Monash IVF Research and Education Foundation.

January 2019 to June 2020 Report.

Monash IVF Group


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JAPAN

A year in review

Comment from the Group CEO (on behalf of the Board)

At the heart of Monash IVF Group is a commitment to "help bring life into the world" by delivering best in class fertility solutions for all, diagnostics, genetics and pathology across our fertility and women's imaging services.

We have a strong expanding footprint of IVF clinics, ultrasound practices and service centers across Australia and Malaysia. Our network includes over 700 dedicated doctors, scientific, nursing, allied health and support staff, complimented with many medical and scientific global leading researchers.

Monash IVF Group are absolutely committed to scientific leadership and clinical research and innovation as a key pillar of our long-term strategy. We will strive to break new ground through world class research and science as we continue to deliver market leading success rates, innovative services and attract partnership opportunities.

The Monash IVF Group Research and Education Foundation (MREF) provides an effective platform to ensure we continue to lead the world on the clinical and scientific front, building on our pioneering heritage, since achieving the world's first IVF pregnancy.

Across 2019 to June 2020, the Group successfully submitted over 90 scientific papers and presentations both locally and internationally.

On behalf of the Monash IVF Group Board, I commend the MREF and relay my thanks to our doctors, scientists, staff and collaborators who have contributed to this strategically important body of work.

Excellence in Research and Education

Monash IVF Research and Education Foundation (MREF)

A word from the Chairman of the Monash IVF Research and Education Foundation Professor Robert McLachlan — Chairman MREF

As Chairman of MREF over the past nine years, I have greatly enjoyed working with my colleagues on the Foundation. The MREF Advisory Board provides outstanding clinical, embryological and medical imaging expertise and all members have worked with enthusiasm and creativity to address our strategic goals. We were all greatly sadden by the passing of Prof Michelle Lane who had made invaluable contributions for many years. The Board has been enhanced by the addition of Dr Mark Green, Deputy Scientific Director, Research (Victoria) and Prof Moira O'Bryan, Head of the School of Biological Sciences, Monash University who both bring a wealth of experience in reproductive biology and medicine. In 2020, the committee welcomed two members from Queensland, A/Prof David Shaker, the Clinical Representative for Queensland and Dr Yanhe Liu, the Scientific Director of Queensland.

I have been gratified by the continued support of the Monash IVF Group Managing Director and the Board of Directors who share our commitment to the work of MREF and who have provided substantial funds across the years. The Monash IVF Group's commitment to research and education has again been evident through 2019 and into 2020 as it maintains its leadership position in assisted reproductive treatment. Our close relationship with Monash and Adelaide Universities along with the Murdoch Children's Health Institute has enhanced research and teaching productivity. Finally, I acknowledge the generous untied research grants received from industry.

The outcomes of papers and presentations across the 18 months to June 30th 2020 and our future research directions are outlined in this report. I express my gratitude to Professor Luk Rombauts, Director of Clinical Research, for his energy and expertise in the development and conduct of our many clinical studies. We both recognise the invaluable work of our dedicated research team; Vivien MacLachlan, Data and Research Manager, Samantha Ter and Dr Nicole McPherson who diligently oversee the clinical studies and deals with the complex demands of the medical, nursing and scientific staff, and human ethics committees.

I would also like to thank all the Monash IVF Group clinical and scientific staff for their contributions to the educational programs we provide to undergraduate, postgraduate and overseas trainees.

Monash IVF Research and Education Foundation Advisory Board

Professor Robert McLachlan

MBBS (Hons), PhD, FRACP, AM

Chairman MREF, Director of Clinical Research, Hudson Institute; Adjunct Professor, Monash Department of Obstetrics and Gynaecology; Medical Director, Healthy Male; Monash IVF Consultant Andrologist

Graduating from Monash University in 1977 and completing advanced training in endocrinology in 1984, Professor Rob McLachlan undertook his PhD studies in reproductive physiology at Prince Henry's Institute and the Department of Anatomy, Monash University. He worked as a visiting scientist at the University of Washington, in Seattle, USA, working on the hormonal regulation of reproductive function. After returning to Australia in 1990, he was a Research Fellow of the NHMRC until 2016 and continues to hold research grants. He has been the Consultant Andrologist to the Monash IVF program since 1991.

He is an Adjunct Professor in the Department of Obstetrics and Gynaecology at Monash University. As Director of Clinical Research at the Hudson Institute at Monash Medical Centre, he conducts NHMRC supported research involving basic and clinical research into male fertility regulation and the role of androgens, and is Deputy Director of Endocrinology, Monash Medical Centre. He has been Medical Director of Healthy Male [formerly Andrology Australia], a Federal government initiative, based at Monash University since 2006, and is committed to research and community and professional education in male reproductive health.

Since 2010, he has made over 80 invited presentations including 22 international meeting presentations (keynotes & plenaries). He has published over 280 original reports, reviews and chapters. He is Section Editor "Male Endocrinology" for www.ENDOTEXT.org. He is a Past President of the Fertility Society of Australia. In 2014 he received the Hoffenberg International Medal, Society for Endocrinology, UK, for outstanding contributions to the field and in 2016 was made a Member (AM) in the General Division of the Order of Australia in recognition of his work in male reproductive health and research. At the 2019 Fertility Society of Australia conference, Rob was awarded a Lifetime Membership as recognition to his contribution to male infertility.

Professor Luk Rombauts

PhD, MD, FRANZCOG, CREI

Research Director, MREF, Group Medical Director , Monash IVF; President of the Fertility Society of Australia, Clinical Adjunct Professor, Department of Obstetrics and Gynaecology, Monash University; Head of Reproductive Medicine, Monash Health; IVF Specialist, Monash IVF Victoria.

Trained in obstetrics and gynaecology at the University of Leuven, Belgium, Prof Rombauts began his clinical and research work at Monash in 1994. After spending a further 2 years in the IVF unit at the Leuven Institute of Fertility and Embryology (Belgium), Prof. Rombauts returned to Melbourne in 1998 to obtain his Certificate of Reproductive Endocrinology and Infertility (CREI). He is now accredited by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists as a training supervisor and examiner for the CREI.

Prof. Rombauts has a strong track record in women's health, clinical and translational research in the field of reproductive medicine. He currently conducts NHMRC funded research into several aspects of female infertility, with a strong focus on the communication between the embryo and the endometrium. Professor Luk Rombauts has published more than 150 articles, reviews and book chapters since 1990. He has a current h-index of 37 (Scopus 2020) and a total of 3731 citations. He has been invited to present lectures at numerous international meetings. He has helped develop clinical guidelines for the management of PCOS, endometriosis and OHSS. He is also an expert advisor for the Endometriosis Phenome and Biobanking Harmonisation Project sponsored by the World Endometriosis Research Foundation.

He is an Adjunct Clinical Professor in the Department of Obstetrics and Gynaecology at Monash University and the Head of Reproductive Medicine at Sothern Health. He is the Group Medical Director and Clinical Research Director of Monash IVF and a Research Fellow of the Hudson Institute for Medical Research. Prof Rombauts was elected as President of the Fertility Society of Australia in 2019. He is the current President-Elect of the World Endometriosis Society and in 2011 he was appointed to the World Endometriosis Research Foundation Board of Trustees. He is also a member of the Endometriosis Australia Advisory Board.

His clinical interests are advanced laparoscopic surgery for endometriosis, male and female reproductive microsurgery, and the management of male and female infertility, including all aspects of IVF.

Professor Beverley Vollenhoven

MBBS (Hons), PhD, FRANZCOG, CREI

Director Teaching and Learning, MREF. Professor, Department of Obstetrics and Gynaecology, Monash University; Head of Gynaecology at Monash Health; IVF Specialist, Monash IVF Victoria

Professor Vollenhoven graduated from Monash University in 1984 and completed her training in Obstetrics and Gynaecology in 1995. She has been a clinician at Monash IVF since 1996 and has a sub-specialty qualification in Reproductive Endocrinology and Infertility (CREI).

Her areas of clinical interest include infertility, polycystic ovarian syndrome, eating disorders, paediatric and adolescent gynaecology and menopause. She also has a clinical and research interest in the cause and treatment of uterine fibroids (leiomyomas); the management of infertility, particularly IVF, ovulation and ovulation disorders (such as PCOS), Turner's Syndrome and menopause. She has more than 150 publications in both journals and books.

Professor Vollenhoven is the Head of Gynaecology at Monash Health and also of the Contraceptive Counselling Clinic and Menopause Clinic, Monash Medical Centre. She is a reproductive endocrinologist in the Long Term Care of Children with Cancer Clinic. She is the deputy head of Obstetrics and Gynaecology at Monash University

She is a Past Chairperson of the Victorian Regional Committee of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists. She is a member of the RANZCOG CREI committee and an examiner for the sub specialist exams. She was a member of the 8th Council of RANZCOG. She is a member of the Advisory Committee on Medicines for the TGA. She is currently on the board for both the Fertility Society of Australia as well as the Australasian Menopause Society. In 2019 she became a member of the Victorian Honour Roll of Women. Professor Vollenhoven was appointed Director of Teaching and Learning, MREF in June 2012.

Professor Michelle Lane

BSc, PhD (1970 – 2020)

Director of Research and Development, Monash IVF Group

Professor Michelle Lane was Director of Research and Development at the Monash IVF Group and Research Leader at the Robinson Research Institute at the University of Adelaide. She published >200 peer reviewed journal articles and >350 abstracts in understanding the preimplantation embryo including in prestigious journals such as Science and Nature Biotechnology. Her translational studies have resulted in 12 patents and she was an inventor of several media sold worldwide for the culture of human embryos and as well as products for vitrification of embryos. She won several awards for her research into improving IVF outcomes, including a new generation of diagnostics for embryo viability as well as understanding lifestyle impacts on fertility, including her leading role in the focus on men's health at conception.

Professor Lane unfortunately passed away on February 4th of 2020. We are very grateful of her contributions in the past 30 years of her career and she will be forever missed.

Associate Professor Deirdre Zander-Fox

BSc (Hon), PhD

Regional Scientific Director of Monash IVF Victoria and KL Fertility, Associate Professor Monash University, University of South Australia and University of Adelaide

Deirdre completed her PhD studies in 2010 through The University of Adelaide's School of Paediatrics and Reproductive Health in which she undertook novel research into the impact of in-vitro stress on preimplantation embryo development, viability and metabolism. She has been a clinical embryologist since 2004 and is currently the Monash IVF Group Regional Scientific Director and oversees Monash IVF Victoria and KL Fertility (Malaysia). She is responsible for Embryology, Genetics, Andrology and Endocrine services within these clinics as well as operational management, QC/QA and new technology implementation. In addition Deirdre supervises numerous PhD and honors students and holds an Adjunct Associate Professor positions at three Universities within Australia (Monash University, University of Adelaide and University of South Australia) as well as NHMRC funding.

Deirdre has authored 31 peer reviewed journal articles and book chapters with her research focusing on improving laboratory technology that will directly benefit infertile patients including cryopreservation, microinjection, culture media design and metabolic screening of embryo culture media. Her basic research interests focus on the impact of the environment during peri and pre implantation development on programming fetal growth and offspring health.

Dr Mark Green

PhD

Deputy Scientific Director of Monash IVF Victoria, Merck Serono Senior Lecturer and Group Leader, as well as Director of Teaching & Learning, School of BioSciences, University of Melbourne

Mark completed his PhD at the University of Nottingham in the UK, before undertaking a two-year postdoctoral fellowship at the University of Missouri, USA. He then moved to New Zealand, to be the inaugural Maurice Paykel Fellow at The Liggins Institute, University of Auckland and subsequently, the inaugural Fertility Associates Fellow, working closely with New Zealand's largest human fertility clinic, to ascertain the effects of reproductive technologies on the phenotype and health of IVF children. During this time, Mark also held a joint appointment as a senior scientist studying the health of cloned animals with AgResearch Ltd. In 2011 Mark was recruited as the Merck Serono Lecturer in Reproductive Biology and group leader in the School of BioSciences, University of Melbourne. Alongside this in 2019, Mark started as the Deputy Scientific Director of Victoria for Monash IVF.

Mark has published more than 50 journal articles and book chapters, with his research frequently featured in the media. He has founded two start-up companies to commercialise his patents in microfluidic sperm sorting technologies. Mark has received national research awards and sits on numerous committees and scientific boards in the reproductive biology discipline. He has successfully secured greater than $10 million in research funding and currently holds NHMRC and ARC research grants. His research focusses on understanding how environmental factors, such as endocrine disruptors, light pollution and heat stress, as well as assisted reproductive technologies affect gamete quality, early embryo development and offspring health.

Associate Professor David Shaker

MBBCh FRCS, FRGOG, FRANZCOG, MMEd (Dundee)

Associate Professor, Department of Obstetrics and Gynaecology, University of Queensland; IVF Specialist, Monash IVF Queensland

Dr Shaker graduated in 1986 and attained Fellowship of the Royal College of Surgeons of Edinburgh, UK (FRCS) in 1993. Later, he attained membership of the Royal College of Obstetricians & Gynaecologists (RCOG) UK in 1995. He received special training in advanced laparoscopic surgery and obtained RCOG certificate of laparoscopic surgical training.

Dr Shaker worked in different consultant positions in UK before moving to Australia in 2007, to take a consultant position at Rockhampton Hospital.

He was appointed as Associate Professor at the University of Queensland in 2013. He also is a member of the board of examiners of Royal Australasian College of Obstetricians and Gynaecologists (FRANZCOG) and the Australian Medical Council Exam (AMC).

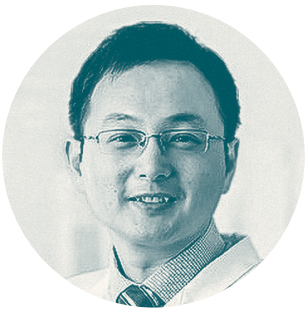
Besides his clinical work, Dr Shaker has special interest in medical education and scholarship in medicine. He completed a Masters degree in medical education at the University of Dundee, UK. His thesis focused on the process of learning and teaching surgical techniques. He also is a member of the Faculty of Surgical Trainers, Royal College of Surgeons Edinburgh, UK and a member of the Editorial Board for the RCOG continuous professional development Journal (The Obstetrician and Gynaecologist).

Dr Shaker currently practices as a private obstetrician and Gynaecologist at Rockhampton and IVF specialist at Monash IVF Rockhampton.

Dr Yanhe Liu

BSc, MSc, MCE, PhD

Scientific Director Monash IVF Queensland; Adjunct Senior Lecturer, University of Western Australia and Edith Cowan University



Yanhe has been a clinical embryologist since 2002, with extensive experience in IVF laboratory management both in Australia and overseas. He achieved his Master's degree in Clinical Embryology at Monash University in 2009, followed by a PhD through Edith Cowan University in 2016 while working part time. His PhD project has focused on time-lapse embryo selection, with 7 resulting publications on the top fertility journals including Fertility and Sterility. Yanhe is currently the Scientific Director QLD at Monash IVF, overseeing the operation and scientific development of Embryology, Andrology and Biochemistry in all our Queensland laboratories. In addition, Yanhe has supervised a number of research students in conjunction with either University of Western Australia or Edith Cowan University.

Yanhe's research interests focus on the clinical introduction of novel techniques to improve IVF success rate. He is an internationally recognised expert in embryo selection, and has been frequently invited to speak at conferences and to participate in the peer review process with a number of top fertility journals (including Human Reproduction, Journal of Assisted Reproduction and Genetics, Human Fertility, and Reproductive Biology). Considering his quality contributions, he was awarded Top Reviewer by Human Reproduction in both 2016 and 2018.

Professor Moira O'Bryan

PhD

Professor and Head of the School of Biological Sciences, Monash University, Victoria.

Moira O'Bryan is a Professor and the Head of the School of Biological Sciences at Monash University. Her research encompasses: germ cell development and the relationship between sperm form and function, the genetic causes of human infertility, and the implications for 'reproductive' proteins on health broadly. She directs a multidisciplinary and highly collaborative research program spanning basic research and clinical medicine. She is a founding member of the International Male Infertility Genomics Consortium, a member of the Australian Research Council College of Experts and the President of the Society for Reproductive Biology.

Education

A word from the Director of Education, Professor Beverley Vollenhoven — Director of Education MREF

Our partnership with Monash University's Education Program in Reproduction and Development (EPRD) continues to develop. Clinicians and embryologists provide teaching for both the Diploma and Masters courses and participate in collaborative research. We are most grateful for the time and effort that our staff put into training the next generation of researchers and health practitioners in reproductive medicine

Our 3rd Biennial Clinical and Scientific meeting in Melbourne, November 2019, was a tremendous success that brought together 130 clinical, scientific and other senior staff for a 2 days meeting of the highest caliber, including MVF group presentations and webinars by leading overseas speakers.

The meeting was very stimulating with three international presentations by Prof Stacey Missmer from Michigan State University (USA), Prof Siladitya Bhattacharya from University of Aberdeen (UK) and Prof Cindy Farquhar from University of Auckland (New Zealand). Many key Monash IVF Group doctors and staff contributed to the symposia, including Prof Rob McLachlan, Prof Beverley Vollenhoven, Prof Luk Rombauts, Prof Kelton Tremellen, Dr Irving Korman, Dr Ross Turner, Dr Kim Matthews, Dr Prue Johnstone, Ms May Kew Loke, Dr Hamish Hamilton, Dr Gareth Weston, Dr Melody Menezes, A/Prof Deirdre Zander-Fox, Ms Kate Watson, Dr Leanne Pacella-Ince, Dr Greg Kesby and Dr Hassan Bakos. The symposium was a great success with the 4th Meeting planned on the April 30 – May 2nd 2021 in Sydney.

Research

A word from the Director of Clinical Research Professor Luk Rombauts — Director of Clinical Research MREF

Sadly, one of the driving forces of our research program, Professor Michelle Lane, passed away and she leaves a big hole to fill. We are very fortunate that she has left a significant legacy behind, not just in terms of scientific discoveries, but also a team of talented young scientific leaders who have eagerly taken up the challenge to continue her work into the future.

After some restructuring across our group, new initiatives are being introduced to further profile our education and research credentials. These initiatives will eventually benefit our patients and the doctors that care for them. Clinical and scientific education is vital to ensure that we stay on top of the latest discoveries in our field. Monash IVF organises regular educational events including a biannual scientific meeting with renowned international guest speakers. The last one was held in Melbourne in 2019 and the feedback was overwhelmingly positive. A further educational initiative is the Monash IVF Group National Journal Club which will offer all staff easy access to a forum to discuss the latest peer-reviewed journal articles.

Professor Moira O'Bryan joined the Monash IVF Research and Education Foundation Committee. She is a world expert in male reproductive physiology and she and Professor Robert McLachlan have collaborated for many years with Monash IVF investigating the genetic causes of male infertility. Another new scientific team member is Dr Mark Green who joins us from Melbourne University. One of his many research interests is the effects of environmental pollutants on human reproduction. Monash IVF Group welcomes them both and looks forward their expert guidance in research and education

Research highlights

2019-June 2020 Research Awards

Professor Beverley Vollenhoven: Victorian Honour roll of Women

The MREF committee would like to congratulate Professor Beverley Vollenhoven on her achievement to be inducted into the Victorian Honour roll of Women 2019. Beverley has been instrumental in ensuring access to critical reproductive and women's health services in Victoria, and has been an advocate for gender equality in science and medicine.

Professor Rob McLachlan: FSA Lifetime award

Professor Robert McLachlan was awarded a Lifetime Membership of the Fertility Society of Australia at its Annual Meeting in 2019. This recognition adds to the General Division of the Order of Australia he received for his significant contributions to medicine in endocrinology, particularly men's reproduction and health & medical research.

Associate Professor Hassan Bakos

Associate Professor Hassan Bakos was awarded the Geoff Driscoll Medal & Best Clinical Paper Award at the Fertility Society of Australia Annual Meeting in 2019, for his paper that explored how sperm can impact early embryo development, titled "Differences in 2-Cell and 4-Cell Embryo Quality in Relation to Sperm Developmental Status as Assessed by Time-lapse Technology." (Awarded the Exchange Lecture with the British Fertility Society)

Monash IVF completed projects

2019 to 2020 Research Projects

Endometrial thickness and its association with uterine hyper-peristalsis in IVF

Dr Michelle Dunn[1], Prof Luk Rombauts[1,2], Dr Shavi Fernando[1], Samantha Ter[2].

[1] Monash Dept Obstetrics and Gynaecology, Clayton; [2]Monash IVF, Clayton.

This cohort study is investigating the subtle muscle contractions of the uterus known as "uterine peristalsis" during the time of implantation of an embryo into the uterus. It is thought that these contractions may be more prominent in women with a thicker endometrium. Although we don't know for sure, these contractions may have the potential to shift the embryos into a different spot than where it was deposited. This study proposes that the thickness of the endometrial lining is related to these contractions; i.e. the thicker the endometrial lining the higher the frequency of the contractions. If a relationship between the thickness of the endometrium is linked to the uterine contractions it could potentially explain why embryos sometimes implant low in the uterine cavity or in rare circumstances end up implanting in the fallopian tube as an ectopic pregnancy. Additionally, this may lead to future studies looking at screening for and potentially treating higher risk women with medications to decrease uterine muscle activity at the time of transfer.

The effects of unrecognised Chlamydial infection on sperm production in human infertility

A/Prof Ken Beagley[1], Dr Danica Hickey[1], Emily Bryan[1], Prof Eileen MacLaughlin[2], Prof Rob McLachlan[3], A/Prof Luk Rombauts[3,4], Samantha Ter[3], Dr Darren Katz[5]

[1] Queensland University of Technology, Brisbane; [2] University of Newcastle, Callaghan; [3] Monash IVF, Clayton; [4]Monash Dept Obstetrics and Gynaecology, Clayton; [5]The Centre for Specialist Men's Health and Fertility, Melbourne.

Chlamydial infections are very common in our community with about 25% of people aged 25-35 yrs having past or current infections. Many people have no symptoms and therefore don't receive treatment and as a result, chronic infections may occur that damages reproductive tissues in females and potentially in males. We now believe that Chlamydial infection of the testis can damage sperm production leading to infertility. The purpose of this research is to investigate whether male infertility can be caused by the sexually transmitted infection, Chlamydia. Testicular tissue obtained after testicular biopsy will be used to find out the effects of possible unrecognized infection on sperm development, and the ways this damage occurs. We hope to develop methods for early diagnosis of infections.

Clinical IVF Genomics: Whole Genome Sequencing (WGS) on IVF Embryos and Patients

Dr Nicholas Murphy[1,2], Jayne Mullen[2], Emma Perry[2], [2]Dr Lee-Yean Low[2], Claire Lillee[2], Dr Elissa Willats[2], Prof Luk Rombauts[1,2]

[1]Monash University, Clayton; [2]Monash IVF, Clayton

IVF clinics offering a Preimplantation Genetic Screening or Diagnosis service, typically offer the detection of an embryo's aneuploidy or a single gene mutation. This project seeks to research incorporating genomic analysis into the PGS/PGD program as a path to offering patients a single comprehensive embryonic DNA test, capable of detecting all known disease-causing genetic mutations relevant to IVF. The significance of this study is fundamental and profound; comprehensive disease screening with simultaneous aneuploidy calling has not been attempted to date and is not offered clinically [1]. This study will sequence genomes of both embryos and patients with the highly desirable aim of obtaining all the diagnostic endpoints relevant to PGD/PGS and in addition, allowing for the determination of genetic variations relevant to IVF treatment. The aim of this work is to be the first group to show as a proof-of-principle that whole genome sequencing can provide a revolutionary step-change in offering extended genetic information for prospective parents and the offspring at an affordable price.

Endometrial junction contractility and IVF outcomes

Dr Sarah Hunt[2], Prof Luk Rombauts[1,2,3], Prof Beverley Vollenhoven[1,2,3], A/Prof Fabricio Costa[1,4]

[2]Monash Dept Obstetrics and Gynaecology, Clayton; [1]Monash University, Clayton; [3]Monash IVF, Clayton; [4]Monash Ultrasound of Women, Clayton.

There is a strong correlation between endometrial combined thickness (ECT) and complications in assisted reproductive therapy (ART), such as placenta previa and ectopic pregnancy. It is hypothesized ECT is a surrogate marker for changes in uterine peristalsis, as visualized by endometrial wave motion on transvaginal ultrasound. There is evidence these changes are associated with uterine function and ART outcome. Uterine peristalsis may be altered in women with endometriosis, adenomyosis and recurrent unexplained implantation failure. This will be a prospective, observational study with the broad goal of determining the clinical value of ECT and/or objective measures of endometrial peristalsis in relation to IVF outcomes. This will be accomplished through three defined aims:

To assess intra-observer and inter-observer variability in measuring ECT and/or objective measures of endometrial peristalsis on transvaginal ultrasound in experienced and less-experienced sonographers / sonologists.

To assess whether ECT and/or objective measures of endometrial peristalsis is different in patients with endometriosis, adenomyosis and unexplained repeat implantation failure compared to fertile controls.

To assess within-patient variability of ECT and/or objective measures of endometrial peristalsis.

It is hoped that this study will provide the diagnostic means to identify subpopulations of patients who would potentially benefit from pharmaceutical interventions aimed at optimizing endometrial peristalsis patterns.

Ongoing projects

Piezo ICSI: Can an alternative type of intracytoplasmic sperm injection (ICSI) for eggs improve fertilisation

Prof Luk Rombauts[1], Prof Michelle Lane[1], Kate Watson[2], A/Prof Deirdre Zander-Fox[1]

[1]Monash IVF Group, Clayton; Monash IVF, Queensland

The standard method for ICSI was developed in the 1990's and involves using a sharp needle to pierce the zona pellucida and the cell membrane in order to place the sperm inside the egg. In addition, it is necessary to aspirate the cytoplasm of the oocyte up into the pipette and then to expel back into the egg, to ensure that the membrane is pierced. This procedure revolutionised the treatment for male infertility. The fertilization rates for this method across the group range between 65-70% and approximately 8-12% of eggs do not survive this piercing method and lyse.

Piezo ICSI which has been used for many years for animal IVF has recently been used in Japan. This method involves ultrasonic movement of a pipette that gently bores its way through first the zona pellucida and then the cell membrane. This method uses a blunt pipette and does not require the cytoplasm to be aspirated. As a result it has been reported that this method enables more gently placement of the sperm in the oocyte and reduces the lysis rate of eggs, overall increasing fertilization rates.

This study is to assess the effect of Piezo ICSI on fertilization rates and degeneration rates in a sibling split study.

Felix- Method for Separating DNA intact sperm to improve IVF Outcomes

A/Prof Hassan Bakos[1], Prof Luk Rombauts[1], Prof Michelle Lane[1,2], A/Prof Deidre Zander-Fox[1], Prof Rob McLachlan[1]

[1]Monash IVF Group , Clayton, NSW; [2]Repromed

Current semen preparation methods in ART do not assess the impact on all sperm molecular aspects that may impact fertilization..Current methods for the selection of sperm for ICSI are usually based on low magnification selection of the morphology of a motile sperm. However, these parameters do not provide any assessment of the molecular health of the sperm. In particular, sperm with high levels of DNA damage are known to result in reduce fertilization rates, poorer embryo development, reduced pregnancy rates and increased levels of miscarriage. Current methods for sperm selection cannot assess DNA damage.

The Felix medical device uses electrophoresis to separate DNA intact sperm. This study will assess the ability of the Felix device to separate DNA intact sperm and to improve IVF outcomes. The initial aim of this study is to assess the impact of Felix method compared with existing sperm selection methodologies. The second aim is to engage in a clinical trial sibling split design will be used to determine the effect of Felix sperm separation on fertilization rates and embryo development. Secondary outcomes will include DNA damage levels in sperm and pregnancy rates.

Establishment and validation of the 'exposome' as a prognostic predictor of female fertility

Dr Mark Green[1,2], Dr Bradley Clarke[3], A/Prof Deidre Zander-Fox[1], Prof Luk Rombauts[1]

[1]Monash IVF, Clayton; [2]School of BioScience University of Melbourne, Parkville; [3]School of Chemistry University of Melbourne, Parkville

There is now an increasing reliance on ART in order to reproduce. It is postulated that rising infertility can be partially attributed to exposure to man-made environmental toxicants, such as endocrine disrupting chemicals (EDCs). The aims of this project are 1) to establish and validate methodologies to quantify the 'exposome', specifically paraben, phthalate and per-/poly-fluoroalkyl substances (PFAS) concentrations in human urine and follicular fluid samples (n=150 patients), and 2) to provide preliminary data to determine whether the exposome can be used as a reliable prognostic marker for egg quality and thus fertility. This research will establish a brand-new academic collaboration. The project outcomes have substantial scope for direct uptake and future investment by Monash IVF, as a clinical test to be offered to patients.

Which factors are associated with repeated implantation failure in couples undergoing IVF/ICSI?

Fabrizzio Horta[1,3], Prof Beverley Vollenhoven[2,3], Prof Ben W Mol[2], Dr Sarah Hunt[2,3], A/Prof Deirdre Zander Fox[3], A/Prof Peter Temple-Smith[1], Dr Sally Catt[1]

[1]EPRD Monash University, Clayton; [2]Monash Dept Obstetrics and Gynaecology, Clayton; [3]Monash IVF, Clayton

Recurrent implantation failure (RIF) refers to the non-occurrence of pregnancy after transfer of at least four good-quality embryos in a minimum of three fresh or frozen cycles. RIF can be the consequence of male contribution/sperm, embryonic or uterine factors including disrupted endometrial receptivity. Sperm DNA damage, thrombophilia and immunological issues as well as factors affecting endometrial receptivity, have been suggested as important to consider in couples with RIF. While many infertile couples with RIF currently are undergoing such testing and subsequent treatment, the scientific knowledge underpinning these tests is lacking. The aim of this study is to assess whether the presence of hereditary and acquired thrombophilia and / or sperm DNA damage are related to RIF in couples with idiopathic infertility. We propose a case-control study with 80 couples (two groups; 40 couples/group). Cases will be couples with RIF, defined as above. Controls will be age-matched couples scheduled for their first IVF cycle. Women with previous ovarian hyperstimulation syndrome, poor responders and women with ≥20 cumulus oocytes complexes retrieved at OPU will be excluded. We propose a novel approach not requiring randomization. Couples in the cases and control group will undergo testing for inherited and acquired thrombophilia and sperm DNA damage.. Chi-square, logistic regression and ROC-analysis will be used to compare the results. In the absence of an association, thrombophilia or sperm DNA damage can be excluded from a role in RIF.

Oocyte DNA repair capacity as a novel marker for female ageing in IVF/ICSI cycles

Fabrizzio Horta[1,3], Prof Beverley Vollenhoven[2,3], A/Prof Peter Temple-Smith[1], Dr Sally Catt[1], A/Prof Deirdre Zander-Fox[3]

[1]EPRD Monash University, Clayton; [2]Monash Dept Obstetrics and Gynaecology, Clayton; [3]Monash IVF, Clayton

Reproductive outcomes for women undergoing ART declines with age. Ageing and oocyte quality have been associated with aneuploidy, however, the factors determining oocyte quality remain unclear. Critical markers of DNA damage response (DDR) have been shown to decrease in the mouse model regardless of the oocyte stage during aging. Furthermore, a diminished DNA repair capacity and negative effects on embryo development have been found in the presence of DNA insults in gametes. This emerging data requires exploratory studies in humans to examine potential novel oocyte quality markers linked to IVF/ICSI clinical outcomes and male/sperm contribution. To examine the potential effect of female age on the DNA repair capacity makers of human oocytes on IVF/ICSI clinical outcomes, we propose a prospective cohort study including women presenting with either primary or secondary idiopathic infertility. Couples will be allocated into three groups according to female age: <30, 30-39 and ≥40 years old. Immature oocytes will be assessed for NADH, ATM and ãH2AX levels and leftover sperm samples used for IVF/ICSI cycles will undergo DNA damage testing. Women with known uterine pathologies, endometriosis, polycystic ovarian syndrome, ovarian hyperstimulation syndrome and poor responders will be excluded. Sample size; 60 couples, 20 couples per study group.

DDR makers will be assessed simultaneously in each oocyte collected. Markers will be analysed using ANOVA and clinical outcomes through Chi-square and logistic-regression analysis. Gamete studies will be conducted at Monash University aiming to develop two publications.

Optimise endometrial receptivity to improve IVF outcomes

Prof Guiying Nie[1], Prof Luk Rombauts[2,3]

[1]Hudson Institute of Medical Research, Clayton; [2]Monash Dept Obstetrics and Gynaecology, Clayton; [3]Monash IVF, Clayton

The success rate of IVF has improved significantly over the last decades, allowing many infertile couples the chance to conceive. However, too many IVF attempts still do not result in a successful pregnancy. Embryo implantation is a crucial event in establishing a pregnancy, and implantation failure is a bottleneck in IVF treatment.

Successful implantation requires coordinated interactions between a high quality embryo and a receptive endometrium that are synchrony in their development. To date, technologies and culture conditions are well advanced to obtain and transfer a high quality embryo, however, capabilities in optimizing and assessing endometrial receptivity are lagging behind largely because the mechanisms governing endometrial transition from a non-receptive to a receptive state is still poorly understood.

The current dogma on endometrial receptivity states that the tissue must up-regulate adhesion molecules so that an embryo can attach and implant. However, our recent studies strongly suggest an opposite mechanism: the human endometrial epithelium innately expresses an anti-adhesion molecule (to be referred to as AAM), and AAM is down-regulated specifically in the endometrial surface epithelium in the mid-secretory phase to open up the window of implantation.

We will determine whether AAM presentation in the luminal epithelium at putative receptivity is linked to implantation failure in IVF patients. We will also investigate how AAM is regulated in the human endometrial epithelial cells for receptivity.

Studies on the genetic basis of male and idiopathic infertility, and the trans-generational health of children conceived through ART

A/Prof Moira O'Bryan[1], Dr Liza O'Donnell[2,3], Prof Robert McLachlan[3,4], Prof. Andrew Sinclair[5]; Dr Alicia Oshlack[5].

[1]Dept. Anatomy and Developmental Biology, Monash University; [2]Monash Institute of Medical Research; [3]Hudson Institute of Medical Research, Clayton; [4]Monash IVF, Clayton; [5]The Murdoch Children's Research Institute.

Infertility affects 1 in 20 Australian men and leads to approximately half of all ART treatments. Male infertility is often due to the failure to produce adequate numbers of motile sperm capable of fertilisation. Genetic factors are suspected to be causal in many cases. Understanding such genetic factors may result in new diagnostic tests and ultimately specific treatments. Such research may also address uncertainties around the possible transmission of infertility to ART conceived offspring. Based on our extensive mouse gene discovery program, we have identified many genes with essential roles in male mouse fertility. As an extension of this work, and using a bioinformatics approach, we are systematically screening human male samples for mutations likely to cause infertility. Recent findings include an evolutionarily conserved association between Sertoli cell only syndrome in mice and humans, and mutations in the ETV5 gene.

Podocalyxin identified as a key negative regulator of human endometrial epithelial receptivity

Prof Guiying Nie[1], Prof Luk Rombauts[2,3], Prof Beverley Vollenhoven[2,3].

[1]Hudson Institute of Medical Research, Clayton; [2]Monash IVF, Clayton; [3] Monash Dept Obstetrics and Gynaecology, Clayton

ART has progressed into an important medical intervention to overcome infertility. However, despite significant advancements in embryo culture, selection and transfer techniques, implantation failure still poses a crucial limiting factor. It is believed that the problem is the "soil for the seeds", the endometrium. For implantation to occur, the endometrium must differentiate into a receptive state. As the embryo first contacts the surface of the endometrial epithelium, this surface must become adhesive for embryo attachment. Although it is known that the endometrial epithelium remodels structurally and functionally to gain receptivity, the exact molecular changes are not well understood. A widely held view is that up-regulation of adhesion-promoting molecules is important, but the details are not well characterized. Our studies discovered a concept contrasting to the commonly held notion of receptivity establishment – the endometrium needs to remove a key negative regulator. This regulator is a membrane protein called podocalyxin, which is expressed in all endometrial epithelial cells and inhibits embryo implantation. During the establishment of receptivity, podocalyxin is down-regulated in the luminal epithelial cells, selectively converting the endometrial surface from a non-receptive to an implantation-permitting state. Our studies further suggest that epithelial podocalyxin may provide a new parameter for optimizing and evaluating endometrial receptivity.

Health and fertility in ICSI-conceived young adult males of severely infertile fathers

Prof Jane Halliday [1], Dr Sharon Lewis [1], Dr Sarah Catford[2], Moira O'Bryan[3],Prof Robert McLachlan[2,4].

[1] Murdoch Childrens Research Institute, Parkville; [2]Hudson Institute of Medical Research, Clayton; [3]Monash University, [4]Monash IVF, Clayton

Infertility is common, affecting 15% of couples and ~65,000 Assisted Reproductive Technology (ART) cycles are undertaken each year in Australia. About one third of cycles are for male factor infertility. In many the reason for reduced sperm number or quality is spermatogenic failure (STF) of unknown cause. Intra-cytoplasmic sperm injection (ICSI) is the commonest ART method. ICSI-conceived offspring of severely infertile men have higher rates of congenital anomalies, which may be due to patient factors and/or the ICSI technique. However, little is known about the health of ICSI-conceived adults, and in particular the health and reproductive potential of ICSI-conceived men. Only one small study to date has assessed semen parameters and reproductive hormones in ICSI-conceived men and suggested higher rates of impaired semen quality compared to spontaneously conceived (SC) peers while metabolic data was similar.

This cohort study aims to evaluate the general health and development, fertility and metabolic parameters and, epigenetic signatures of ICSI-conceived sons whose fathers had poor semen quality due to spermatogenic failure compared to three age-matched control groups, [1] ICSI-conceived sons whose fathers with obstructive azoospermia (OAZ), [2] IVF-conceived sons and [3] spontaneously conceived sons, recruited from other studies.

Of 1112 ICSI parents including fathers with STF and OAZ, 78% (n=867) of mothers and 74% (n=823) of fathers were traced and contacted. ICSI sons were recruited from March 2017 to July 2020. Based on preliminary participation rates, we estimate the following sample size will be achieved for the ICSI study group: mothers n=275, fathers n=225, sons n=115. Outcome measures include validated survey questions, physical examination, reproductive hormones, serum metabolic parameters and semen analysis. For epigenetic and future genetic analyses, ICSI sons provide specimens of blood, saliva, sperm and seminal fluid while their parents provide a saliva sample.

The primary outcomes of interest are the number of mother-reported hospitalisations of the son; son-reported quality of life; prevalence of moderate-severe oligozoospermia (sperm concentration <5 million/ml); and DNA methylation profile. Data analysis is currently underway. The new knowledge generated from these results will direct research into treatment safety and patient counselling.

CSF3 Receptor blockade to restore endometrial receptivity in idiopathic infertile women

Dr Tracey Edgell[1], Prof Luk Rombauts[2], Prof Beverley Vollenhoven[2]

[1]Hudson Institute for Medical Research, Clayton; [2]Monash IVF, Clayton

Despite improved embryo technologies IVF fails to fulfil its promise for many women. Women often undergo multiple cycles without achieving a pregnancy. Increasingly it is recognized that the maternal endometrium is a critical component in achieving pregnancy success. Our published studies have identified that CSF3 to significantly elevated within the uterine cavity of idiopathic infertile women (Edgell et al, Cytokine. 2018;111:222-229). In these infertile women the CSF3 receptor (CSF3R) is found reduced or absent from the endometrial tissue. Functional studies have demonstrated that CSF3 significantly impacts both endometrial cell and trophoblast cell behaviours. Together the data demonstrates the importance of the CSF3 axis during the early stages of embryo attachment and invasion.

This study examined the potential to target the excess CSF3 concentrations to improve endometrial receptivity using specific antibodies to blockade the receptor, preventing its reduce/loss from the endometrial surface. Utilising antibodies directed to the CSF3 receptor, we examined CSF3R expression on endometrial cells following exposure to elevated concentrations of CSF3. It was observed that the molecular mass of CSF3 receptor protein evident on endometrial cells differed to the multiple forms that are widely characterised in immune cells. Studies of proliferation and adhesion of endometrial and trophoblast cells elicited a small but not statistically significant change in cell behaviours. Outcomes of the study were potentially impacted by poor antibody recognition of the novel endometrial form of CSF3R

Long-term influence of Fertility Treatment on cardiovascular events – The LIFE registry

[1]Dr Stephanie Yiallourou, [1]A/Prof Melinda Carrington, [1]Dr Jocasta Ball, [2]Prof Luk Rombauts, [3]Dr Daniel Rolnik, [1,3,4,5]Mr Andre Rodrigues, [3,4,5]A/Prof Fabricio da Silva Costa

Pre-Clinical Disease and Prevention Unit, Baker Heart and Diabetes Institute, Melbourne; Monash IVF, Clayton; Monash Medical Centre, Clayton; Monash Ultrasound for Women, Clayton; Monash University, Clayton

Approximately 55,000 women undergo assisted reproductive technology treatments per year in Australia. Since its conception 40 years ago, Monash IVF has been responsible for 35,000 births in Australia. Despite the obvious beneficial outcomes, concerns for the long-term effects of fertility treatment on cardiovascular disease (CVD) risk have arisen. In the short-term, fertility treatment has direct effects on the vasculature and inflammatory processes causing pro-thrombotic events. These adverse cardiovascular consequences may lead to cardiovascular complications later in life. Currently, long-term data on the incidence of CVD in women who have undergone fertility treatment, specifically at the age of peak cardiovascular risk, is lacking.

This registry could become an asset to be used in multiple, future research projects to follow women and their offspring in longitudinal research studies and further investigate obstetric complications associated with in-vitro fertilisation (IVF) pregnancies, in particular pre-eclampsia and fetal growth restriction – the most important causes of maternal morbidity and perinatal mortality. The creation of the LIFE registry in the immediate future will allow for important and relevant research into long-term cardiovascular outcomes. Findings from this study have capacity to inform safety of treatment and long-term interventions to improve the cardiovascular health of mothers and their offspring.

A longitudinal investigation into maternal cardiovascular changes in pregnancies conceived through assisted reproductive technologies from pre-conception until the postpartum period (CONCEIVE-IVF)

A/Prof Fabricio da Silva Costa[1,2], Dr Sebastian Hobson[2,3], Prof Euan Wallace[2,3], Dr Ryan Hodges[2,3], A/Prof Andre La Gerche[4], Prof Christoph Lees[5], Dr Fung Lin Foo[5], Prof Luk Rombauts[6]

[1]Monash Ultrasound for Women, Clayton; [2]Monash Health, Clayton; [3]Monash University, Clayton; [4]Baker IDI Heart & Diabetes Institute; [5]Queen Charlotte & Chelsea Hospital; [6]Monash IVF, Richmond

The CONCEIVE-IVF study has been designed in order to determine how much a women's heart and blood vessel health contributes to poor pregnancy outcomes when she falls pregnant using IVF and related infertility treatments. This study will be conducted over the course of two-years by Monash Health, Monash IVF and Monash Ultrasound for Women in collaboration with the Baker IDI Heart and Diabetes Institute and the Centre for Fetal Care at Queen Charlotte's & Chelsea Hospital in the United Kingdom.

Overall, the CONCEIVE-IVF study aims to assess whether and how cardiovascular changes from preconception and through early pregnancies achieved through ART are associated with adverse pregnancy outcomes, specifically: miscarriage, preterm birth, preeclampsia (PE) and/or small for gestational age (SGA <5th growth centile). We hypothesise that miscarriage and preterm birth along with early-onset PE in association with SGA, or SGA at any gestation is associated with inadequate cardiac output (CO) increase from pre-conception through the first trimester of pregnancy, when compared to normal outcome pregnancies. Also, that late-onset PE in association with LGA, or LGA at any gestation is associated with a higher increment of CO from preconception through first trimester, when compared to normal outcome pregnancies. Using novel robust techniques for cardiovascular assessment, our hope would be that this study could identify future pregnancies at risk for adverse outcomes, along with the opportunity for prevention strategies along with earlier detection and treatment for affected pregnant women.

Contributions to Scientific Literature

The following compiles a portfolio of contributions to the scientific literature by Monash IVF doctors, staff and key collaborators for 2019 to June 2020. The list represents our commitment to broad range of research interests spanning reproductive biology, genetic and molecular, andrology, clinical and psychological based research.

Peer Reviewed Journal Articles/Publications

1. Abel K, Healey M, Finch S, Osianlis T, Vollenhoven B. Associations between embryo grading and congenital malformations in IVF/ICSI pregnancies. Reproductive BioMedicine Online. 2019;39(6):981-989.
2. Bardin M, Ritchie D, McLachlan R, Yates C. Acute myeloid leukaemia presenting with diabetes insipidus. Internal Medicine Journal. 2019;49(6):785-788.
3. Beyer C, Lewis A, Willats E, Mullen J. Preimplantation genetic testing using Karyomapping for a paternally inherited reciprocal translocation: a case study. Journal of Assisted Reproduction and Genetics. 2019;36(5):951-963.
4. Bryan E, McLachlan R, Rombauts L, Katz D, Yazdani A, Bogoevski K et al. Detection of chlamydia infection within human testicular biopsies. Human Reproduction. 2019;34(10):1891-1898.
5. Catford S, O'Bryan M, McLachlan R, Delatycki M, Rombauts L. Germ cell arrest associated with aSETX mutation in ataxia oculomotor apraxia type 2. Reproductive BioMedicine Online. 2019;38(6):961-965.
6. Davenport M, Healey M, MacLachlan V, Talmor A, Vollenhoven B. GnRH-agonist trigger in 'freeze-all' cycles: improves pregnancy rates and patient safety. Fertility and Sterility. 2019; 112(3):e206.
7. Fernando S, Rombauts L, Wallace E, White N, Hong J, da Silva Costa F. OC04.03: The effect of melatonin on ultrasound markers of follicular development: a double-blind placebo-controlled randomised trial. Ultrasound in Obstetrics & Gynecology. 2017; 50:7-8.
8. Gardner D, Zander-Fox D, Bakos HW, McPherson N and Pacella-Ince L (2020) In memory of Michelle Lane: 1970 – 2020. Reproductive Biomedicine Online; 40(6):753-754.
9. Horta F, Vollenhoven B, Healey M, Busija L, Catt S, Temple-Smith P. Male ageing is negatively associated with the chance of live birth in IVF/ICSI cycles for idiopathic infertility. Human Reproduction. 2019;34(12):2523-2532.
10. Horta F, Catt S, Ramachandran P, Vollenhoven B, Temple-Smith P. Female ageing affects the DNA repair capacity of oocytes in IVF using a controlled model of sperm DNA damage in mice. Human Reproduction. 2020; 35(3):529-544.
11. Hunt S, Vollenhoven B. Fertility preservation in women with cancer and afterward. Climacteric. 2019;22(6):579-583.
12. Hogg K, Rizio T, Manocha R, McLachlan R, Hammarberg K. Men's preconception health care in Australian general practice: GPs' knowledge, attitudes and behaviours. Australian Journal of Primary Health. 2019;25(4):353.
13. Juonala M, Lewis S, McLachlan R, Hammarberg K, Kennedy J, Saffery R, McBain J, Welsh L, Cheung M, Doyle LW, Amor DJ, Burgner DP, Halliday J. American Heart Association ideal cardiovascular health score and subclinical atherosclerosis in 22–35-year-old adults conceived with and without assisted reproductive technologies. Human Reproduction. 2020 Jan;35(1):232 -239.
14. Kemper J, Vollenhoven B, Talmor A. Preimplantation Genetic Testing for Aneuploidy. Obstetrical & Gynecological Survey. 2019;74(12):727-737.
15. Kennedy A, Stern C, Tong S, Hastie R, Agresta F, Walker SP, Brownfoot FC, MacLachlan V, Vollenhoven BJ, Lindquist AC. The incidence of hypertensive disorders of pregnancy following sperm donation in IVF: an Australian state-wide retrospective cohort study. Human Reproduction. 2019;34(12):2541-2548.

16. Kieu V, Healey M, Vollenhoven B. Oral complementary medicine use and first-cycle in vitro fertilisation – What are the effects on the oocyte, the embryo and the pregnancy rate?. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2019;59(5):712-716.
17. Lantsberg D, Fernando S, Cohen Y, Rombauts L. The role of fertility preservation in women with endometriosis: A systemic review. Gynecology. 2020; 27(2): 362-372.
18. Leonardi M, Reid S, Lu C, Gerges B, Chang T, Rombauts L, Healey M, Chou D, Choi S, Al-Mashat D, Ahmed S, Magotti R, Nader R, Adno A, Condous G. Diagnostic Accuracy and Reproducibility of Predicting Cul-de-Sac Obliteration by General Gynaecologists and Minimally Invasive Gynaecologic Surgeons. Journal of Obstetrics and Gynaecology Canada. 2019;41(4):443-449.e2.
19. Murphy NM, Samarasekera TS, Macaskill L, Mullen J, Rombauts LJF. Genome sequencing of human in vitro fertilization embryos for pathogenic variation screening. Scientific Reports. 2020;10:3795.
20. Norman R, Alvino H, Hull L, Mol B, Hart R, Kelly TL, Rombauts L. Human growth hormone for poor responders: a randomized placebo-controlled trial provides no evidence for improved live birth rate. Reproductive BioMedicine Online. 2019;38(6):908-915.
21. Novakovic B, Lewis S, Halliday J, Kennedy J, Burgner D, Czajko A, Kim B, Sexton-Oates A, Juonala M, Hammarberg K, Amor DK, Doyle LW, Ranganathan S, Welsh L, Cheung M, McBain J, McLachlan R, Saffery R. Assisted reproductive technologies are associated with limited epigenetic variation at birth that largely resolves by adulthood. Nature Communications. 2019 Sept;10(1).
22. Ratner R, Tsaltas J, Vollenhoven B. Hysteroscopy and the risk of gas embolism: A review. Journal of Endometriosis and Pelvic Pain Disorders. 2019;:228402651987240.
23. Raad G, Mouchantaf L, Azoury J, Azoury J, Azoury J and Bakos HW. The Impact of Four Sperm Preparation Techniques on Sperm DNA Fragmentation, Motility and Concentration: A Prospective Study. Human Reproduction. 2019; 34 (1): 179-180.
24. Takamura M, Zhou W, Rombauts L, Dimitriadis E. The long noncoding RNA PTENP1 regulates human endometrial epithelial adhesive capacity in vitro: implications in infertility. Biology of Reproduction. 2019;.
25. Wang Y, Logan S, Stern K, Wakefield C, Cohn R, Agresta F, Jayasinghe Y, Deans R, Segelov E, McLachlan RI, Gerstl B, Sullivan E, Ledger WE, Anazodo A. Supportive oncofertility care, psychological health and reproductive concerns: a qualitative study. Supportive Care in Cancer. 2020; 28: 809-817.
26. Xiao J, Healey M, Talmor A, Vollenhoven B. When only one embryo is available, is it better to transfer on Day 3 or to grow on?. Reproductive BioMedicine Online. 2019;39(6):916-923.

Presentations- National Conferences and Meetings

1. Alesi R. Caring for the patient when things go wrong in the laboratory. Scientists in Reproductive Technology; 2019, May 4 -5: Gold Coast, Australia.
2. Bakos H. Latest advancements in Male fertility. CREI trainee Weekend; 2019, Mar 2: Sydney, Australia.
3. Bakos H. Sperm selection – state of the art and emerging approaches. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
4. Hunt S. Endometritis and Infertility receptivity. Fertility Society of Australia; 2019, Sept 15 - 18: Hobart, Australia.
5. Johnston P. Male factor subfertility in provincial Victoria. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
6. MacLachlan R. Male fertility – a look under the cover. CRH Forum, Hudson Institute of Medical Research; 2019, Nov 13: Melbourne, Australia.
7. Matthews K. A tale of three DSDs in one day!. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
8. Turner R. A Surrogacy saga!. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
9. Vollenhoven B. MHT in difficult circumstances. Australasian Menopause Society, Menopause Essential; 2019, May 25: Melbourne, Australia.
10. Vollenhoven B. SPRMs in gynaecology. Spark your Curiosity, Merck Serono Australia; 2019 June 15: Sydney, Australia.
11. Vollenhoven B. Update on Endometriosis. Provincial Fellows RANZCOG Webinar; 2019, Aug 26.
12. Vollenhoven B. Selective Progesterone Receptor Modulators. Australasian Menopause Society Meeting; 2019, Sept 6 - 8: Hobart, Australia.
13. Vollenhoven B. Research Informed Management of Infertility. Hudson Public Forum; 2019, Sept 17: Melbourne, Australia
14. Vollenhoven B. Fertility Preservation. Community Cancer Nurses; 2019, Nov 28.
15. Vollenhoven B. Infertility Investigations prior to referral. Jean Hailes Clinicians Education Update; 2020, May 13.
16. Watson K. Buying babies – Purchasing donor gametes. Scientists in Reproductive Technology; 2019, May 4 -5: Gold Coast, Australia.
17. Watson K. Is CRISPR the future of IVF?. Scientists in Reproductive Technology; 2019, Nov 22: Melbourne, Australia.
18. Watson K, Pacella-Ince L, Hamilton H. Embryoscope: Do they really improve embryo quality: MVF experience. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
19. Weston G. Gender fluid ART and LBGTIQ. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
20. Zander-Fox D. PGT 3.0 – What will cell-free assessment deliver now and into the future?. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
21. Zander-Fox D. Piezo ICSI Update. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.

Presentations- International Conferences and Meetings

1. Rombauts L. How bias limits the surgeon's skills. 14th World Congress of Endometriosis; 2020, May 8-11: Shanghai, China.
2. Rombauts L. How bias limits the surgeon's skills. AGES WES Focus meeting; 2019, August 2-3; Melbourne, Australia.
3. Rombauts L. Mild endometriosis: Does it matter? SEED meeting; 2019, May 18-19: Sydney, Australia.
4. Rombauts L. Endometriosis and infertility: management options. The 24th Annual conference of Indian Society of Assisted Reproduction; 2019, March 1-3: Mumbai, India.
5. Patlamazoglou L. Coming to terms with Infertility. International surrogacy conference; 2019, June 1-2: Melbourne, Australia.

Poster presentations and Abstracts- National Conferences and Meetings

1. Demmers KJ. Proposed Certification Scheme for Medical Laboratory Scientists and Technicians. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
2. Huston W, Rombauts L, Vollenhoven B, Allan J. The Uterine Microbiome. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
3. Kieu V & Vollenhoven B. IVF after renal transplantation: A literature review of cases. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
4. Nguyen AW, Rombauts L, Mol BW. Estimating the need for assisted reproductive technology in Australia. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
5. Raad G, Nader C, Azoury J, Azoury J, Azoury J, Bakos HW. Differences in 2-Cell and 4-Cell embryo quality in relation to sperm developmental status as assessed by time-lapse technology. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
6. Watson K, Korman I, Zander-Fox D. Handling the Zona free patient: Use of time lapse incubation and ingle-step culture to achieve a viable pregnancy in a zona free patient; Fertility Society of Australia 2019, Sept 15 - 18: Tasmania, Australia.
7. Watson K. Does Time lapse incubation improve embryo quality?. Monash IVF Clinical Education evening meeting; 2019, Nov 24-26: Melbourne, Australia.

Poster presentations and Abstracts- International Conferences and Meetings

1. Davenport MK, Healey M, MacLachlan VB, Talmor AJ, Vollenhoven BJ. GnRH-Agonist trigger in 'freeze all' cycles: improves pregnancy rates and patient safety. ASRM Scientific congress & expo; 2019 Oct 13-16; Philadelphia, USA.
2. Davenport MK, MacLachlan VB, Vollenhoven BJ, Talmor AJ, Healey M. How we trigger matters: intranasal GnRH agonist trigger may reduce oocyte maturation compared to subcutaneous administration in ICSI cycles. ASRM Scientific congress & expo; 2019 Oct 13-16; Philadelphia, USA.
3. Horta F, Vollenhoven B, Healey M, Busija L, Catt S, Temple-Smith P. Male ageing negatively affects the chances of live birth in IVF/ICSI cycles for idiopathic infertility. 35th Annual meeting of ESHRE; 2019 Jun 24-26: Vienna, Austria.
4. Raad G, Mouchantaf L, Azoury J, Azoury J, Azoury J, Bakos H. The impact of four sperm preparation techniques on sperm DNA fragmentation, motility and concentration: A prospective study. 35th Annual meeting of ESHRE; 2019 June 23-26: Vienna, Austria.

Books and Book Chapters

None

MREF external research grants attracted in 2019 – June 2020

Professor Robert McLachlan

NHMRC Research Grants

2017– 2019

NHRMC Project Grant #1140706, Chief Investigator (CIC). "Health and fertility of young men conceived using intra-cytoplasmic sperm injection"

2016 - 2019

NHMRC Project Grant #1124606, Associate Investigator (AI). "The importance of the blood-testis barrier in human infertility"

2016 – 2021

NHMRC Project Grant #1120356, Associate Investigator (AI). "The genetic causes of male infertility"

Medical Research Future Fund [MRFF] Research Grant

2020-2023 MRFF Emerging Priorities and Consumer Driven Research initiative #EPCD000007, Chief investigator (CIB). "Men And Infertility over the Lifecourse (MAIL)'

Professor Luk Rombauts

NHMRC Research grants

2019-2021

NHMRC Project Grant #1156666 (CIB). "The magic shield of the human uterus and fate of embryo implantation"

2019-2020

NHMRC Development Grant #1159714 (CIC). "Validation of a Prognostic Assay for Embryo Transfer"

2018-2021

NHMRC Project Grant #1139568 (CIC). "Human embryo's secret weapon for implantation"

2018-2020

NHMRC Development Grant #1136065. "Improving oocyte mitochondrial DNA copy number to enhance female reproductive capacity"

2017-2020

NHMRC Development Grant. Associate Investigator (AI). "Improving oocyte mitochondrial DNA copy number to enhance female reproductive capacity"

2017-2021

NHMRC Project Grant #1139568, Associate Investigator (AI). "Human embryo's secret weapon for implantation"

2016 – 2021

NHMRC Project Grant #1120689, Associate Investigator (AI). "Facilitating endometrial receptivity to improve pregnancy outcomes"

2016-2019

NHMRC Project Grant #1098321 (CID). "Critical regulators of endometrial receptivity"

ESHRE Research grants

2017-2020

Chief Investigator (CIB). "Elucidating a new mechanism of endometrial receptivity establishment in women and its clinical significance"

Professor Beverly Vollenhoven

NHMRC Research grants

2020 – 2023

NHMRC New Ideas Grant #1185467 (CIB). "Pregnancy and childhood outcomes associated with novel medication use in early pregnancy following IVF-assisted conception"

2019 - 2020

NHMRC Development Grant. "Validation of a prognostic assay for embryo transfer outcome"

2018 – 2020

NHMRC Grant #1139489. "Reappraisal of the mechanisms underlying implantation success or failure"

2017 – 2020

NHMRC Project Grant #1139489, Associate Investigator (AI). "Reappraisal of the mechanisms underlying implantation success or failure"

Media / Press

News Medical Life sciences (2019). Study highlights potential impact of chlamydia infection on men's fertility. [online]. Available at: https://www.news-medical.net/news/20191009/Study-highlights-potential-impact-of-chlamydia-infection-on-mens-fertility.aspx [Accessed 2020 Jan 13].

Monash IVF Research and Education Foundation.
January 2019 to June 2020 Report.

Repromed Scientific Advisory Committee (SAC)

Professor Kelton Tremellen.

Reproductive Endocrinology And Infertility Subspecialist, MB BS(Hons) PhD FRANZCOG CREI

Medical Director – South Australia, Chairman SAC

Kelton Tremellen is a specialist Gynaecologist who also holds a sub-specialty qualification in Reproductive Endocrinology and Infertility (CREI). He also completed a PhD in Reproductive Immunology at the University of Adelaide.

Professor Tremellen is a Medical Director at Repromed, Adelaide and Professor of Reproductive Medicine, Flinders University. He has an active research interest in the fields of oxidative stress as a cause of male infertility, immune mediated implantation failure, ovarian reserve and the effect of nutritional supplements on fertility.

Professor Tremellen was the first to introduce AMH as a test of ovarian reserve to Australia in 2004 and is also the inventor of the male fertility pill Menevit (http://www.elevit.com.au/product-range/menevit/) marketed in Australiasia by Bayer Consumer Care.

Associate Professor Deirdre Zander-Fox

BSc (Hon), PhD

Regional Scientific Director of Repromed, Monash IVF QLD (until November 2019), Associate Professor Monash University, University of South Australia and University of Adelaide

Deirdre completed her PhD studies in 2010 through The University of Adelaide's School of Paediatrics and Reproductive Health in which she undertook novel research into the impact of in-vitro stress on preimplantation embryo development, viability and metabolism. She has been a clinical embryologist since 2004. She is responsible for Embryology, Genetics, Andrology and Endocrine services as well as operational management, QC/QA and new technology implementation. In addition Deirdre supervises numerous PhD and honors students and holds an Adjunct Associate Professor positions at three Universities within Australia (Monash University, University of Adelaide and University of South Australia) as well as NHMRC funding.

Deirdre has authored 31 peer reviewed journal articles and book chapters with her research focusing on improving laboratory technology that will directly benefit infertile patients including cryopreservation, microinjection, culture media design and metabolic screening of embryo culture media. Her basic research interests focus on the impact of the environment during peri and pre implantation development on programming fetal growth and offspring health.

Dr Leanne Pacella-Ince

BHSc (Hons), PhD

Scientific Director Repromed (from November 2019) and Fertility Tasmania

Leanne joined Repromed in 2007 and is the Scientific Director of Repromed and Fertility Tasmania. A fully qualified Embryologist, prior to becoming the Deputy Scientific Director of Dulwich Leanne was the Genetics Co-ordinator for Repromed.

Completing her PhD under the supervision of Professor Michelle Lane and Associate Professor Deirdre Zander-Fox in 2014 through the University of Adelaide's School of Paediatrics and Reproductive Health for which she was awarded the Dean's Commendation for Thesis excellence. Her PhD focused on the contribution of perturbed granulosa and cumulus cell metabolism and mitochondrial protein levels to the poor IVF outcomes seen in women undergoing IVF with either reduced ovarian reserve or advanced maternal age.

In 2016, Leanne was awarded the Scientist in Reproductive Technology Established Scientist Award. With published papers in peer reviewed journals, Leanne is also an honors supervisor through the Adelaide University's Department of Obstetrics and Gynecology as well as an Australian Institute of Medical Scientists Assessor for IVF Embryologists.

Heavily involved in the implementation of new technology designed to provide better outcomes, Leanne is passionate about patient care and improving success rates.

Hamish Hamilton

Regional Manager - Repromed and Womens Imaging

Hamish has over 15 years of experience working with Monash IVF. He joined the Group in 2005 and has since held leadership positions in science, ultrasound and fertility across South Australia, Victoria, Northern Territory, Queensland and New South Wales.

Carole Tilbrook

Senior Fertility Nurse Specialist- Repromed

Gillian Homan

Fertility Nurse. SAC Executive Assistant

Associate Professor Mark Nottle.

SAC External independent representative

Principal Research Fellow, Adelaide Medical School, Faculty of Health and Medical Sciences, The University of Adelaide.

The SAC would like to recognise the invaluable work of Dr Nicole McPherson who diligently oversees recruitment for the clinical studies and deals with the complex demands of the medical, nursing and scientific staff, and human ethics committees.

2019 – June 2020 Research Projects

Ongoing research

Efficacy of PIEZO ICSI to improve fertilisation rates of oocytes

A/Prof Deirdre Zander-Fox[1], Dr Francesca Bell[2], Kevin Lam[2], Professor Michelle Lane[1], Dr Leanne Pacella-Ince[2], Dr Hamish Hamilton[1], Professor Kelton Tremellen[2]

[1]Monash IVF Group, Richmond; [2]Repromed, Dulwich

The first pregnancies using intracytoplasmic sperm injection (ICSI) were reported in 1992. Since that time ICSI has transitioned from being used to treat severe male factor infertility to being used as a treatment of choice for many other reasons including failed IVF insemination, embryo genetic testing and low oocyte number. In addition, the usage of ICSI has increased significantly with some countries reporting that ICSI is used in 100% of ART cycles. Although ICSI is a revolutionary technology in the field of ART, it is still invasive in its nature and the method, which involves aspiration of the cytoplasm, can result in increased rates of oocyte degeneration after the microinjection process is complete. PIEZO-ICSI is a modified microinjection process that uses a piezoelectric actuator is used to move the capillary in an ultra-rapid fashion resulting in microdrilling of the zona.

This form of microinjection has been used successfully in various animal models to improve survival post microinjection. In addition, limited reports out of Japan have demonstrated that a significantly higher survival rate post injection was seen for oocytes being injected with PIEZO-ICSI rather than conventional ICSI and fertilisation rates were also higher and PIEZO-ICSI increased the quality of D3 embryos compared to conventional ICSI and also resulted in increased pregnancy rates and live birth rates. Therefore, a clinical trial was undertaken to test the hypothesis that PIEZO-ICSI technology will increase fertilisation rates and decrease oocyte degeneration rates compared to conventional ICSI as well as improving embryo quality and pregnancy rates compared to a prospectively matched cohort.

Acrosome reacted sperm – an innovative way to improve ICSI technology

Dr Nicole McPherson[1,2,3], Dr Hamish Hamilton[1], Kevin Lam[1], Marg Szemis[1].

[1]Repromed, Dulwich; [2]School of Medicine, University of Adelaide, Adelaide; [3]Freemasons Centre for Men's Health, University of Adelaide, Adelaide.

Before sperm has the capacity to fertilise and conceive a healthy embryo and fetus, it must first undergo post ejaculation maturation (capacitation, hyperactivation and acrosome reaction) which is initiated in the oviduct and by the cumulus oocyte complex. However, the current protocol for ICSI completely ignores this post ejaculation sperm maturation, with direct injection of sperm into the oocyte irrespective if their acrosomal status. This means that the oocytes receive a number of proteins and sperm plasma membrane components that it would not 'normally' receive. In rodent models it has been shown that injection of sperm that had not undergone this post ejaculation maturation (to mimic what is currently injected during ICSI) resulted in slower embryo cleavage and reduced pregnancy rates compared with embryos produced from natural mating. In addition, in the human injection of acrosome reacted sperm resulted in a 4-fold increase in morula implantation rates compared with non-acrosome reacted sperm. These data suggest that while the oocyte has some capacity to deal with the incorporation of these 'extra' sperm molecules their addition is clearly having lasting effects to the developing embryo. Therefore, we hypotheses that inducing post ejaculation sperm maturation and the acrosome reaction in vitro prior to ICSI will increase blastocyst formation, implantation rates and live births.

Creating a Monash IVF Group Biobank to identify causes and early detection of major obstetrical syndromes

Dr Deirdre Zander-Fox[1,2], Dr Melody Menezes[3,4], A/Prof Fabricio da Silva Costa[3,5,6], Dr Todd Fullston[1,2], Dr Leanne Pacella[1]

[1]Repromed, Dulwich; [2]The University of Adelaide, Adelaide; [3]Monash Ultrasound for Women, Clayton; [4]Murdoch Children's Research Institute, Parkville; [5]Monash Medical Centre, Clayton; [6]Monash University, Clayton.

During pregnancy small fragments of cell-free DNA (cfDNA) from both mother and fetus circulate in maternal peripheral blood. The Monash IVF group has recently established the nestTM Non-Invasive Prenatal test (NIPT) which analyses these cfDNA fragments to screen for the most common chromosome conditions in pregnancy (i.e. Trisomy 21 (Down syndrome), Trisomy 18 (Edward's syndrome), Trisomy 13 (Patau syndrome) and sex chromosome aneuploidy). As part of the nest NIPT both cfDNA and maternal serum will be collected for analysis. We are requesting funding to set up a biobank of samples collected as part of the nest NIPT which will then be used for multiple research projects into the major
obstetrical syndromes – particularly pre-eclampsia and intrauterine growth restriction. These hypertensive disorders are the most frequent medical complications in pregnancy and the most important cause of maternal morbidity and perinatal mortality. The nest NIPT has afforded a unique opportunity for the Monash IVF group to have access to maternal history, ultrasound characteristics, maternal/fetal cfDNA, RNA and maternal serum. The creation of a biobank to store DNA, RNA and serum will allow for important and relevant research to be done into the causes and early detection of these significant and common obstetric syndromes.

GIRRTH – improving IVF/ICSI treatment outcomes in obese men

Dr Nicole McPherson[1,3,4,5], Prof Michelle Lane[2], Dr Tod Fullston[1], Dr Deirdre Zander-Fox[1], Prof Gary Wittert[4], Dr Margaret McGee[4]

[1]Repromed, Dulwich; [2]Monash IVF Group, Richmond; [3]School of Medicine, University of Adelaide, Adelaide; [4]Freemasons Foundation Centre for Men's Health, University of Adelaide, Adelaide; [5]Robinson Research Institute, University of Adelaide, Adelaide

One quarter of all male patients attending fertility treatment are now obese. We know that obesity in men significantly reduces live birth rates following IVF/ICSI (3) likely due to increases in sperm reactive oxygen species (ROS), which is independently linked to reduced pregnancy rates following ART. Therefore, reducing sperm ROS concentrations in these obese men prior to treatment should theoretically improve pregnancy outcomes. In rodent models of male obesity, lifestyle interventions to reduce adiposity and restore obesity related co-morbidities reduces sperm ROS concentrations and restores embryo quality and pregnancy rates. However, it is not known in humans whether sperm ROS concentrations can also be modified by lifestyle interventions to reduce weight and improve obesity related co-morbidities.

NEST4E- Non-invasive preimplantation Genetic Testing (PGT) for blastocysts that are not suitable for standard biopsy and PGT.

Professor Michelle Lane[1], Professor Kelton Tremellen[2], A/Prof Deirdre Zander-Fox[1], Dr Leanne Pacella-Ince[2], Dr Francesca Bell[2]

[1]Monash IVF Group, Richmond; [2]Repromed, Dulwich

Maternal age remains the primary determinate of IVF success rates most likely as a result of the increases in embryo aneuploidy with increasing age of the women. To counteract this, there has been the introduction of preimplantation genetic screening where cells from the embryo are removed and assessed using molecular techniques to determine the chromosome number of the embryo. A major limitation of the current technology is that only expanded blastocysts can be biopsied, meaning around 1/3 of embryos are not able to be tested. As a result, many older women who would most benefit from the technology have their screening cancelled as the embryos are frequently not of sufficient quality to be biopsied. It is therefore desirable to develop a non-invasive test for embryo ploidy. The advantages of this technology are therefore 2-fold; (i) non-invasive, (ii) used for embryos that are not suitable for biopsy. The purpose of this study is to implement a clinic trial for a non-invasive Preimplantation Genetic Testing (PGT) method for human embryos that are unable to be biopsied (but are still suitable to be frozen) and screened by the standard PGT technology by screening DNA isolated from the culture media to assess the ploidy status of those embryos.

Contributions to Scientific Literature

Peer Reviewed Journal Articles/Publications

1. Campbell J, McPherson N. Influence of increased paternal BMI on pregnancy and child health outcomes independent of maternal effects: A systematic review and meta-analysis. Obesity Research & Clinical Practice. 2019;13(6):511-521.
2. Evans A, de Lacey S, Tremellen K. Corrigendum to: Australians' understanding of the decline in fertility with increasing age and attitudes towards ovarian reserve screening. Australian Journal of Primary Health. 2019;25(1):97.
3. McPherson N, Shehadeh H, Fullston T, Zander-Fox D, Lane M. Dietary Micronutrient Supplementation for 12 Days in Obese Male Mice Restores Sperm Oxidative Stress. Nutrients. 2019;11(9):2196.
4. McPherson NO, Tremellen K. Increased BMI 'alone' does not negatively influence sperm function – a retrospective analysis of men attending fertility treatment with corresponding liver functions results. Obesity Research & Clinical Practice. 2020 Mar; 14(2): 164-167.
5. Pearce K, Estanislao D, Fareed S, Tremellen K. Metabolic Endotoxemia, Feeding studies and the use of Limulus Amebocyte (LAL) Assay; Is it fit for purpose?. Diagnostics (Basel). 2020 Jun; 10(6): 428.
6. Pearce K, Hill A, Tremellen K. Obesity related metabolic endotoxemia is associated with oxidative stress and impaired sperm DNA integrity. Basic and Clinical Andrology. 2019;29(1).
7. Pearce K, Tremellen K. The Effect of Macronutrients on Reproductive Hormones in Overweight and Obese Men: A Pilot Study. Nutrients. 2019;11(12):3059.
8. Tremellen K, Hill A, Pearce K. Mechanistic insights into the aetiology of post-prandial decline in testosterone in reproductive-aged men. Andrologia. 2019;51(10).
9. Tremellen K, Pearce K. Small intestinal bacterial overgrowth (SIBO) as a potential cause of impaired spermatogenesis. Gut. 2020 Feb.
10. Tremellen K, Woodman R, Hill A, Shehadeh H, Lane M, Zander-Fox D. Use of a male antioxidant nutraceutical is associated with superior live birth rates during IVF treatment. Asian Journal of Andrology. 2020;.
11. Rezaei M, Winter M, Zander-Fox D, Whitehead C, Liebelt J, Warkiani M, Hardy T, Thierry B. A Reappraisal of Circulating Fetal Cell Noninvasive Prenatal Testing. Trends in Biotechnology. 2019;37(6):632-644.

Presentations- National Conferences and Meetings

1. Hardy T. Preconception Screening. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
2. McPherson N. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
3. Pacella-Ince L. What about the age of the blastocyst: day4,5,6,or 7?. Fertility Society of Australia; 2019, Sept 15 - 18: Tasmania, Australia.
4. Tremellen K. New solutions to the big problem of obesity and male reproductive health. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
5. Tremellen K. Caesarian section defect as a cause of recurrent IVF failure. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.

Presentations- International Conferences and Meetings

1. Hardy T, Ledger W, Scott H. Karyomapping using whole genome sequencing data: preclinical validation of a personalized approach to PGT-M. Preimplantation genetic diagnosis international society PDGIS; 2019 Apr 15 – 18: Geneve, Switzerland.
2. Pacella-Ince L. Overcoming challenges in Embryo Culture with Optimised QA/QC. Indian Society for Assisted Reproduction ISAR. 2020 March 6: India.
3. Pacella-Ince L. Preimplantation Genetic Aneuploidy screening: Is it delivering on its promise?. Indian Society for Assisted Reproduction ISAR. 2020 March 6: India.
4. VerMilyea M et al. Artificial intelligence technology can predict human embryo viability across multiple laboratories with varying demographics with high accuracy and reproducibility. 35th Annual Meeting ESHRE; 2019, June 23-26: Vienna, Austria.

Poster presentations and abstracts- International Conferences and Meetings

None

Books and Book Chapters

None

A/Prof Deirdre Zander-Fox NHMRC Research Grants 2019

NHRMC Project Grant #1171821, Chief Investigator (CIC). "Genome-wide Non-Invasive Prenatal Testing based on Circulating Fetal Trophoblastic cells"

New South Wales research

Associate Professor Hassan Bakos

B.HLTH.SC. (HONS.), PH.D.(MED), GRAD.CERT.MGT, CPMgr

Scientific Director Monash IVF NSW & ACT; Conjoint Associate Professor, University of Newcastle

Associate Professor Hassan Bakos completed a Bachelor of Health Sciences and Honours Degree in Obstetrics and Gynaecology, University of Adelaide. In 2010, he completed a PhD in Reproductive Medicine for which he was awarded a special commendation from the Dean of Graduate Studies and the Robert Seamark award for the most outstanding graduating postgraduate candidature.

In 2011, Hassan was appointed as Deputy Scientific Director at Repromed where he supervised of the Andrology and Pathology services as well as performing clinical embryology procedures including ICSI and embryo biopsy. In 2015, he was appointed as Scientific Director for the Monash IVF Group in Sydney and is currently responsible for the scientific directorship and operations of six MVF laboratories across New South Wales and the Australian Capital Territory, including embryology, andrology and endocrinology services.

A/Prof. Bakos has held adjunct academic positions at the University of Adelaide and University of Sydney. His qualifications extend to a Graduate Certificate in Management. He is also a past Honorary Treasurer of Scientists in Reproductive Technology.

A/Prof. Bakos has won a number of scientific awards both nationally and internationally, including the Society for Reproductive Biology Oozoa award, the American Society for Reproductive Medicine Travelling Scholar award. In 2019 he was awarded the Fertility Society of Australia Geoff Driscoll medal.

2019 – June 2020 Research Projects

Ongoing research

Neurophysiology of cognitive behavioural therapy, deep breathing and progressive muscle relaxation used in conjunction with assisted reproductive technology treatments

A/Prof Hassan Bakos1 and Dr Georges Raad2

[1]Monash IVF Group NSW, [2]Al-Hadi Laboratory and Medical Centre, Beirut, Lebanon

It has been recommended recently that psychosocial support should be offered as a complementary therapy during infertility treatments. In this effect, the efficiency of different psychological interventions, such as cognitive behavior therapy (CBT), deep breathing (DB), and progressive muscle relaxation (PMR), was evaluated in the context of ART treatment.

Applying these techniques was associated with mood improvements and a decline in stress biomarkers, and, hypothetically, reducing stress biomarkers associated with ART treatment. Accordingly, this study will ensure that these interventions reach their full potential and therefore improve clinical outcomes.

The impact of four sperm preparation techniques on sperm quality

A/Prof Hassan Bakos[1] and Dr Georges Raad[2]

[1]Monash IVF Group NSW, [2]Al-Hadi Laboratory and Medical Centre, Beirut, Lebanon

Current methods for the selection of sperm for IVF and ICSI remain relatively under-researched and there is little known about the impact of these methods on the molecular health of sperm. In particular, sperm with high levels of DNA damage are known to be associated with poorer pregnancy outcomes.

The aim of this study was to assess the impact of four sperm preparation techniques on sperm motility, sperm vacuoles, DNA fragmentation, intracellular ROS, acrosome reaction and mitochondrial activity. The results of the study will help optimize the existing sperm selection methods and establish an evidence based approach to determine the safest methodology to select sperm for ART treatment.

Kuala Lumpur research

Dato' Dr Prashant Nadkarni

MBBS (MAL), FRCOG (UK)

Medical Director & IVF specialist, KL Fertility Malaysia.

Dr. Prashant obtained his specialist qualification (MRCOG) in 1989 and chose to further sub-specialise in the field of infertility. He was fortunate to be selected to train with Prof. Ian Craft, one of IVF's early pioneers. He spent the next two years (1989-1991) at the London Fertility & Gynaecology Centre in Harley St., where he was involved in cutting-edge infertility research and treatments which have now become a routine part of infertility management. Dr. Prashant was seconded to Dubai to set up the center from scratch. This fertility centre grew to become one of the largest fertility centres in the Middle East doing over 500 IVF and GIFT cycles a year.

Upon his return to Malaysia in 1997 he re-joined University Hospital and set up the IVF unit there. As Associate Professor, he was responsible for teaching students and resident doctors, and to this day, maintains an active interest in research and training. He is regularly invited to speak at public forums as well as at medical conferences on fertility issues.

On a national front he is actively involved in helping to set standards in fertility practice and serves on several technical committees for the Ministry of Health, Academy of Medicine Malaysia, Ministry of Science, Technology & Innovation and the Malaysian Society for Quality in Health.

In recognition of his fertility-related work for the Tunku Azizah Fertility Foundation (TAFF) as well as his voluntary involvement at various national-level fertility initiatives, he was awarded a Dato' title by the Sultan of Pahang. He has also been awarded the Fellowship of the Royal College of Obstetricians & Gynaecologists in the UK.

Contributions to Scientific Literature

Peer Reviewed Journal Articles/Publications

1. Keen SP, Yeong TH, Siew-Keah L. Semen parameters in male partners of infertile couples in Malaysia. Medical Journal of Malaysia. 2019; 74 (1).

Presentations- National Conferences and Meetings

1. Loke MK. Does information change patients preference for double embryo transfer. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.

Presentations- International Conferences and Meetings

1. Sim PK, Sivasengaran S, Lee SK, Loke MK, Nadkarni P. Association between races and semen quality in fertility evaluation at a single fertility center in Malaysia. The 9th Congress of ASPIRE; 2019, May 2-5: Hong Kong, China.
2. Syed Tahir SNA, LEE SK, Nadkami P, Lim YH, Loke MK, Wiao WAM. Does information change patient's preference for double embryo transfer between year 2015 and 2018?.The 35th Annual meeting of ESHRE; 2019, June 23-26: Vienna, Austria.

Poster presentations and Abstracts- International Conferences and Meetings

1. Keen SP, Yeong TH, Siew-Keah L. Semen parameters in male partners of infertile couples in Malaysia. 27th International Congress of OGSM; 2019 July 18-21: Penang, Malaysia.

Monash & Sydney Ultrasound for Women

A/Prof Simon Meagher

BSc (Hons), MB BCH BAO, FRCPI, FRCOG, FRANZCOG, DDU, COGU

Medical Director of Monash Ultrasound for Women, Victoria; Lecturer, Monash University

As Medical Director of Monash Ultrasound for Women, Dr Simon Meagher oversees a team of 50 sonologists, sonographers, genetic counsellors, phlebotomists and administrative staff in delivering a tertiary level ultrasound service across south east Melbourne. Dr Meagher has dedicated 25 years of his term as Director, teaching and lecturing in obstetric and gynaecological ultrasound both locally and overseas.

In 2015 he was awarded 'Sonologist of The Year' by the Australian society of Ultrasound in medicine (ASUM) in recognition of his commitment to hands on training within the hospital setting at the Mercy Hospital for Women, his commitment and contributions to ASUM and the International Society of Ultrasound in Obstetrics and Gynaecology.

Dr Meagher has delivered over 700 lectures, across 15 countries, and 40 cities worldwide. He has conducted predominantly clinical research in obstetric ultrasound, with a focussed interest in early pregnancy screening and diagnosis. He has published 70 articles in peer review journals, including 15 in the last 3 years focusing on first trimester pregnancy screening and diagnosis. Dr Meagher has described five original sonographic fetal markers during the first and second trimesters of pregnancy. He is now focusing his interest on aneuploidy and embryo development from seven to 10 weeks as we approach the dawn of a new era of genetic screening via free fetal DNA analysis.

Dr Meagher has taken on multiple leadership positions - early in his career as the Chair of the Standards of Practice Committee at ASUM, examiner and executive board member for the ASUM Diploma of diagnostic ultrasound and later as council member of ASUM. Thereafter he served as Chairman of the Victoria Obstetric Sonologists group and on several task force and education committees at the International Society of Ultrasound in Obstetric and Gynaecological Ultrasound.

Dr Meagher is consultant sonologist at the Perinatal department, Mercy Hospital for Women, Melbourne.

Dr Melody Menezes

BSc(Hons), GDipGenetCouns, PhD, FHGSA

Scientific Director at Monash Ultrasound for Women

Melody is the Head Genetic Counsellor and Scientific Director at Monash Ultrasound for Women. She is also a Senior Lecturer at the University of Melbourne for the Master of Genetic Counselling and Master of Genomics and Health courses, and an Editor of the Journal of Genetic Counselling. Melody's research and clinical interests include prenatal screening and testing, disability issues, and the ethical, legal and social aspects of genetic testing. She has a particular interest in Non-Invasive Prenatal Testing (NIPT) and has a number of publications looking at NIPT in the Australian population.

A/Prof Andrew McLennan

BSc MB BS (Hons) FRANZCOG MRCOG COGU

Clinical Associate Professor, Department of Obstetrics, Gynaecology and Neonatology, Northern Clinical School, Obstetrician Gynaecologist Sonologist, Sydney Ultrasound for Women

Associate Professor Andrew McLennan is a specialist obstetrician and gynaecologist whose particular interest is in prenatal diagnosis and ultrasound. He is a consultant to the Maternal Fetal Medicine Unit at Royal North Shore Hospital, a Clinical Associate Professor at the University of Sydney and a Sonologist at Sydney Ultrasound for Women.

In a national first, Andrew introduced Nuchal Translucency (NT) screening for Down syndrome to Australia, helping to revolutionize the way prenatal screening for chromosome abnormality is conducted. He is the founding Chairman of the National Early Pregnancy Assessment Program and the past President of the Australian Association of O&G Ultrasonologists.

Andrew has been involved in educating doctors and sonographers in Australia and South-East Asia in the conduct of early pregnancy screening for fetal chromosome abnormalities and adverse pregnancy outcomes. He is actively involved in research into early diagnosis of fetal abnormalities and quality assurance in ultrasound.

2019 – June 2020 Research Projects

Completed research

Non-invasive prenatal testing with cell-free DNA for fetal trisomies 21, 18 and 13, in an ART population.

Dr Fabricio Costa[1], Andrew McLennan[2], Dr Simon Meagher[1], Dr Melody Menezes[1], Prof Jon Hyett[3].

[1]Monash Ultrasound for Women, Clayton; [2]Sydney Ultrasound for Women, Burwood; [3]Royal Prince Alfred Hospital, Sydney.

ART pregnancies have reduced first trimester combined screening (FTCS) PAPP-A levels leading to an increased likelihood of receiving a false-positive result. Non-invasive prenatal testing (NIPT) is a recently available advanced screening test which involves testing cell-free DNA (cfDNA) in the maternal plasma. These cells are released from the placenta (fetal genetic material) into the maternal circulation and this allows the detection of common autosomal trisomies (21, 18, and 13) with a high level of accuracy in singleton pregnancies. The objective of this study is to assess the performance of screening by NIPT for trisomies using a chromosome-selective sequencing method of cfDNA in maternal plasma obtained from an ART population undergoing routine screening at 11-13 weeks' gestation. A prospective chart review will be conducted to collect clinical data on patients who will have undergone combined FTCS and NIPT. From the 300 patients studied a high risk on FTCS is expected in 24-30 cases (~8-10%). We will compare the risk scores, between FTCS and NIPT.

The establishment of a normal range of embryonic heart rates in IVF pregnancies at seven weeks' gestation in an Australian population: embryonic heart rate as a determinant of first trimester loss

Presanna Sujenthiran[1], Dr Martha Finn[1], Dr Simon Meagher[1], Paul Lombardo[2].

[1]Monash Ultrasound for Women, Richmond; [2]Dept. Medical Imaging and Radiation Sciences, Monash University.

ART births now account for ~3.6% of Australian births with almost 10,000 born each year. The 7 week ultrasound has become a definitive time to confirm a live intrauterine gestation for ART patients and it is therefore crucial to have established ultrasound parameters at this gestation. The boundary between normal and slow early embryonic heart rate (EHR) has not been well established in ART pregnancies. The study aims to establish a normal range of embryonic heart rates at 7 weeks gestation in ART singleton pregnancies as well as to analyse whether the EHR between 6W1D (i.e. 6 weeks and one day) and 7W6D in singleton ART pregnancies is useful in predicting the likelihood of first trimester loss. The range of EHRs will be evaluated to determine whether they form a normal distribution. The primary outcomes include successful first trimester pregnancy, confirmed by the standard 12 week ultrasound examination or miscarriage confirmed by ultrasound or medical documentation.

PeTALS: A longitudinal study exploring women's experiences following a prenatal diagnosis of fetal abnormality

Dr Melody Menezes[1], Professor Sylvia Metcalfe[2], Dr Jan Hodgson[2], Professor Jane Fisher[3], A/Prof Kerry Petersen[4], A/Prof Jane Halliday[2].

[1]Monash Ultrasound for Women, Richmond; [2]Murdoch Children's Research Institute, Parkville; [3]Jean Hailes Clinical Research Unit, Monash University, Clayton; [4]School of Law, La Trobe University, Melbourne.

Advances in genetic technologies are rapidly expanding the availability and accuracy of prenatal tests. In Australia, ~4% of babies are born with a fetal abnormality, many of which are diagnosed during pregnancy. Our multidisciplinary team will use a collaborative approach to understand how pregnant women are cared for following the diagnosis of a fetal abnormality, and to develop appropriate evidence-based models of supportive care. This study will be the first in Australia to investigate women's experiences of a prenatal diagnosis (PND) of fetal abnormality immediately following diagnosis. The study aims to (1) explore the psychosocial impact of a PND of fetal abnormality on women; (2) identify the social and professional supports utilised and needed by women and (3) describe the longer term outcomes for women who receive a diagnosis of a fetal abnormality. The project will add to the existing knowledge in this under-researched field and contribute directly to improving the social and clinical care of women together with the education of the health professionals who care for them.

2019 – June 2020 Research Projects

Ongoing research

Reproducibility of three-dimensional ultrasound of the junctional zone in myometrial pathology and their correlation with pregnancy rates

Dr Lufee Wong[1,2], A/Prof Fabricio Costa[1,2], Prof Luk Rombauts[2,3], Prof Beverley Vollenhoven[2,3], Dr Hugo Fernandes[2,3,4], A/Prof Martin Healey[3,4], A/Prof Evdokia Dimitriadis[5], A/Prof Wellington Martins[6].

[1]Monash Ultrasound for Women, Richmond;[2]Monash Medical Centre, Clayton;; [3]Monash IVF, Clayton; [4]The Royal Women's Hospital, Parkville; [5]Hudson Institute, Clayton; [6]Faculty of Medicine of Ribeirao Preto, University of Sao Paulo, Brazil.

During pregnancy, the endometrial-myometrial junction, or junctional zone (JZ), is fundamental to the process of implantation and placentation. Consequently, any myometrial disorders, such as adenomyosis, can disrupt the process, leading to infertility and various pregnancy complications. While magnetic resonance imaging (MRI) can be used in the assessment of the JZ, it is not readily available, expensive and can be claustrophobic for some patients. Three-dimensional (3D) ultrasound has made it possible to assess minor changes in the JZ. A consensus statement in 2015 on the classification system of myometrial disorders aims to assess the JZ using standardized nomenclature. This study aims to evaluate the reproducibility of this evaluation of the JZ using 3D-ultrasound, as well as the correlation of the JZ changes with pregnancy rates. Being able to accurately diagnose adenomyosis will help in the diagnosis and counseling of patients with infertility before undergoing IVF cycles.

Furthermore, recent studies have identified that small non-coding RNA, microRNA (miR), are differentially expressed in human endometrium across the menstrual cycle suggesting they are hormonally controlled. Uterine miR expression levels are altered in a number of uterine disorders and a recent study demonstrated that miR levels in human endometrium correlate with serum levels in women with primary infertility. We propose that similarly miR levels in serum may reflect alterations in the JZ and may be useful in the diagnosis of adenomyosis in conjunction with 3D-ultrasound.

Performance and characteristics of non-invasive prenatal testing (NIPT) in assisted reproductive technology (ART) conceptions

Dr Melody Menezes[1,2], Mr Tim Lee[3], Prof Jane Halliday[2,4], A/Prof Lisa Hui[2,4,5], Dr Sharon Lewis[2,4], A/Prof Fabricio da Silva Costa[1,3,6]

[1]Monash Ultrasound for Women, Clayton; [2]Murdoch Children's Research Institute, Parkville; [3]Monash University, Clayton; [4]The University of Melbourne, Parkville; [5]Mercy Hospital for Women, Heidelberg; [6]Monash Medical Centre

During pregnancy small fragments of cell-free DNA (cfDNA) from both mother and fetus circulate in maternal peripheral blood. Non-Invasive Prenatal testing (NIPT) analyses these cfDNA fragments to screen for the most common chromosome conditions in pregnancy (i.e. Trisomy 21 (Down syndrome), Trisomy 18 (Edward's syndrome), Trisomy 13 (Patau syndrome) and sex chromosome aneuploidy). To date, Monash Ultrasound for Women (MUFW) has screened over 7000 pregnancies with NIPT; approximately 20% of which are ART conceptions. Despite the high uptake of NIPT among women with ART conceptions, there is currently no reliable performance data or evidence to support the use of NIPT in this particular population.

As leaders in the field of IVF, and recently having developed NIPT within the Monash IVF group, we are in the unique position of having fertility, ultrasound and NIPT data for all of our patients. It is a known challenge for researchers to ensure complete clinical follow up of cases, in particular, identifying false negative cases of NIPT. Victoria is in a unique position to perform complete follow-up due to existing pre- and post-natal databases. Generating evidence on the performance of NIPT in the ART population will allow the Monash IVF group to play an important role in evidence-based practice and innovation in this rapidly advancing area.

Validation of prospective first trimester screening for preterm preeclampsia in the Australian population

Dr Daniel Lorber Rolnik[1], A/Prof Fabricio da Silva Costa[1,2], A/Prof Andrew McLennan[3]

[1]Monash Health, Clayton; [1,2]Monash Ultrasound for Women, Clayton; [3]Sydney Ultrasound for Women, Sydney

Despite all the research published in the last three decades on screening and prevention of preeclampsia, the condition remains as one of the main causes of maternal and perinatal morbidity and mortality worldwide. It affects 2-8% of all pregnancies and it is responsible for one out of five maternal deaths and 15% of the premature deliveries. This research aims to assess and validate in the Australian population a previously published first trimester algorithm for prediction of preeclampsia that combines maternal characteristics, uterine artery Doppler, mean arterial pressure and biochemistry (pregnancy associated plasma protein-A - PAPP-A – and placental growth factor - PlGF). This algorithm detects 75-80% of all cases of preeclampsia requiring premature delivery and more than 90% of the cases that will require delivery before 34 weeks, with a false-positive rate of 10%. The algorithm was recently evaluated in a European multicentre prospective study, and seems to be far superior than screening by maternal factors alone. However, there is only one study validating this predictive test in the Australian population and no studies adding PlGF to the algorithm.

First trimester screening for preterm preeclampsia is routinely offered as part of the 11-14 weeks' ultrasound at Monash Ultrasound for Women (MUFW) and at Sydney Ultrasound for Women (SUFW) and more than 20,000 women were prospectively screened since June 2013 in both services. Furthermore, recent clinical trials and meta-analyses have shown that initiation of low-dose aspirin before 16 weeks for patients at high risk reduces by more than 60% the incidence of preterm preeclampsia.

Contributions to Scientific Literature

Peer Reviewed Journal Articles/Publications

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12. Smet ME, Scott FP, McLennan AC. Discordant fetal sex on NIPT and ultrasound. Prenatial Diagnosis. 2020 Mar.
13. Wertaschnigg D, Ramkrishna J, Ganesan S, Tse C, Scheier M, Volpe N, Ghi T, Meagher S, Rolnik DL. Cranial sonographic markers of fetal open spina bifida at 11 to 13 weeks of gestation. Prenatal Diagnosis. 2019 Nov; 40(3): 365-372.
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Presentations- National Conferences and Meetings

1. Kesby G. Meeting the challenges of consumerism and regulation in reproductive medicine. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
2. McLennan A. Extending the scope of NIPT. Roche NIPT Expert Symposium; 2019, July 16.
3. McLennan A. First trimester screening in the Molecular Age. RANZCOG NSW Fellows Education; 2019, Aug 21.
4. McLennan A. Combined aneuploidy screening in the NIPT era. World Federation for Ultrasound in Medicine and Biology; 2019, Sep 6.
5. McLennan A. Rare autosomal trisomies. Repromed Reproductive Genetic forum; 2019, Nov 9.
6. McLennan A. Prenatal aneuploidy screening and diagnosis. RANZCOG Fellowship Exam revision course; 2019, Nov 20.
7. Menezes M. Genetic carrier screen/ triple screen. Monash IVF Group Clinical meeting; 2019 Nov 22-24: Melbourne, Australia.
8. Menezes M. Prenatal genetic counselling in a brave new world. ISUOG First Trimester Ultrasound Symposium; 2019, May 4-5: Melbourne, Australia.
9. Menezes M. NIPT and the Importance of Ultrasound. Vietnamese Australian Health Professionals Association; 2019, Oct 20: Melbourne, Australia.
10. Menezes M. Expert Panel. Repromed Reproductive Genetics Forum; 2019, Nov 9. Adelaide.
11. Menezes M. Genetic Counselling in Private Ultrasound. ASGC Webinar Series: 2019, Nov 20.

Presentations- International Conferences and Meetings

1. Ekelund CK, Rode L, Tabor A, Hyett J, McLennan A. First trimester placental growth factor level and adverse obstetric outcomes.29th World Congress on Ultrasound in Obstetrics and Gynecology; 2019, Oct 12-16: Berlin, Germany.
2. McLennan A. First trimester PlGF levels and adverse perinatal outcome. International Society of Ultrasound in Obstetrics and Gynecology ASM; 2019, Oct 13: Berlin, Germany.
3. Menezes M, Meagher S, Humnabadakar K, Tse C, Maxfield M, Rolnik D et al. Pregnancy outcomes following the detection of early fetal oedema on pre-NIPT ultrasound. Human Genetics Society of Australasia 43rd Annual Scientific Meeting; 2019, Aug 3-6: Wellington, New Zealand.


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