In this issue #43

$14.7 million for the Synchrotron provides new hope for cancer treatment

$14.7 million funding from the Federal Government's National Health and Medical Research Council and the State Government will allow upgrades to the medical beamline at the Australian Synchrotron enabling it to become one of the most advanced medical beamlines in the world.

MIMR is leading a collaborative project using the Synchrotron that could see cancer patients withstand radiotherapy treatment at much higher radiation levels and suffer fewer side effects.

Institute Director, Professor Bryan Williams, said that, up until now, the project team have had to travel to the Japanese Synchrotron to undertake their preliminary research.

"Upgrading the beamline at the Australian Synchrotron means our researchers can now base their research here in Melbourne.

"We hope to be working with cancer models at the Synchrotron within the next three months," Professor Williams said.

Professor Peter Rogers, the project's Chief Investigator, will exploit the latest in science technology using the Australian Synchrotron. He believes that his team will be the first to explain how and why patients could safely undergo radiotherapy at 400 times higher than the current clinical dose.

In April, the Cancer Council of Victoria announced that MIMR will receive a further $206,500 grant from their Venture Grants Scheme for this important research project. This grant is in addition to the funding provided by the Cancer Council of Victoria since 2007 and will enable Professor Rogers to continue his research into improved radiotherapy treatments into 2010.

"Approximately 50 percent of cancer patients receive radiotherapy. The major limitation of current radiotherapy treatment is devising ways to administer enough radiation to kill the tumour without destroying the surrounding, healthy tissue," he said.

Cancer patients undergoing radiotherapy currently receive broad x-ray beams, with treatment spread over a number of days to allow the healthy tissue to recover between doses.

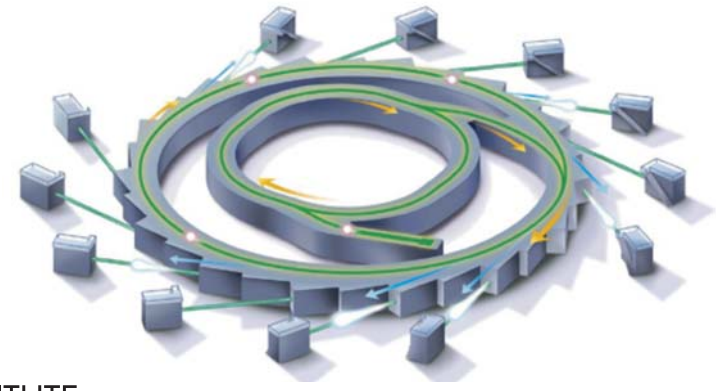
The research project will explore the phenomenon whereby splitting the powerful synchrotron x-ray beam into narrow microbeams dramatically changes the effects of radiation on tumour and healthy tissues.

Using mouse models, Professor Rogers investigated this process, called Microbeam Radiation Therapy (MRT). He administered MRT at 400 times the normal clinical dose. His results showed that the cancer died, and the healthy tissue completely recovered within six weeks.

"For reasons we still don't understand, MRT only hits 20 percent of the tumour, yet the entire tumour dies and the healthy tissues are less affected, despite receiving much higher levels of radiation. Once our project clarifies the cellular and molecular responses that occur, the implications for treating human cancer patients are enormous."

"To achieve our aim of developing more effective radiotherapy treatments, we need to understand why normal tissue is resistant to MRT, but tumours are not. We can then use these findings to design MRT treatment that optimises the benefits of radiotherapy for certain cancer patients," Professor Rogers said.

Continued on Page 2



From the Director's Desk:

The last three months have seen major changes within the Centre for Reproduction and Development.

Associate Professor Kate Loveland has moved with her group to join Monash University's Department of Biochemistry and Molecular Biology and Associate Professor Moira O'Bryan has moved with her group to Monash University's Department of Anatomy and Cell Biology. Both groups will benefit from being located at Clayton campus, within close proximity to collaborators in other Monash University departments. While the groups are no longer located at MIMR, they will maintain strong links with the Institute and we anticipate future collaborations with them.

After 15 years at MIMR, Associate Professor David Phillips has moved to Latrobe University in Bundoora to become the Director of Research.

Centre Director, Professor Michael Holland has joined the University of Queensland as Professor of Reproduction and Animal Biotechnology in the School of Veterinary Science. Michael was the Director of the Centre for Reproduction and Development since 2005 and was instrumental in leading the merger of the Centre for Early Human Development with the Centre for Molecular Reproduction and Endocrinology following the departure of Professor Alan Trounson to lead the Monash Immunology and Stem Cell Laboratories. Under Michael's leadership this Centre continued active engagement in the Dairy Cooperative Research Centre, pioneering reproductive technology studies in the bovine model and provided an active node in the ARC Centre of Excellence in Biotechnology and Development. Stem cell research also flourished under his leadership.

I take this opportunity to wish each of these researchers the best of luck in their new roles.

While these changes have had a significant impact on the Centre for Reproduction, it offers us the opportunity to review the Centre's activities and to recruit a new Centre Director to drive the strengths and talents of existing researchers and expand the Centre's research base.

In a move that could help advance our own stem cell research, President of the United States of America, Barack Obama, recently announced changes to the stem cell legislation in the US. The March announcement has seen the reversal of the Bush Administration decision to ban Federal funding for research using embryonic stem cells. President Obama's decision to back this important area of research offers Australian scientists the potential to create international collaborations with researchers in the United States.

The April announcement by the Federal and State Governments to fund the upgrade of the medical beamline, equipment, laboratories and clinical facilities at the Australia Synchrotron will greatly enhance the research conducted at MIMR into radiation therapies.

We are hopeful that this research will provide better outcomes for patients undergoing radiation treatment for cancer.

Professor Bryan Williams,
Institute Director

What is the Synchrotron?

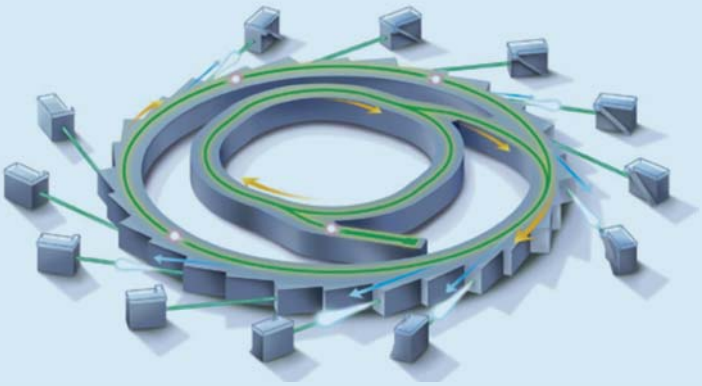
From Page 1

A synchrotron is a large machine (about the size of a football field) that accelerates electrons to almost the speed of light. As the electrons are deflected through magnetic fields, they create extremely bright light.

The light is channelled down beamlines to experimental workstations where it is used for research.

In addition to medical research, synchrotron technology is used worldwide to:

- Develop new fibre from wool
- Make better chocolate
- Clean up polluted wetlands
- Explore for gold deposits
- Improve fuel efficiency
- Create flat screen displays for mobile phones, televisions and computers
- Undertake crime scene investigations



Picture: Illustration of the Australian Synchrotron
Source: Australian Synchrotron **www.synchrotron.org.au**


Professor Gail Risbridger

A moment with:

Professor Gail Risbridger

Director, Centre for Urological Research

Scientists and clinicians working in the Centre for Urological Research (CURe) investigate the three clinical conditions that affect the prostate gland: prostate cancer, benign prostate hyperplasia (BPH) and prostatitis. These are all common conditions that have an immeasurable impact on quality of life for men and their families.

Prostate cancer is the most common cancer among men. Each year, 18,700 new cases are diagnosed in Australia alone.

It is an exciting time to be an investigator in this field; Professor Gail Risbridger, Director of CURe, gives her thoughts:

Debate continues over the suitability of the current Prostate Specific Antigen (PSA) testing for men. To screen or not to screen, that is the question?

Although there is currently no other better, non-invasive test for prostate cancer, recent evidence from two major studies have failed to justify the use of PSA for screening. A European study reported a reduction in mortality due to screening whereas a US study did not. However, both of them highlighted the issue of over-diagnosis as a result of screening and the consequent interventions (and side effects) that would not occur otherwise. So, in 2009, the dilemma of PSA screening for prostate cancer remains unresolved, and ultimately means we need more research.

A promising new treatment [Abiraterone] for patients with advanced prostate cancer was in clinical trial, tell us your thoughts?

Advanced prostate cancer can be difficult to treat and is eventually fatal. There is no question that new treatments are needed to treat this stage of the disease.

The 2008 clinical trials in the US and UK tested a new treatment for patients with advanced prostate cancer with a drug called Abiraterone. This drug turns off hormone production. Hormones drive tumour growth and patients with advanced disease commonly have what is called hormone ablation therapy. This therapeutic approach has been used for decades, but only recently did we realise that the tumour cells are clever and have adapted to their environment by simply making their own hormones rather than getting them from the circulation Exciting work, but the job does not stop there because only about half of the men responded to this treatment and there are side effects. Nevertheless, this is progress!

What do you think will be important steps in the future?

Whilst total androgen blockade is effective, there are significant side effects in these men, including osteoporosis and metabolic syndrome, that require treatment.

A great strength of the research program at CURe lies in our training in cancer biology together with endocrinology, biology and physiology. At CURe we study tumour biology but always in the context of the tumour being located in the prostate gland where benign disease may also be present, and where the man is ageing and will show significant changes to normal physiology. In this way, we can ensure that potential treatments for prostate cancer will not exacerbate other diseases that might be present, such as BPH.

For more information on prostate cancer, PSA testing and a range of conditions that affect men go to: **www.andrologyaustralia.org.**

VALE

George Limb

16 November 1935 - 7 March 2009

George Limb will be remembered by his family and friends as a man of great intelligence, strength and vision.

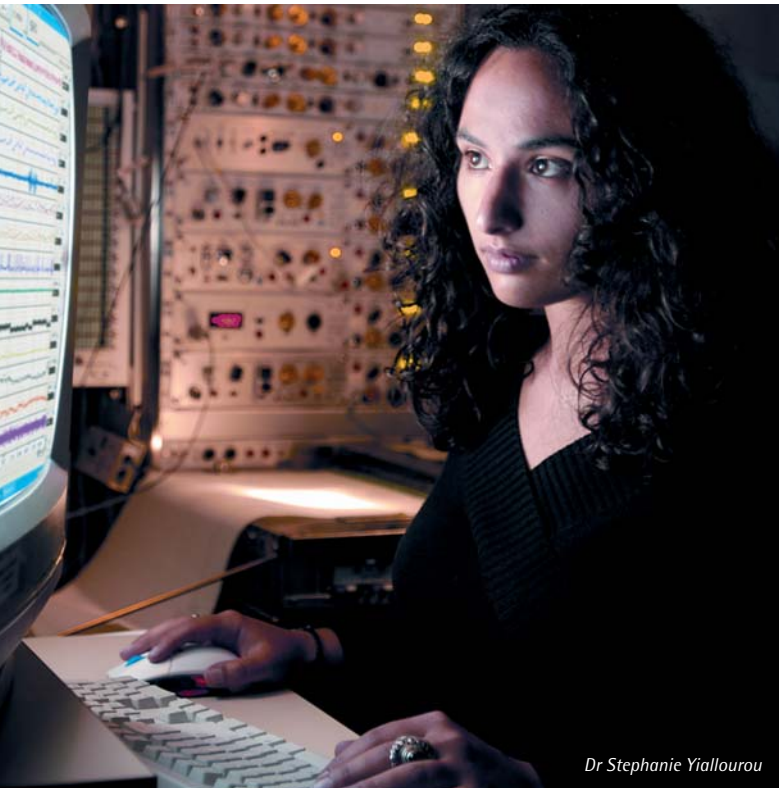
At MIMR, we remember George for the legacy that he leaves behind him. In 2007, George and his wife Janet provided funding to establish the Limb Family Foundation Scholarship for two PhD students studying prostate cancer research.

Prostate cancer is a disease affecting older men, but George had the insight and vision to make an impact across the generations. By providing this scholarship for two young researchers, he and his family are assisting the education of the next generation of researchers, whose work will benefit the older generation of people impacted by prostate cancer.

George was a familiar face at MIMR, he took great interest in what was happening at the Institute and took the time to get to know Sherin Hussain and Sarah Wilkinson, the Limb Family Foundation Scholars.


Sarah Wilkinson, Janet Limb, Professor Gail Risbridger, George Limb and Sherin Hussain

George Limb will be sadly missed by all who knew him but his memory will live on through the scholarships he and his family have provided.



Dr Stephanie Yiallourou

New Kaarene Fitzgerald Fellow announced

Dr Stephanie Yiallourou has been appointed the Kaarene Fitzgerald Fellow for 2009-2011. The Fellowship is a collaboration between MIMR and SIDS and Kids Victoria. It recognises the work of Kaarene Fitzgerald AC who founded SIDS and Kids and was a tireless supporter of research into the prevention of Sudden Infant Death Syndrome (SIDS).

Stephanie completed her PhD in 2008 in the Ritchie Centre for Baby Health Research investigating the effects of sleeping position on cardiovascular control during sleep in infants and the implications for SIDS. Stephanie returned to the Ritchie Centre at the beginning of 2009 as a Research Fellow after the birth of her son.

This appointment will allow Stephanie to continue working towards further understanding the mechanisms involved in SIDS.

Study shows maternal smoking increases risk of SIDS

A study conducted in the Ritchie Centre for Baby Health Research has shown that maternal smoking impairs an infant's ability to arouse from sleep, a critical response linked with the cause of Sudden Infant Death Syndrome (SIDS).

Scientific Director of the Ritchie Centre, Associate Professor Rosemary Horne, and PhD student, Heidi Richardson, compared the arousal responses of infants born to mothers who smoked during pregnancy with infants who had non-smoking mothers. The study reviewed babies at three stages from two weeks to six months, covering the peak incidence period for SIDS.

This research has shown that maternal smoking can impair the arousal pathway of seemingly normal infants, which may increase their risk for SIDS.

While public education campaigns have reduced the number of SIDS related deaths in Australia over the past 10 years, there are still around 70 SIDS deaths each year in Australia.

This study highlights the importance of public education of the risks of maternal smoking to infants.

The results of this study "Maternal Smoking Impairs Arousal Patterns in Sleeping Infants" were published in *SLEEP*, Vol. 32(4), 515-521, 2009

MIMR Researcher WOWs International Organisation

Drs Caroline Gargett and Dharani Hapangama

Dr Caroline Gargett, from the Centre for Women's Health Research, is one of a team to be awarded the prestigious Wellbeing of Women (WOW) award with her international collaborators.

The team, led by Dr Dharani Hapangama from Liverpool University, comprises Dr Caroline Gargett from MIMR, Professor Philip S Rudland and Dr Siobhan Quenby from Liverpool University, Dr Gabriele Saretzki and Professor Thomas von Zglinicki from Newcastle University, are studying the role of cell fate regulators of endometrial stem cells in developing endometriosis, with the view to developing potential therapeutics.

Dr Gargett gained international recognition for her research identifying two types of stem cells in the endometrium or lining of the uterus. She was also the first person to isolate these cells for use in research into common gynaecological disorders such as endometriosis and pelvic floor prolapse.

Endometriosis is a common and painful condition affecting 10% of young women of reproductive age. It can cause severe abdominal and back pain and fertility issues.

Endometriosis occurs when endometrial cells are found outside uterus in the abdominal cavity. These cells can form lesions on tissue or organs and continue to grow causing severe pain.

Currently there is little known about why women develop endometriosis and its progression. This has hampered the development of effective diagnostics and therapeutic treatments. Diagnosis of endometriosis requires invasive techniques and current treatment options are inadequate providing only temporary relief of symptoms

The WOW award will enable Dr Gargett and her team of collaborators to conduct research which may provide new insights into the mechanisms involved in normal growth of endometrium in healthy women compared to the abnormal endometrial growth associated with endometriosis.

This research may also provide new markers for the development of non-invasive tests for diagnosing endometriosis and new targets to develop more effective treatments which will bring relief to the large number of women who suffer with endometriosis.

In April Dr Dharani Hapangama visited MIMR from Liverpool University to work with Dr Gargett to establish this important project at the Institute. She will return to MIMR again later in 2009.

MIMR - the Place to Be

Increasing numbers of overseas researchers and students are coming to MIMR to gain experience in our laboratories.

In recent months we have welcomed two international visitors to the Institute; Dr Reidun Aesoey is visiting the Centre for Urological Research (CURe) and Damien Bertheloot is visiting the Centre for Cancer Research (CCR).

Reidun completed her PhD studies in Norway before joining the Karolinska Institute in Stockholm, Sweden. She joins MIMR as part of the Endocrine Society's International Endocrine Scholars Program which matches exceptional researchers to laboratories outside their home country. It aims to foster the talents of young endocrinologists and develop them as future leaders in their field.

Reidun has joined CURe to work as a postdoctoral researcher for two years with Professor Gail Risbridger in prostate cancer research.

As part of her research, Reidun is examining the mechanisms involved in the development of androgen-resistant prostate cancer, with the aim of developing new treatments for the disease.

"I chose to come to MIMR for this postdoctoral position due to the exciting research that is being undertaken by Professor Gail Risbridger's group and because of their excellent international reputation" said Reidun.

"It's a great opportunity for me to evolve as a researcher and will help for me to establish my own research group when I return home"

The Endocrine Society's International Endocrine Scholars Program provides benefits to both the scholar and the Institute.

"By developing the researcher's career, we create the potential for future international collaborations with them and their research institutes" said Professor Risbridger.

Reidun Aesoey and Damien Bertheloot

In March, Damien Bertheloot from the Montpellier University of Science in Montpellier, France joined CCR for six months to work in Professor Bryan Williams's lab as part of his Masters of Biotechnology - Cell Engineering course.

He is working on a project that is defining the role of the protein MDA5 in type 1 diabetes.

Damien applied to come to MIMR because he was interested in gaining experience outside of France in biotechnology, to improve his English and to increase his knowledge and research experience.

"This traineeship will be a real benefit for my professional future. It is important for me to learn biology and more specifically biotechnologies from a medical applications perspective" said Damien.

Ten Years of DNA Sequencing

This year marks the tenth anniversary of the establishment of the DNA Sequencing Centre within the Monash Health Research Precinct (MHRP). The MHRP incorporates MIMR, Prince Henry's Institute (PHI) and the Monash Medical Centre.

In 1999, with a grant from the Wellcome Trust, combined with funding from both MIMR and PHI, the Wellcome Trust Sequencing Centre was established. The Centre was the first of its kind for the Precinct. Complementary genomic services including mutation detection and gene expression have since been introduced.

In 2006, the Centre received a generous grant from the Gandel Charitable Trust to purchase a new Genetic Analyzer. The centre was renamed the Gandel Charitable Trust Sequencing Centre in recognition of this gift.

The Sequencing Centre provides researchers with an essential tool for determining the exact order of the three billion bases that make up the genes in the 24 chromosomes in the human genome. This process is crucial to understanding conditions such as male infertility, cancer, diabetes and inflammation.

Demand for DNA Sequencing for medical research and clinical diagnosis continues to grow and in 2008 the Collier Charitable Trust generously provided funding to the Centre enabling the purchase of a second 16 capillary Genetic Analyzer.

"The MHRP is committed to fostering the translation of basic research knowledge into clinical practice resulting in improved patient outcomes. Sharing technologies such as DNA Sequencing will facilitate collaboration between the clinical and research areas of the Precinct, a key to achieving this aim" said Vivien Vasic, Gandel Charitable Trust Sequencing Centre Manager.


Dr Mandar Joshi

Mandar Joshi – the Victor Y-H Yu Fellow

Postdoctoral Fellow, Dr Mandar Joshi, is the inaugural recipient of the Victor Y-H Yu Fellowship.

The Victor Y-H Yu Fellowship was established through a substantial personal gift from Professor Victor Yu who identified the need for financial support to promote research in perinatal medicine and science.

Professor Yu hopes that by providing this scholarship opportunity he can encourage high calibre researchers and clinicians to conduct research into conditions affecting infants.

Dr Mandar Joshi joined the Ritchie Centre for Baby health Research in March, coming from Columbus Ohio in the United States. He has spent the past three years working as a postdoctoral scientist at the Nationwide Children's Hospital in Ohio studying the cardiovascular and pulmonary system of preterm infants.

"It's an honour to be appointed as the first Victor Y-H Yu Fellow. Victor is an amazing man who has had such an incredible career both clinically and in research," said Mandar.

Mandar's research is focused on understanding the inflammatory mechanisms associated with cardiovascular and pulmonary disease in infants and children. These conditions affect thousands of infants in Australia each year.

Complications of the heart and lungs are the leading causes of death in infants and children. Many children with these complications in their childhood will develop severe cardiovascular diseases in adulthood. Mandar hopes that by developing an understanding of cardiovascular disease, it will assist with the development of therapies specifically for neonates, infants and children who are affected.

"The Fellowship has given me the chance to work not only on basic laboratory research but also clinical research, which is extremely exciting."

"This project provides the opportunity to work in close collaboration with clinicians at Monash Newborn at the Monash Medical Centre on research that could translate to clinical therapies in the near future," said Dr Joshi

Professor Victor Y-H Yu AM

Over his 30-year career, Professor Victor Y-H Yu AM contributed immeasurably to the increased survival rate of preterm infants in Australia and around the world. His pioneering contributions in this field have resulted in the introduction and establishment of neonatal intensive care units as standard hospital practice in Australia.

Former Clinical Director of the Ritchie Centre, Professor Yu AM (MBBS, MSx (Oxon) MD, FRACP, FRCP (Lond, Edin, Glasg) FRCPSH, DCH, GradDipCS) did his clinical and research training in neonatology at Oxford University and McMaster University before his appointment as Director of Neonatal Intensive Care at Monash Medical Centre in 1976. He went on to become Professor of Neonatology in 1996 at Monash University.

Throughout his career, Professor Yu placed great importance on fostering the talents of young clinicians and scientists. He was supervisor for postgraduate neonatal training to more than 200 overseas paediatricians from 41 countries.

Upon retiring in January 2008, Professor Yu became an Honourary Research Fellow at the Monash Institute of Medical Research and the Victor Y-H Yu Research Fellowship was established.


Professor Victor Y-H Yu AM

Ectopic Pregnancy

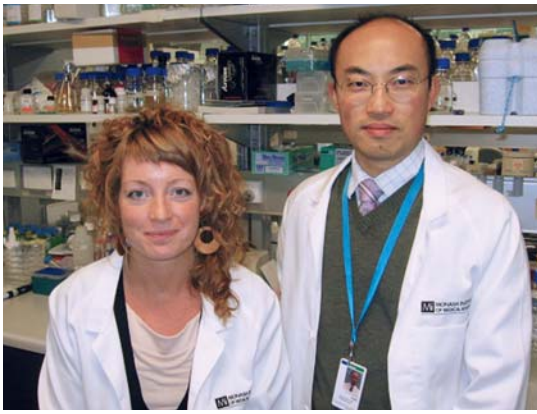
MIMR researchers, Drs Stephen Tong and Ulrika Nilsson, are investigating the potential to develop a non-surgical medical treatment for ectopic pregnancies.

Ectopic pregnancies are conceptions that implant in the fallopian tube. They can erode blood vessels causing catastrophic bleeding. While prompt management makes deaths rare in the developed world, fatalities still occur as evidenced by a tragic case that occurred this year in country Victoria.

Approximately 2% of all pregnancies are ectopic, which in Victoria equates to around 1,500 cases each year. Ectopic pregnancies are a life-threatening condition that place a significant burden on the health system.

Currently, most are treated with surgery where commonly, the entire fallopian tube is also removed. This new research project is investigating the possibility of developing a medical treatment that blocks a vital pathway essential to placenta health – epidermal growth factor. Blocking this pathway should cause death of placental tissue, arresting ectopic tissue growth.

The translation of these research findings to clinical application would revolutionise the treatment of ectopic pregnancies. Since some



Dr Ulrika Nilsson and Dr Stephen Tong

epidermal growth factor inhibitors can be taken orally – and are already used for cancer treatment- the exciting possibility exists of replacing invasive surgery with a tablet.

This research has been funded by the Helen MacPherson Smith Trust and Monash University Faculty of Medicine, Nursing and Health Sciences.

MIMR Alumna Wins US Award

Dr Denise Goldman

MIMR Alumna Dr Denise Goldman has received the US Endocrine Society First Author Student Award for her publication "Evidence that Androgens Regulate Early Developmental Events, Prior to Sexual Differentiation" (*Endocrinology* 149: 5-14, 2008).

Denise completed her PhD studies at MIMR in 2006, under the supervision of Dr John Morrison and Emeritus Professor David de Kretser AC. Her PhD project was entitled "A potential role for androgens in mouse embryogenesis"

Androgens are known to play a vital role in normal fetal development. However, prior to Denise's research, there was little understanding about how androgens affected the formation and development of the early embryo.

Research has shown that mice with targeted disruption of androgen receptors developed cardiac abnormalities in adulthood. Denise's PhD studies examined the influence of androgens on the differentiation of cardiac cells. Her research showed that androgens enhance differentiation of mouse embryonic stem (mES) cells to cardiomyocytes, or contracting cardiac cells, and that the mES cells are capable of androgen production.

The publication in *Endocrinology* was the culmination of her PhD research which identified the unique action of androgens at the earliest stages of embryonic development. The paper shows that androgens not only affect in vitro differentiation but are also in fact secreted from ES cells.

Since completing her PhD, Denise has spent time doing postdoctoral research into neural stem cell biology at the National Institute for Medical Research in the UK. She is now working in business development for biomedical research at the Royal National Institute for Deaf People in the UK.

Contact us:

Monash Institute of Medical Research
Monash Medical Centre,
246 Clayton Road, Clayton,
Victoria 3168, Australia

www.monashinstitute.org

Freecall: 1800 424 055
Telephone: 03 9594 7109
Facsimile: 03 9594 7114
Donation hotline: 1800 424 055
Email: moreinfo@med.monash.edu.au