y, Hagedorn M, Qin Z, Bischof J (2017) Gold nanorod induced warming of embryos from the cryogenic state enhances viability. *ACS Nano* **11**(8), 7869–7878. doi:10.1021/acsnano.7b02216

Kim B-J, Choi Y-M, Rah S-Y, Park D-R, Park S-A, Chung Y-J, Park S-M, Park JK, Jang KY, Kim U-H (2015) Seminal CD38 is a pivotal regulator for fetomaternal tolerance. *Proceedings of the National Academy of Sciences of the United States of America* **112**(5), 1559–1564. doi:10.1073/pnas.1413493112

Kumar N, Singh AK (2015) Trends of male factor infertility, an important cause of infertility: a review of literature. *Journal of Human Reproductive Sciences* **8**(4), 191–196. doi:10.4103/0974-1208.170370

Lawrence BM, O'Donnell L, Smith LB, Rebourcet D (2022) New insights into testosterone biosynthesis: novel observations from HSD17B3 deficient mice. *International Journal of Molecular Sciences* **23**(24), 15555. doi:10.3390/ijms232415555

Lemaître J-F, Ronget V, Tidière M, Allainé D, Berger V, Cohas A, Colchero F, Conde DA, Garratt M, Liker A, Marais GAB, Scheuerlein A, Székely T, Gaillard J-M (2020) Sex differences in adult lifespan and aging rates of mortality across wild mammals. *Proceedings of the National Academy of Sciences of the United States of America* **117**(15), 8546–8553. doi:10.1073/pnas.1911999117

MacLean G, Li H, Metzger D, Chambon P, Petkovich M (2007) Apoptotic extinction of germ cells in testes of *Cyp26b1* knockout mice. *Endocrinology* **148**(10), 4560–4567. doi:10.1210/en.2007-0492

McNally R, Alqudah A, Obradovic D, McClements L (2017) Elucidating the pathogenesis of pre-eclampsia using *in vitro* models of spiral uterine artery remodelling. *Current Hypertension Reports* **19**(11), 93. doi:10.1007/s11906-017-0786-2

Mitchell M, Bakos HW, Lane M (2011) Paternal diet-induced obesity impairs embryo development and implantation in the mouse. *Fertility and Sterility* **95**(4), 1349–1353. doi:10.1016/j.fertnstert.2010.09.038

Mukherjee S, Darzi S, Paul K, Cousins FL, Werkmeister JA, Gargett CE (2020) Electrospun nanofiber meshes with endometrial MSCs modulate foreign body response by increased angiogenesis, matrix synthesis, and anti-inflammatory gene expression in mice: implication in pelvic floor. *Frontiers in Pharmacology* **11**, 353. doi:10.3389/fphar.2020.00353

Nakamura M (2009) Sex determination in amphibians. *Seminars in Cell & Developmental Biology* **20**(3), 271–282. doi:10.1016/j.semcdb.2008.10.003

Nasir BF, Black E, Toombs M, Kisely S, Gill N, Beccaria G, Kondalsamy-Chennakesavan S, Nicholson G (2021) Traumatic life events and risk of post-traumatic stress disorder among the Indigenous population of regional, remote and metropolitan Central-Eastern Australia: a cross-sectional study. *BMJ Open* **11**(4), e040875. doi:10.1136/bmjopen-2020-040875

Netherton J, Ogle RA, Hetherington L, Silva Balbin Villaverde AI, Hondermarck H, Baker MA (2020*a*) Proteomic analysis reveals that Topoisomerase 2A is associated with defective sperm head morphology. *Molecular & Cellular Proteomics* **19**(3), 444–455. doi:10.1074/mcp.RA119.001626

Netherton JK, Hetherington L, Ogle RA, Gavgani MM, Velkov T, Villaverde AIB, Tanphaichitr N, Baker MA (2020*b*) Mass spectrometry reveals new insights into the production of superoxide anions and 4-hydroxynonenal adducted proteins in human sperm. *Proteomics* **20**(2), 1900205. doi:10.1002/pmic.201900205

Nolan-Isles D, Macniven R, Hunter K, Gwynn J, Lincoln M, Moir R, Dimitropoulos Y, Taylor D, Agius T, Finlayson H, Martin R, Ward K, Tobin S, Gwynne K (2021) Enablers and barriers to accessing healthcare services for Aboriginal people in New South Wales, Australia. *International Journal of Environmental Research and Public Health* **18**(6), 3014. doi:10.3390/ijerph18063014

Nygaard I, Barber MD, Burgio KL, Kenton K, Meikle S, Schaffer J, Spino C, Whitehead WE, Wu J, Brody DJ (2008) Prevalence of symptomatic pelvic floor disorders in US women. *JAMA* **300**(11), 1311–1316. doi:10.1001/jama.300.11.1311

Parker G, Le Grice J (2022) Sized out: fatness, fertility care, and reproductive justice in Aotearoa New Zealand. In 'Reproductive citizenship'. (Ed. RM Shaw) pp. 153–178. (Palgrave Macmillan)

Paul K, Darzi S, Werkmeister JA, Gargett CE, Mukherjee S (2020) Emerging nano/micro-structured degradable polymeric meshes for pelvic floor reconstruction. *Nanomaterials* **10**(6), 1120. doi:10.3390/nano10061120

Pilmis B, Jullien V, Sobel J, Lecuit M, Lortholary O, Charlier C (2015) Antifungal drugs during pregnancy: an updated review. *Journal of Antimicrobial Chemotherapy* **70**(1), 14–22. doi:10.1093/jac/dku355

Pulotu-Endemann FK (1995) 'Fonofale: model of health.' (Fuimaono Karl Pulotu-Endemann)

Rarere M (2022) The importance of whakapapa for understanding fertility. *Genealogy* **6**(2), 26. doi:10.3390/genealogy6020026

Rebourcet D, O'Shaughnessy PJ, Monteiro A, Milne L, Cruickshanks L, Jeffrey N, Guillou F, Freeman TC, Mitchell RT, Smith LB (2014) Sertoli cells maintain leydig cell number and peritubular myoid cell activity in the adult mouse testis. *PLoS ONE* **9**(8), e105687. doi:10.1371/journal.pone.0105687

Righarts A, Dickson NP, Ekeroma A, Gray AR, Parkin L, Gillett WR (2021) The burden of infertility in New Zealand: a baseline survey of prevalence and service use. *Australian and New Zealand Journal of Obstetrics and Gynaecology* **61**(3), 439–447. doi:10.1111/ajo.13323

Robertson HA, Colbourne RM, Graham PJ, Miller PJ, Pierce RJ (2011) Experimental management of Brown Kiwi *Apteryx mantelli* in central Northland, New Zealand. *Bird Conservation International* **21**, 207–220. doi:10.1017/S0959270910000444

Rossitto M, Déjardin S, Rands CM, Le Gras S, Migale R, Rafiee M-R, Neirijnck Y, Pruvost A, Nguyen AL, Bossis G, Cammas F, Le Gallic L, Wilhelm D, Lovell-Badge R, Boizet-Bonhoure B, Nef S, Poulat F (2022) TRIM28-dependent SUMOylation protects the adult ovary from activation of the testicular pathway. *Nature Communications* **13**(1), 4412. doi:10.1038/s41467-022-32061-1

Schjenken JE, Moldenhauer LM, Sharkey DJ, Chan HY, Chin PY, Fullston T, McPherson NO, Robertson SA (2021) High-fat diet alters male seminal plasma composition to impair female immune adaptation for pregnancy in mice. *Endocrinology* **162**(10), bqab123. doi:10.1210/endocr/bqab123

Sever DM (2002) Female sperm storage in amphibians. *Journal of Experimental Zoology* **292**(2), 165–179. doi:10.1002/jez.1152

Shaw RM, Fehoko E (2023) Epistemic injustice and body mass index: examining Māori and Pacific women's access to fertility treatment in Aotearoa New Zealand. *Fat Studies* **12**, 338–352. doi:10.1080/21604851.2022.2063507

Shen S, Khabani A, Klein N, Battaglia D (2003) Statistical analysis of factors affecting fertilization rates and clinical outcome associated with intracytoplasmic sperm injection. *Fertility and Sterility* **79**(2), 355–360. doi:10.1016/S0015-0282(02)04675-7

Skerrett-Byrne DA, Nixon B, Bromfield EG, Breen J, Trigg NA, Stanger SJ, Bernstein IR, Anderson AL, Lord T, Aitken RJ, Roman SD, Robertson SA, Schjenken JE (2021) Transcriptomic analysis of the seminal vesicle response to the reproductive toxicant acrylamide. *BMC Genomics* **22**(1), 728. doi:10.1186/s12864-021-07951-1

Skinner MK (2011) Role of epigenetics in developmental biology and transgenerational inheritance. *Birth Defects Research Part C: Embryo Today: Reviews* **93**(1), 51–55. doi:10.1002/bdrc.20199

Smith P, Wilhelm D, Rodgers RJ (2014) Development of mammalian ovary. *Journal of Endocrinology* **221**(3), R145–R161. doi:10.1530/JOE-14-0062

Sugrue VJ, Zoller JA, Narayan P, Lu AT, Ortega-Recalde OJ, Grant MJ, Bawden CS, Rudiger SR, Haghani A, Bond DM, Hore RR, Garratt M, Sears KE, Wang N, Yang XW, Snell RG, Hore TA, Horvath S (2021) Castration delays epigenetic aging and feminizes DNA methylation at androgen-regulated loci. *eLife* **10**, e64932. doi:10.7554/eLife.64932

Tiegs AW, Scott RT (2020) Evaluation of fertilization, usable blastocyst development and sustained implantation rates according to intracytoplasmic sperm injection operator experience. *Reproductive BioMedicine Online* **41**(1), 19–27. doi:10.1016/j.rbmo.2020.03.008

Undin M, Lockhart PJ, Hills SFK, Armstrong DP, Castro I (2021) Mixed mating in a multi-origin population suggests high potential for genetic rescue in North Island Brown Kiwi, *Apteryx mantelli*. *Frontiers in Conservation Science* **2**, 702128. doi:10.3389/fcosc.2021.702128

Upton R, Clulow S, Mahony MJ, Clulow J (2018) Generation of a sexually mature individual of the Eastern dwarf tree frog, *Litoria fallax*, from cryopreserved testicular macerates: proof of capacity of cryopreserved sperm derived offspring to complete development. *Conservation Physiology* **6**, coy043. doi:10.1093/conphys/coy043

Upton R, Clulow S, Calatayud NE, Colyvas K, Seeto RGY, Wong LAM, Mahony MJ, Clulow J (2021) Generation of reproductively mature offspring from the endangered green and golden bell frog *Litoria aurea* using cryopreserved spermatozoa. *Reproduction, Fertility and Development* **33**(9), 562–572. doi:10.1071/RD20296

Varas Enriquez PJ, McKerracher LJ, Elliot MG (2018) Pre-eclampsia and maternal–fetal conflict. *Evolution, Medicine, and Public Health* **2018**(1), 217–218. doi:10.1093/emph/eoy029

Watkins AJ, Dias I, Tsuro H, Allen D, Emes RD, Moreton J, Wilson R, Ingram RJM, Sinclair KD (2018) Paternal diet programs offspring health through sperm- and seminal plasma-specific pathways in mice. *Proceedings of the National Academy of Sciences of the United States of America* **115**(40), 10064–10069. doi:10.1073/pnas.1806333115

Wilhelm D, Yang JX, Thomas P (2013) Mammalian sex determination and gonad development. *Current Topics in Developmental Biology* **106**, 89–121. doi:10.1016/b978-0-12-416021-7.00003-1

Yang D, Dai F, Yuan M, Zheng Y, Liu S, Deng Z, Tan W, Chen L, Zhang Q, Zhao X, Cheng Y (2021) Role of transforming growth factor-β1 in regulating fetal-maternal immune tolerance in normal and pathological pregnancy. *Frontiers in Immunology* **12**, 689181. doi:10.3389/fimmu.2021.689181

Yang R, Li Q, Zhou Z, Qian W, Zhang J, Wu Z, Jin L, Wu X, Zhang C, Zheng B, Tan J, Hao G, Li S, Tian T, Hao Y, Zheng D, Wang Y, Norman RJ, Li R, Liu P, Qiao J (2022) Changes in the prevalence of polycystic ovary syndrome in China over the past decade. *The Lancet Regional Health - Western Pacific* **25**, 100494. doi:10.1016/j.lanwpc.2022.100494

Young CD, Bird RJ, Hohmann-Marriot BE, Girling JE, Taumoepeau MM (2022) The revitalised fonofale as a research paradigm: a perspective on pacific sexuality and reproduction research. *Pacific Dynamics* **6**(2), 186–201. doi:10.26021/10639

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