

## Award-winning research gives hope to children of uncertain sex

Professor Peter Koopman, from the Institute for Molecular Bioscience (IMB) at The University of Queensland, has been awarded the GlaxoSmithKline Australia Award for Research Excellence for his pioneering research that offers hope to children born with sexually ambiguous genitalia and other sexual development conditions.

"It is usually the first question new parents are asked – is it a boy or a girl? But when it is not possible to determine a baby's sex it is upsetting for families and raises questions about whether to assign a gender immediately or wait until a child gets older," Professor Koopman said.

"These conditions are common, almost always traumatic for the families involved and require significant healthcare resources through corrective surgery, hormone therapy, psychological support and other related treatments."

Professor Koopman is the second IMB researcher to receive the prestigious Award in the last three years, following Professor Melissa Little's win in 2005 for her work on renal disease.

Following his discovery of SRY, a gene which sets an embryo down the pathway of male development, Professor Koopman has made a number of discoveries relating to how we become male or female, which have implications for intersex conditions as well as testicular cancer.

"My work is essentially a study of how testes or ovaries develop in the embryo. The genetic controls that underpin development are complex and the pathway often breaks down, which can result in a broad spectrum of intersex conditions including a child of uncertain sex," Professor Koopman said.

Identifying the genes involved in this process and understanding how they work is the first step in understanding what happens when the process breaks down.

Tony Briffa, of the Melbourne-based Androgen Insensitivity Syndrome (AIS) Support Group Australia, and Genetic Support Network of Victoria commented on the award.

"The AIS Support Group Australia congratulates Professor Peter Koopman on his award, and encourages more researchers to consider the human aspects of genetic conditions," Mr Briffa said.

"Intersex conditions result in considerable difficulties for families and are more common than most people think. Sexual identity issues, sexual dysfunction, infertility, body image, cancer, osteoporosis and social difficulties are all likely consequences.

"This research increases our understanding of sexual development and has the potential to improve outcomes for people with these conditions."

Professor Koopman discovered that sex determination in mammals hinges on the action of Y-chromosomal gene, SRY, by adding the gene to mice with an XX genome, which would normally develop as female. The resulting mice were born male.

This experiment also showed that SRY does not act alone, but rather initiates a cascade of genetic steps that leads to the formation of the testes. This led to the discovery of another gene, Sox9, which acts downstream from SRY in the sex-determining pathway. Unlike SRY, which is found only in mammals, Sox9 is likely to be the universal regulator of male sex determination in all animals that have a backbone or spine.

Recently Professor Koopman has been working to understand the complex developmental networks within the gonads that tell cells whether to become sperm or eggs. It is believed that these signals going awry may be a trigger for testicular cancer.

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Professor Koopman with the GlaxoSmithKline Award for Research Excellence.  
Photo courtesy of GlaxoSmithKline.

# Graduate to Group Leader

Professor Brandon Wainwright, IMB Director, takes great pleasure in announcing the appointment of Dr Matt Sweet to the position of IMB Group Leader.

Group Leaders are the senior scientists of the IMB, who head the laboratories and are responsible for directing and overseeing all of the research that takes place among their group.

"Dr Sweet is a classic IMB success story," Professor Wainwright said. "He undertook his PhD at the IMB's precursor, the Centre for Molecular and Cellular Biology, and after working overseas, has returned to rise through the ranks and become a Group Leader."

Dr Sweet, who was previously a Senior Research Officer in Professor David Hume's group, was appointed Group Leader after Professor Hume left the IMB to run a new research centre in Scotland, as reported in the last issue of Output.

Dr Sweet's group primarily focuses on how innate immune cells detect invading pathogens and the impact of innate immune cell activation on both acute and chronic inflammation.

Innate immune cells, such as macrophages, are able to detect distinct components of invading pathogens to trigger the most appropriate immune response. This includes both the containment of the infectious agent, as well as the activation of an "antigen-specific" immune response to destroy the pathogen.

"Such processes underlie the basis of resistance and susceptibility to infectious disease, and for this reason have obvious importance to human health," Dr Sweet said.

Whilst innate immune cell activation is required for effective control of infectious disease, inappropriate activation of these cells is responsible for the development and severity of both acute inflammatory diseases (e.g. septic shock) and chronic inflammatory diseases (e.g. Rheumatoid Arthritis, asthma).

Most anti-inflammatory agents have significant side effects associated with them or are ineffective in many chronic disease states. There is therefore a need to develop alternative approaches to treat inflammatory disease. To do so, Dr Sweet and his team are characterizing the molecular pathways by which innate immune cells drive inflammation.

"The dual strengths of chemistry and biology at the IMB will hopefully enable both the identification of such pathways as well as the development of novel therapeutic agents to treat inflammatory disease," Dr Sweet said.



Dr Matt Sweet

# IMB researcher honoured with leading fellowship

IMB researcher Professor Peter Koopman has received one of Australia's most prestigious fellowships, being named an Australian Research Council (ARC) Federation Fellow.

Professor Koopman was recognised at a ceremony at Parliament House in Canberra on the 22nd of May, along with the other 19 Fellows named.

Federation Fellows are considered to be world leaders in their chosen fields of research, and the program is aimed at attracting some of the world's best research talent to Australia, as well as offering opportunities for top Australian researchers to continue their work here.

Professor Koopman said his research was looking to develop and use new and vastly more efficient ways of identifying which of our 30 000 genes are important for embryonic development.

"What we are trying to do is reveal their specific function and identify control mechanisms that can go awry to cause birth defects," he said.

His research will suggest new ways to diagnose and deal with these conditions, and will be applicable to: stem cell technologies, tissue regeneration, cancer biology, conservation, pest management and livestock breeding.

Professor Koopman is world-renowned in the field of developmental biology, and was part of the team that discovered the gene that determines gender in mammals, which has been called one of the most important biological discoveries of the 20th century.

Professor Koopman was one of three 2007 Federation Fellows from Queensland, all from The University of Queensland. The others were Professor Gerard Milburn (quantum physics) and Professor John Quiggan (economic risk modelling), both of whom were awarded second Federation Fellowships.

Professor Koopman joins Professors John Mattick and David Fairlie as current IMB Federation Fellows. IMB joint appointees Professors Kevin Burrage and Alan Mark, and affiliate Dr Bostjan Kobe, are also Federation Fellows.



Professor Peter Koopman is congratulated by the Hon. Julie Bishop, Minister for Education, Science and Training.

# Prestigious international grant to researcher

An IMB researcher has received a \$408 800 grant from the prestigious international Human Frontier Science Program (HFSP).

Professor Rob Parton will share the grant with international collaborators in France and India.

The HFSP supports international collaborations in basic research focused on the complex mechanisms of living organisms. Particular emphasis is placed on bringing scientists from a range of fields, such as physics, chemistry, mathematics, computer science, bioinformatics, nanoscience and engineering, together with biologists.

Australia is a member of HFSP through the National Health and Medical Research Council (NHMRC).

Announcing the results of the latest HFSP round, National Health and Medical Research Council CEO Professor Warwick Anderson said that the awards provide valuable opportunities for Australian researchers to work in multidisciplinary teams at the international forefront of research.

"Our researchers are among the best in the world and the HFSP awards mean that they get the chance to further their work through international collaborations," Professor Anderson said.

The program supports cutting-edge life sciences research and involves more than 30 countries worldwide.

Professor Parton was awarded his grant to study endocytosis to better understand how healthy cells work and what goes wrong in disease conditions.

Endocytosis describes the process whereby animal cells are constantly sampling their environment and engulfing parts of their surface membrane.

This is essential for cells to take up nutrients, to respond to signals in the outside world, and for cell movement. Endocytosis is also used by pathogens, such as viruses, as a way to enter cells.

"We have discovered an unusual endocytic route into the cell which is driven by lipids," Professor Parton said.

"This lipid-driven endocytosis will be explored using a truly interdisciplinary approach at the interface between theoretical physics and experimental sciences (physics, biology and chemistry)."

The team will combine theoretical models for lipid-driven membrane deformation with experiments to study lipids in artificial membranes.

The insights from these studies will be complemented by parallel studies of the endocytic pathways in animal cells using state-of-the-art microscopic techniques.

"This unique program of research will lead to a new level of understanding of the intricate workings of the cell, the fundamental unit of life," Professor Parton said.



## Renal research boosted with \$1 million grant

An attempt to stem the rising tide of renal disease among Australians has earned an IMB researcher a \$1 million Queensland State Government Project Innovation Funds grant.

Professor Melissa Little will use the grant to develop cell-based regenerative therapies for chronic kidney disease, a condition that costs Australia \$1.8 billion per year.

The project will investigate ways in which damaged kidneys could repair and regenerate themselves, and the triggers needed to begin this process.

While treatments for chronic kidney disease do exist, namely dialysis and transplantation, both have drawbacks.

Dialysis limits the quality of life for patients, is very expensive, and has limited effect. While transplantation is far more effective, only one in four patients will be lucky enough to receive a donated kidney.

With the incidence of renal disease increasing by eight per cent a year in Australia, these current treatments will not cope with the rate of increase in patient numbers.

It is predicted that 600,000 Australians are at risk of chronic kidney disease as a result of smoking, obesity, hypertension, age, or Aboriginal or Torres Strait Islander heritage.

This is especially a problem in Queensland, because of the State's relatively large aboriginal population – the rate of chronic kidney disease in the Aboriginal and Torres Strait Islander population is 13 times that of the Caucasian population.

Clearly, more effective treatments that can be accessed by a higher number of patients are needed, something Professor Little recognised several years ago. She had been working on kidneys "one way or another" for all of her career, but it was only relatively recently that she made a conscious decision to work towards the development of therapies for kidney disease.

"About five or six years ago I was looking at my career and querying whether my research on kidney development was of value to society," Professor Little said. "I realised that the developmental processes I was discovering would allow us to understand renal disease and potential regeneration."

Since then, she has been an active advocate for the development of novel therapies, founding the Renal Regeneration Consortium, a multidisciplinary partnership between researchers in Queensland and Victoria.

She also established Nephrogenix Pty Ltd, a company that commercialises the research outcomes of the Renal Regeneration Consortium. No existing group, nationally or internationally, has developed such a comprehensive program in the development of regenerative medicine strategies for renal disease.

Professor Little's expertise has also recently been recognised with her appointment to the position of Chief Scientific Officer of the Australian Stem Cell Centre. For more details, please see story below.



## IMB researcher to direct Australian stem cell science

An IMB researcher has been appointed to the position of Chief Scientific Officer of the Australian Stem Cell Centre (ASCC).

Professor Melissa Little will be seconded to the ASCC until mid-2011 from her current position at the IMB, where she leads a team of researchers investigating the potential of stem cells in treating chronic kidney disease.

Professor Little will continue running her research program at IMB as she takes on her new role heading the scientific program at the ASCC, developing strategy, scientific review and management.

Another major part of her role will involve consolidating the Brisbane-based groups funded by the ASCC to form a Brisbane node, which will be run out of The University of Queensland's Australian Institute for Bioengineering and Nanotechnology (AIBN).

The ASCC funds stem cell researchers from around Australia, with two major geographical groups in Melbourne, where the Centre is headquartered, and Brisbane.

"We aim to provide this rapidly developing Brisbane group with more resources, specific support services and direction, all leading towards more cohesive national research results," Professor Little said.

"We are also looking to develop synergy across the entire scientific program of the ASCC, engaging all of our researchers, no matter where they are based, enabling the long-term vision of the Centre and capitalising on the national and local geographical advantages these growing groups offer.

"Australians have high expectations of stem cell research. We need to be both clever and resourceful in all areas of science management to ensure results that can be delivered as soon as possible and are of the highest quality."

UQ's Deputy Vice-Chancellor (Research), Professor David Siddle, congratulated Professor Little on her appointment.

"It is testament to the high regard in which Professor Little is deservedly held that she has been chosen to direct the scientific future of the Australian Stem Cell Centre," Professor Siddle said.

"Stem cell research has the potential to yield treatments for many diseases that afflict the Australian population. Formation of a Brisbane node will enhance the capacity of all Brisbane-based stem cell research groups, allowing them to achieve their goals more rapidly."

"This will be particularly beneficial for UQ, as it will strengthen the ties between UQ's flagship bio-research institutes and other UQ research groups, all of which are currently conducting remarkable research into stem cells."

Professor Siddle said examples of this research included Professor Little's own work on chronic kidney disease, research by Professor Julie Campbell from the AIBN into using stem cells to bioengineer blood vessels for transplantation, and Dr Rod Rietze's research on brain stem cells at the Queensland Brain Institute (QBI).

For more details on Professor Little's research into chronic kidney disease, please see above story "Renal research boosted with \$1 million grant."



## Using yeast in the fight against viral infection

An IMB researcher is studying yeast with hopes of finding better ways of preventing viruses.

Dr Alan Munn said that currently there were no treatments for viruses in the way antibiotics could be used to treat bacterial infections.

"When we get a bacterial infection, such as strep throat, our doctor will prescribe us with an antibiotic and we quickly get better," Dr Munn said.

"Antibiotics work because they effectively kill many different types of bacteria without harming the cells in our body. When we get a viral infection like influenza it's a different story."

Dr Munn said viruses can enter our cells and hide, making it difficult to develop a treatment that would kill them without also killing the cells that harbour them.

"One way around this would be to perturb the ability of cells to harbour viruses, but we would need to do this without harming the cells themselves," he said.

"Unfortunately, viruses use many types of cellular machinery that are essential for life, including those involved in making molecules such as DNA and proteins."

A recent advance is the discovery of a new class of cellular machinery called ESCRT (pronounced "escort"), which is used by many different viruses to infect cells.

"Viruses now known to use ESCRT include those that cause AIDS, Ebola, glandular fever, herpes, respiratory infections and hepatitis," Dr Munn said.

"The exciting thing about this discovery is that some cells can survive without key ESCRT components. In theory, this means that a drug targeting ESCRT could prevent viruses from entering cells without harming the cells."

"The research in my laboratory at the IMB uses yeast in the aim of discovering ways of targeting ESCRT so that it cannot be used by viruses but can still perform its normal cellular roles."

"We use yeast because it is easy to study and many molecular processes have been conserved between yeast and humans."

Dr Munn (*pictured below*), who was recently involved in organising the 23rd International Conference on Yeast Genetics and Molecular Biology, said that any drug that could result from his and others' work would be many years away.



## In Brief

Professor Mark Ragan (pictured below) has been elected to the Bioinformatics Australia Management Committee. Professor Ragan will serve from 2007-2009, and is the second IMB researcher serving on the committee. Dr Rohan Teasdale was elected to the inaugural committee, and is serving from 2005-2008.



Two IMB staff members have received 2008 Churchill Fellowships. Angela Gardner, Finance Manager, and Dr Jeremy Barker, CEO of the Queensland Facility for Advanced Bioinformatics, won the Fellowships from the Winston Churchill Memorial Trust.

The fellowships provide financial support for the Fellow to travel overseas and gain experience in their area of expertise that could not be gotten in Australia.

Ms Gardner will travel to the United States of America and the United Kingdom to study the establishment of collaborative print/poetry small press for emerging practitioners, while Dr Barker (pictured below) will also travel to the USA and UK, to study bioinformatics.



The KOALA Child Obesity Program (reported in IMB Output 8) has begun recruiting for participants.

The study requires children aged between 6 and 10 who are ready to improve their health and fitness and who are overweight or at risk of obesity.

For more information please visit the KOALA website on <http://koala.imb.uq.edu.au/Koala/> or contact the Project Coordinator Denise Mitchell on: 07 3840 2757 or email [denise.mitchell@mater.org.au](mailto:denise.mitchell@mater.org.au)

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Mr Paul Lirette, Managing Director, GlaxoSmithKline Australia, said the company is committed to supporting innovation, research and development for the wellbeing and economic benefit of all Australians.

"The GlaxoSmithKline Award for Research Excellence is awarded annually in recognition of distinguished discoveries in scientific and medical research which have the potential to lead to significant benefits in human health," Mr Lirette said.

"Professor Koopman is a deserving winner of the award as his pioneering work has the potential to improve human health in a number of important areas including sexual development, fertility and oncology," said Mr Lirette.

Future challenges for Professor Koopman and his team include searching for other genes important for male sex determination and testis development and learning more about the development of the ovaries.

"We aim to find genes and to deduce how and where they fit into the regulatory network. Ovarian development has remained mysterious despite big advances in the study of other tissues. We aim to shed light on the genes that regulate the early development of the ovary too."

Although Professor Koopman was honoured to receive the Award, he said it was other factors that spurred on his research efforts.

"A major motivator for me is to be involved in work that makes a real difference to people's lives. Research is a painstaking process but the belief that my work will benefit people is what keeps me so passionate about it. It is an honour that these efforts are to be acknowledged by way of such a prestigious award."

Recipients of the GlaxoSmithKline Award for Research Excellence receive an honorarium of \$50,000 to acknowledge their discovery and contribution to science and help further their work. The Award is regarded as one of the most prestigious within the Australian research community. A requirement of the Award is that the majority of the research is undertaken in Australia.



## IMB Graduates

Twelve IMB PhD students graduated on Friday July 20 at The University of Queensland mid-year graduations.

"Completing a PhD takes persistence, passion and dedication, and we are very proud of all of our students who graduated this semester," IMB Director, Professor Brandon Wainwright, said.

"Although their theses covered a wide range of topics in the molecular biosciences, what each of our graduates had in common was the high quality of their research.

"We would like to congratulate all of them on their achievement."

IMB Graduates and their thesis titles for Semester One, 2007 are:

Daniel Barry - Structural and dynamic studies of the cyclotides and their precursors

Myrna Constantin - Transcriptional Regulation of the c-fms promoter by the ETS family of transcription factors

Melissa Davis - Defining the Membrane Organisation of Eukaryotic Proteins

Tamarind Hamwood - The Structural Basis for Interaction Between Colony-Stimulating Factor-1 and its receptor, CSF-1R

Falak Helwani - Cortactin regulates actin cytoskeletal dynamics at E-cadherin adhesive contacts

Lita Imperial - Novel Peptides from *Conus planorbis*, *Terebra subulata* and *Hastula hectica*

Shannon Joseph - The Exocytic and Endocytic Trafficking of E-cadherin in Epithelial Cells

Erica Lovelace - The Structure, Activity and Engineering of Two Disulfide-Bonded Conotoxins

Jyotsna Pippal - Understanding the Role of PPAR-alpha in the Regulation of Lipid and Carbohydrate Metabolism in Skeletal Muscle Cells

Ranjala Ratnayake - Chemistry and Bioactivity Studies of Australian Microorganisms

Ivana Saska - Biosynthesis of Circular Proteins in Plants

Andy Wu - In vitro and in vivo characterisation of cellular responses to PHPV and Hydroxyapatite/PHBV composites as bone biomaterials

Pictured right (top to bottom): Dr Manuel Plan, Dr Shannon Joseph, Dr Tamarind Hamwood.

