IMB annual report 2011

DISCOVER ◆ INVENT ◆ CURE

THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

INSTITUTE FOR
MOLECULAR BIOSCIENCE

DISCOVER ◆ INVENT ◆ CURE

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Clare Smith, Lucid Photography (pgs 1,2 9-11, 14-19, 22-25, 28-32, 37, 40)
Chris Stacey (pgs 5, 33, 34)
Justine Walpole (pg 34)

COVER IMAGE

Joannah Underhill:
Molecular Regeneration
(76 x 76cm,
ink, acrylic & oil on canvas)

Molecular Regeneration *is a visual representation of the potential that all cells have for regeneration. It is inspired by the artist's ongoing exploration and observation of molecular and sub-cellular processes through microscopic images.*

We thank the following major supporters for their generosity in 2011:

Australian Government
National Health and Medical Research Council
NHMRC

Australian Government
Australian Research Council

Queensland Government

Australian Cancer Research Foundation

Cancer Council Queensland

JAMES S. MCDONNELL FOUNDATION

DR. ROSAMOND SIEMON

MR AND MRS GOLDING

THE SIMON AXELSEN MEMORIAL FUND

The ATLANTIC Philanthropies

wellcome trust

IMB annual report 2011 contents

director's report

The IMB had another excellent year in 2011, despite several challenges. UQ was affected during the January floods that covered much of Queensland, though the IMB was not directly affected by flood damage. Despite this, integral services were lost and staff and students were unable to use the facilities for several days. Many of our employees volunteered to provide food, money and support to stranded overseas students and IMB operational staff ensured that essential materials and data were not lost, despite long periods of power outage. A special mention must go to John Ford, Maintenance Manager (Institutes), who slept in the building to ensure our vital research was safe and secure.

A different challenge came in April, when the scientific community was warned by credible sources that the National Health and Medical Research Council (NHMRC), which provides the bulk of funding for medical research in Australia, was facing large cuts in the upcoming federal budget. Researchers participated in a nationwide campaign to raise public awareness of the importance of medical research to Australia, including health and economic benefits. IMB staff and students helped organise a rally in Brisbane, which was attended by over 1000 people and attracted good media coverage. After several weeks of a sustained campaign, the cuts were not included in the budget, but the threat emphasised the need for institutes to seek varied sources of funding.

In response to this, the IMB appointed a new Deputy Director (Advancement), Ms Amanda Whelan, to prepare the Institute for a multi-million-dollar five-year campaign in co-ordination with UQ. Ms Whelan has a wealth of experience in public administration and campaign management; I am confident she will further the Institute's strategic relationships and create new avenues of funding and support for the critical research performed at the IMB. Already as part of our new communications and marketing plan, IMB has adopted a logo and slogan, DISCOVER INVENT CURE, both unveiled in this publication.

The year ended on a positive note, with excellent results in the Australian Research Council (ARC) and NHMRC grant rounds. IMB achieved a 50% success rate for ARC grants, compared to a national average of 21.95%, and received a quarter of the funding awarded to UQ by the NHMRC in the October grant round, including five of the seven Research Fellowships received by the University. The Institute also contributed to UQ being ranked the top Australian university in life sciences, and 26th in the world, in the 2011 Times Higher Education discipline rankings.

Engagement with industry is another measure of our success in performing cutting-edge science. 2011 was a good year in these terms. In June we announced our expanding collaboration with Pfizer, the world's largest biopharmaceutical company, to develop new peptide-based medicines for the treatment of major diseases and in November we hosted the Industry Affiliates Program with over a hundred external attendees including scientists from Pfizer, Genentech and Novartis. We are seeking to expand industry engagement in 2012 and look forward to initiating new collaborations.

I thank the advisers, supporters, staff and students of the Institute for their hard work over 2011. It has certainly paid off this year, and will continue to do so in the future.

Professor Brandon Wainwright
IMB Director

institute profile

THE UNIVERSITY OF QUEENSLAND'S IMB

is committed to improving quality of life for all by pursuing discoveries through fundamental research, inventing sustainable technologies, and advancing cures for cancer, pain and infectious disease.

2011 BY THE NUMBERS:

- AUD $70 million annual budget
- $220 million annual economic impact on QLD community
- 95% of budget spent on research and support
- 44% of 2011 budget from NHMRC & ARC competitive grants
- 34 Laboratory Heads (Faculty), 22 supported by external research fellowships
- 155 current PhD & Honours students, 319 former PhD students
- 150 postdoctoral researchers
- 41 countries represented by IMB Faculty, staff and students
- 6000 visitors to IMB in 2011

1 **Professor Mark Ragan**
Head, Genomics and Computational Biology Division

2 **Professor David Fairlie**
Head, Chemistry and Structural Biology Division

3 **Professor Jennifer Stow**
Deputy Director (Research)

4 **Professor Brandon Wainwright**
Director

5 **Professor Peter Koopman**
Head, Molecular Genetics and Development Division

6 **Professor Alpha Yap**
Head, Molecular Cell Biology Division

7 **Amanda Whelan**
Deputy Director (Advancement)

8 **Dr Ian Taylor**
Deputy Director (Operations)

the year IN REVIEW

(L-R) Professor Matt Cooper (see May story), Dr Tim Mercer (see August story) and Professor Jenny Martin (see first September story).

january

The University of Queensland's St Lucia and Gatton campuses were inundated in flooding that affected much of the State. The IMB was not water-damaged, but staff and students were unable to access the building for five-and-a-half days. Despite the extensive damage to the University, teaching, learning and research resumed within a week of the peak of the flood.

march

Professor Alpha Yap and PhD student **Sabine Mangold** found a new way in which the proteins that adhere cells together to form healthy tissues can come apart. This discovery will open new avenues to understanding how these proteins are disturbed in diseases such as cancer.

Dr Joshua Mylne and **Professor David Craik** discovered how protein ring that can block cancer enzymes is naturally produced in sunflower seeds. Despite its potential, this protein has not been broadly adopted by drug designers because of the expense of producing it using traditional methods, a disadvantage that is overcome if the drug is grown in plant seeds.

april

IMB scientists joined medical researchers from around Australia to protest planned cuts to the National Health and Medical Research Council (NHMRC) budget. IMB personnel teamed with counterparts from the Queensland Institute of Medical Research to organise a rally in the Brisbane CBD, which attracted over 1000 people including members of the public, politicians and researchers. After a sustained campaign, the NHMRC budget received a small increase instead of a large cut.

may

The UK's Wellcome Trust awarded $5 million to **Professor Matt Cooper** (pictured above left) to develop a treatment for drug-resistant bacteria. Professor Cooper, along with collaborators at UQCCR and the Royal Brisbane and Women's Hospital, will use the funding to modify an existing antibiotic into a new drug that weakens the structures in bacteria that cause resistance.

The University of Queensland launched the Q-Index to provide each academic with an individual composite index of research and teaching performance. An awards ceremony was held to honour researchers with high scores. Seven IMB researchers were in the top 25 at the university: **Professors Paul Alewood**, **David Craik**, **David Fairlie**, **Peter Koopman**, **John Mattick**, **Rob Parton** and **Alpha Yap**. Four laboratory heads made the top 10 for research income (**Professors David Craik, David Fairlie**, **Sean Grimmond** and **Jennifer Stow**), while **Professors Craik** and **Mattick** ranked in the top 10 for publication output. **Professor Craik** also reached the top 10 for research higher degree completions.

june

Professors David Fairlie and **David Craik** teamed with Pfizer, the world's largest biopharmaceutical company, to develop new medicines for the treatment of major diseases. They hope to deliver a new generation of orally active therapies for diabetes and cardiovascular disease.

Dr Kelly Smith (Wicking lab) won the Postdoctoral Research Award at the Queensland Health and Medical Research Awards for identifying a new gene in zebrafish, wickham, that causes a heart valve defect. Dr Smith is hopeful studying how wickham helps heart valves develop and how this process can be disrupted will give scientists insights into diagnosing and treating congenital heart disease.

The **EMBL Australia Mirror of EMBL-EBI**, a new national facility housed at IMB, was opened in June. The mirror will provide Australian researchers faster and easier access to richer biological data by mirroring the most-used data services of the European Bioinformatics Institute.

july

Eleven students from IMB graduated at the mid-year University of Queensland graduation ceremonies: Drs Alhadi Bustamam, Joao Fidalgo, Caroline Hendry, Angela Jeanes, Pei Low, Rodrido Morales, Philip Nguyencong, Jonathan Robson, Tom Whitington and MPhil graduates Joo Young Choi and Nurul Mohamed. To read more about Dr Hendry, please turn to page 56.

august

An international research team, spearheaded by **Dr Tim Mercer** (pictured above middle) of IMB, unlocked the blueprints to the 'power plants' of the cell in an effort that will provide clues on treating a range of degenerative diseases. The team mapped the transcriptome, which reveals the genes that are active at particular points in time, of the human mitochondrion, which supplies energy to the body's cells.

september

Professor Jenny Martin (pictured above right) was named a leading female scientist, winning the Biotechnology Outstanding Achievement Award at Queensland's Women in Technology Awards. Professor Martin was recognised for her significant and highly influential research contributions, as well as for playing a leadership role in the scientific community.

A project exploring how to manipulate the development of the lymphatic vascular system to block the spread of cancer cells won a UQ Foundation Research Excellence Award. **Dr Mathias Francois** will use the $90,000 award to develop molecular and pharmacological tools to understand how lymphatic vessels form and spread.

Following the protests in April, the Federal Government announced an independent review on health and medical research in Australia. IMB's **Professor Melissa Little** was chosen for the six-member panel, which will be chaired by the 2011 Australian of the Year, Simon McKeon.

october

Professor John Mattick was part of a team of researchers that discovered a new genetic mechanism behind the extraordinary plasticity of the brain, which underpins our ability to learn, remember and think.

IMB researchers received $13.2 million in fellowships and grants from the National Health and Medical Research Council, accounting for five of the seven fellowships awarded to UQ, including one to **Professor Mike Waters**, who received four grants totalling nearly $2 million.

november

A new method for examining genetic information allowed researchers to delve further than ever before into the human genome and revealed the enormous complexity of gene structure and activity in the body. IMB's **Dr Tim Mercer**, **Dr Marcel Dinger**, **Ms Jo Crawford** and **Professor John Mattick** teamed up with researchers from Harvard University and RocheNimblegen Inc. to develop the method.

Researchers from the IMB received $5.62 million from the Australian Research Council in their major annual funding round. The Institute had a 50% success rate for Discovery projects, compared to a national average of 21.95%.

Later in the month, the Australian Research Council offered over $2.7 million in fellowships to support IMB researchers to investigate heart development, the reproductive system and tiny molecules that could be the key to treating previously incurable diseases.

An exhibition involving two IMB scientists demonstrated the beauty that can be found down the lens and in the lab. The *Incredible Inner Space* exhibition, displayed at Questacon in Canberra, showcased 28 images taken by scientists across Australia, including **Darren Brown** and **Dr Michael Landsberg** of IMB.

december

An IMB team led by **Professor Rob Parton,** which included **Professors Alpha Yap** and **Kirill Alexandrov**, was awarded $7.1 million by the NHMRC to research the changes that occur on the surface of cells in cancer, immunity and muscular dystrophy. **Associate Professor Mark Smythe** was awarded $417,340 to develop new treatments for asthma, a condition that affects over two million Australians.

Eleven IMB PhD students graduated at the end-of-year University of Queensland graduation ceremonies: Drs Muharrem Akcan, Paulo Amaral, Laura Cascales Bolano, Kai-En Chen, Lisa Crowther, Margaret Hardy, Sabine Mangold, Samantha Murphy, Ritesh Raju, Daniel Shaw and Evan Stephens.

international collaboration

IMB researchers have collaborations around the world in the areas of cancer, pain, infection, genetic disease and sustainability.

EUROPE

GERMANY
Universities of Bonn, Munster, Bielefeld, Leipzig, Bruker BioSpin (Rheinstetten) Ludwig-Maximilian University (Munich), Karlsruhe Institute of Technology (Munich), Leibniz Institute for Age Research (Jena), Clondiag (Jena), Hans Knoll Institute (Jena), Max Planck Institute for Experimental Medicine, (Göttingen), University of Freiburg (Freiburg im Breisgau), Goethe University (Frankfurt), Biocentre Wuerzburg, Saarland University (Saarbruecken), University of Lubeck, University Hospital Jena, Cellzome (*UK/Germany*)

UK
Imperial College London, University College London, Queen Mary University of London, Kings College London, Medical Research Council (London), Food & Environment Research Agency (London), Birbeck University (London), Cambridge University, Sanger Centre (Cambridge), Oxford University, MRC Human Genetics Unit (Edinburgh), Edinburgh University, University of Essex, Sheffield University, University of Strathclyde (Glasgow)

SWITZERLAND
University of Basel, University of Geneva Medical School, University Hospital Zurich

FRANCE
University of Paris, VenomeTech (Valbonne), University of Nice, Institut de Génétique Humaine (Montpellier), INSERM (Paris)

SPAIN
Noscira (Madrid), Hospital del Mar Research Institute (Barcelona)

AUSTRIA
Institute of Science and Technology (Vienna), Medical University of Graz

THE NETHERLANDS
Erasmus University (Rotterdam), Utrecht University, Academic Medical Centre (Amsterdam)

DENMARK
University of Copenhagen

RUSSIA
Russian Academy of Science (Moscow)

ASIA

SOUTH KOREA
Hanyang University (Seoul)

JAPAN
University of Kyushu (Fukuoka), National Research Institute for Child Health and Development (Tokyo), Kinki University (Higashi-saka), Kyoto University, Tokyo Medical and Dental University, Nagasaki University

CHINA
Hong Kong University, Institute of Microbiology, Chinese Academy of Sciences (Beijing)

NEW ZEALAND
University of Otago (Dunedin)

SAUDI ARABIA
King Abdullah University of Science and Technology (Thuwal)

SINGAPORE
National University of Singapore, A*STAR

MALAYSIA
Sarawak Biodiversity Centre (Kuching)

NORTH AMERICA

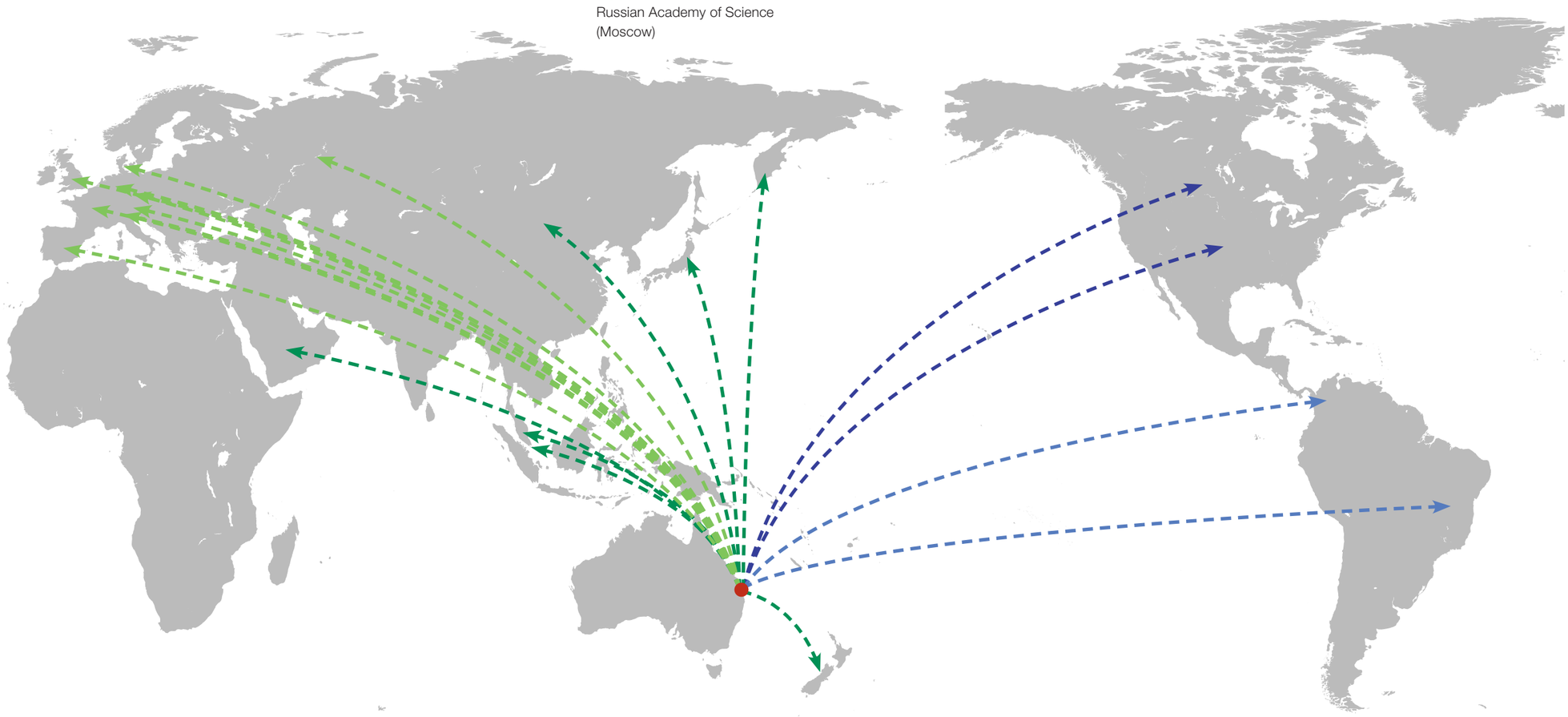
USA
Columbia University (New York), Yale University (New Haven, Connecticut), Harvard University (Cambridge, Massachusetts), Massachusetts Institute of Technology, University of Wisconsin, University of Tennessee (Oak Ridge), Missouri Public Service Commission (Jefferson City) University of Texas Health Science Center at Houston, Case Western Reserve University (Cleveland, Ohio) Florida Atlantic University (Boca Raton), University of Utah (Salt Lake City), University of California San Francisco, University of California Santa Cruz, National Institutes of Health (Bethesda, Maryland), Johns Hopkins University (Baltimore, Maryland), The Hamner Institute for Health Science (Durham, North Carolina), University of Colorado, The Scripps Research Institute (La Jolla, California), Baylor College of Medicine (Houston, Texas), Lewis & Clark College (Portland, Oregon), Iowa State University (Ames), University of North Florida (Jacksonville), Lerner Research Institute (Cleveland, Ohio), Medical College of Wisconsin (Milwaukee), Washington State University (Pullman), University of Minnesota (Minneapolis), University of North Carolina, University of Texas (San Antonio), Texas Tech Uni (Abilene), Pfizer (Groton & Boston, Massachusetts), Alere (San Diego, California), Wayne State University (Detroit, Michigan)

CANADA
University of Western Ontario (London), University of Calgary (Alberta), Laval University (Quebec City)

SOUTH AMERICA

BRAZIL
Centro de Pesquisas René Rachou (Fiocruz)

COLUMBIA
Universidad del Rosario (Bogota)



Artist Joannah Underhill is collaborating with Dr Nick Hamilton (middle) and John Griffin to produce molecular artworks (see report below and on page 40).

DIVISION OF genomics & computational biology

MARK RAGAN
(Division Head)
TIM BAILEY
SEAN GRIMMOND
NICK HAMILTON
JOHN MATTICK
ROHAN TEASDALE

Joint Appointment
PHIL HUGENHOLTZ
Affiliate Appointment
JANE HUNTER

Our researchers study the structure and organisation of genomes, the regulation of genes and the localisation of gene product by application of high-throughput sequencing, imaging, computation and bioinformatics.

All our labs are supported by external competitive funding, including from the National Health and Medical Research Council, Australian Research Council, US National Institutes of Health, Queensland Government and others. Professor John Mattick held an NHMRC Australia Fellowship, and Professor Sean Grimmond an NHMRC Senior Research Fellowship. Professor Ragan's research attracted support from the James S. McDonnell Foundation (USA). John Mattick was named as the new Executive Director of the Garvan Institute, Sydney, and we farewelled John, who will become an IMB Honorary Professor, at the end of 2011.

In June, nearly a hundred stakeholders joined Professors Max Lu (UQ), Nadia Rosenthal and Richard Larkins (EMBL Australia), Dr Ewan Birney (EBI) and Dr Geoff Garrett (Queensland Chief Scientist) in launching the EMBL Australia EBI (European Bioinformatics Institute) Mirror. This facility, together with the National Computational Infrastructure Specialised Facility in Bioinformatics also located at UQ, enables Australian researchers to access very large, complex data, and carry out customised, secure analyses jointly over public EBI and their own data. Next year the Mirror will integrate bioinformatic tools not available at the main EBI site in the UK.

Although ARC funding has ended, the ARC Centre of Excellence in Bioinformatics continues as a partnership among UQ, the University of Newcastle and Macquarie University to coordinate advanced education and training in bioinformatics. We again hosted the annual Winter School in Mathematical and Computational Biology, attracting 306 registrants from 45 institutions across Australia and six overseas countries (4-8 July 2011). For the first time, Bioplatforms Australia and EMBL Australia were supporting partners. We hosted a two-day workshop sponsored by Microsoft Biology Foundation on Libraries for Bioinformatics. In December 2011, UQ approved a new Master of Bioinformatics program to begin in 2012.

Laboratory Heads from our Division were published in several high-ranking international journals in 2011 including *Bioinformatics* (Bailey), *Cell* (Mattick), *Nature* (Mattick), *Nature Biotechnology* (Mattick), *Nature Cell Biology* (Hamilton) and *PLoS Computational Biology* (Ragan). Dr Nick Hamilton's innovative research project with artist Joannah Underhill, whose artwork is featured on the cover of this year's annual report, was also named one of the top ten collaboration with 'pizazz' in the country by *The Australian* (see page 40 for more details.)

Genetic map reveals clues to degenerative disease

An international research team, spearheaded by Dr Tim Mercer of the IMB, has unlocked the blueprints to the 'power plants' of the cell in an effort that will provide clues on treating a range of degenerative diseases.

The scientists, from the Universities of Queensland, Western Australia and Washington (Seattle), mapped the transcriptome of the human mitochondrion, which supplies energy to the body's cells.

Professor John Mattick of the IMB, one of the leaders of the study, said the genome was like a static set of plans for the mitochondria's genetic function, while the transcriptome revealed which genes were active at particular points in time.

"This is the first highly detailed map of the human mitochondrial transcriptome, as well as insights into its control mechanisms, and will provide an important resource for the future study of mitochondrial function and disease," Professor Mattick said.

"By examining which genes are being expressed under various environmental conditions, such as in healthy cells versus infected cells, we can determine the changes in gene activity that may indicate or cause disease."

Mutations in mitochondrial DNA lead to a range of disorders, many of which affect the nervous and muscular systems. The information the team has compiled will provide an improved framework to analyse how genetic mutations in the mitochondria affect gene activity and thus the body itself.

The study was published in leading science journal *Cell*, while the data sets are accessible at the mitochondria-specific genome browser http://mitochondria.matticklab.com.

The work was supported by the Australian Research Council, the National Health and Medical Research Council, the Queensland Government, the Australian Stem Cell Centre and the US National Institutes of Health.

Queensland Centre for Medical Genomics (QCMG)

QCMG was established to lead Australia's contribution to the International Cancer Genome Consortium, which aims to sequence 50 different types and sub-types of cancer. QCMG is sequencing the genomes of 500 pancreatic and ovarian tumours and adjacent normal tissue. In 2011, the Centre completed the first 100 pancreatic tumour/normal pairs, and defined new pathways that escaped detection in previous studies due to the smaller number of samples studied. QCMG has continued to invest in new technology to ensure we maintain our leadership in the next-generation sequencing space with several 5500xl and Ion Torrent PGMs installed in 2011.

Investment has also been made in automated robotics to allow sufficient scaling to process the required number of samples for the ICGC project. QCMG has made tremendous strides in developing, refining and implementing world-class data-processing pipelines making us a clear leader in Australia and an equal to many of the much larger centres worldwide.

The ICGC's ultimate aim is to create comprehensive atlases of the molecular changes arising in human tumours, including changes arising from the genetic code, gene activity and non-genetic factors. QCMG will process 370 matched tumour-normal pancreatic cancer pairs and 130 ovarian cancer tumour-normal pairs for Australia's component of the ICGC project.

mark ragan

COMPUTATIONAL SYSTEMS BIOLOGY

The structure, function and fate of living cells are determined by complex networks of interactions among biomolecules. These networks cannot be observed directly, but must be reverse-engineered from genome-scale data. We develop and apply approaches based on mathematics, statistics, computer science and bioinformatics to infer and analyse these networks from individual samples or patients. We're particularly interested in understanding how networks of gene regulation differ between normal and cancerous states. For this we collaborate with biologists and clinicians in projects on breast, ovarian, pancreatic and prostate cancer. Likewise, the spread of drug resistance and virulence among infectious-disease bacteria can be drawn as a graph and studied mathematically. Using high-performance computers, we identify features of these networks that help us understand and predict properties of cells, organisms and communities.

lab members

Research Officers: Dr Cheong Xin Chan, Dr Melissa Davis, Dr Stefan Maetschke, Chenwei Wang
Queensland Facility for Advanced Bioinformatics Senior Team: Jeremy Barker (CEO), Dr Dominique Gorse (General Manager)
NCI SF Bioinformatics / EMBL Australia EBI Mirror Team: Gavin Graham, Dr David Green (Project Manager), Dr Gerald Hartig, Elham Gharazi
Sabbatical Visitors: A/Prof James Hogan (QUT), Prof Heru Suhartanto (University of Indonesia), Dr Yun Tu (Chongqing University)
Manager, ARC Centre of Excellence in Bioinformatics: Lanna Wong
PhD Students: Piyush Madhamshettiwar, Chang Jin Shin, Elizabeth Skippington
Doctor of Biotechnology Students: Ning Jing, Paul Voigt, Yun Xiao
International Trainees: Pallavi Awasthi (Indian Institute of Science), Chang Liu (Qingdao University), Olivier Poirion (ENSAIA Nancy), Martin Simonsen (Aarhus University)
Undergraduate Research Trainees: Akash Boda, David Derry, Anh Phuong Le (National University of Singapore), Maisarah Mahbob

timothy l. bailey

PATTERN RECOGNITION & MODELLING IN COMPUTATIONAL BIOLOGY

We develop and utilise computational methods to understand biological processes, especially the regulation of gene expression, which shows which genes are active at any point in time. Knowing how gene expression is regulated is essential to understanding cellular processes such as reproduction and metabolism. Currently, we focus on three areas. The first is the regulation of transcription, by which the information in genes is transcribed into a format that can be transported around the cell. This is the initial process through which the information in genes influences physical changes in the body. Secondly, we study the organisation and stability of proteins in the cell nucleus, the control centre of the cell. The third area on which we focus is the formation of triple-stranded DNA. By studying transcription, sub-cellular protein organisation and protein stability, we focus on three key steps in gene expression. Our work on triple-stranded DNA is partly motivated by recent evidence that suggests that these, too, may play a role in gene expression.

In 2011, we continued to collaborate with three groups at UQ to unravel the roles of key regulators of development. This work studied the molecular program controlling the development of three types of cell: red blood cells, neurons and kidney cells. We developed and published a number of computational methods for studying the regulation of transcription, and also published on modeling the import and location of proteins in the cell nucleus. Finally, we continued our study of the possible roles of triple-stranded DNA. We also continued our development of a method for testing triple-helix formation in vitro.

lab members

Research Fellow: Dr Mikael Boden
Research Officers: Dr Chris Leat, Dr Philip Machanick, Dr Kai Willadsen
PhD Students: Tom Whitington, Robert McLeay, Fabian Buske, Ahmed Mehdi
Honours Student: Ralph Patrick
Undergraduate Intern: Gabriel Cuellar
Programmer: James Johnson

sean grimmond

QUEENSLAND CENTRE FOR MEDICAL GENOMICS (QCMG)

The Queensland Centre for Medical Genomics (QCMG) is focused on surveying genomic and gene activity information, as well as how non-genetic factors influence physical traits using next-generation sequencing and microarrays. The combined data sets are then integrated to enable us to define the molecular networks controlling biological processes (such as cell division and specialisation) and disease states (pancreatic, prostate, colorectal, brain, ovarian and breast cancer). This systems-wide approach will provide the means to identify key genes driving specific physical traits and enable us to model the different layers of control guiding biological states.

For more on the QCMG, please see page 8.

We are continuing to survey gene activity in specific biological states using a next-generation sequencing approach (RNAseq) in an effort to put newly discovered gene products into a functional context. We are actively engaged in RNAseq studies to create a human and mouse tissue gene activity atlas, studying gene activity complexity in stem cells and we are surveying gene activity during the cell cycle.

lab members

Executive Officer: Dr Peter Wilson
Executive Secretary: Deborah Gwynne
Senior Bioinformatics Manager: John Pearson
Sequencing Manager: David Miller
Senior Research Officers: Dr Nicole Cloonan, Dr Nic Waddell, Dr Karin Kassahn, Dr Lynn Fink, Dr Sarah Song
Research Officers: Dr Katia Nones, Dr Craig Nourse, Dr Conrad Leonard, Dr Jason Steen, Dr Felicity Newell
Research Assistants: Angelika Christ, Anita Steptoe, Suzanne Manning, Shivangi Wani, Ehsan Nourbakhsh, Ivon Harliwong, Senel Idrisoglu, Scott Wood, Darrin Taylor, Oliver Holmes, Matthew Anderson, Qinying Xu
PhD Students: Mellissa Brown, David Wood, Alan Robertson, Keerthana Krishnan

nick hamilton

MODELLING, VISUALISATION AND CLASSIFICATION OF BIO-IMAGING

Modern scientific methods that allow researchers to rapidly perform millions of tests are leading to massive image sets in need of new methods of analysis. Scientists can now produce 3D time-lapse footage of live cells and organs that shows the interactions and dynamics of multiple proteins at high resolution. The core of my group's research is to develop the methodologies, tools and mathematical models needed to enable the full benefit of these rich advanced new data sources to be realised in areas such as drug and genomic discovery.

As a Strategic Partner of the ARC Centre of Excellence in Bioinformatics, the group leads research on The Visible Cell® project, which provides complete 3D computational models of mammalian cells at a range of resolutions, incorporating data on gene products, molecular interactions, pathways, networks and processes. The goal is to generate an environment in which multiple sources of bio-data can be easily integrated, queried, mathematically modelled and visualised to generate and test biological hypotheses.

The group has two key streams of research in the analysis of multi-dimensional bio-imaging. The first is in developing software to automatically classify, measure and extract key information that describes the biological systems being observed. The second is in building mathematical models of the cellular and organ level systems observed based on the methodologies of the first stream. Recent predictive models include: models of cell proliferation in developing and diseased kidneys; models of fluid dynamics and their relation to structural development in zebrafish blood vessels; and rate models of molecules involved in *Salmonella* infection of cells and drug internalisation. The group is strongly multidisciplinary and collaborative, with a focus on delivering novel methodologies and tools to be used by researchers.

lab members

Research Officers: Dr Daniel Marshall, Oliver Caincross
Co-supervised PhD Students: Mitchell Stanton-Cook, Intan Ruhaiyem
Interns: Hadrien Mary, Franziska Curran
Visiting Researcher: Dr John Belward

john mattick

THE CENTRAL ROLE OF RNA REGULATION IN HUMAN DEVELOPMENT AND COGNITION

It appears that the genetic programming of humans and other complex organisms has been fundamentally misunderstood for the past fifty years, because of the assumption that most genetic information is transacted by proteins. The human genome contains about 20,000 conventional protein-coding genes, surprisingly about the same number and with largely similar functions as those in tiny worms that have only 1,000 cells. On the other hand, the extent of non-protein-coding DNA, traditionally thought to be junk, increases with increasing complexity, reaching 98.8% in humans. Moreover, it is now evident that these non-coding sequences are transcribed in a dynamic manner, to produce tens, if not hundreds of thousands, of noncoding RNAs, and that most complex genetic phenomena are RNA-directed, which suggests that there exists a vast hidden layer of regulatory RNAs that control human development and brain function

The outcomes of the Mattick lab's research will be to expand our understanding of human evolution, development, brain function and disease. For a list of notable achievements from the lab in 2011, please see pages 3 and 4.

lab members

Senior Research Officer: Dr Marcel Dinger
Research Officers: Joanna Crawford, Dr Timothy Mercer, Dr Ryan Taft
Senior Research Assistant: Ke-Lin Ru
PhD Students: Paulo Amaral, Pierre Cattenoz, Anupma Choudhary, Michael Clark, Dennis Gascoigne, Chol Hee Jung, Darren Korbie, Ganqiang Liu, Satu Nahkuri, Martin Smith, Selene Fernandez Valverde, Darya Vanichkina
Honours Student:
Rebecca Johnston

rohan teasdale

ENDOSOMAL DYNAMICS AND PATHOGEN INVASION

The endosomal/lysosomal system of mammalian cells is a highly dynamic organelle, and the trafficking pathways within the endosomal system are fundamental for a wide variety of key cellular processes. My group is developing cellular and computational approaches to identify novel mammalian proteins associated with the endosomal system.

The regulated movement of membrane receptors and ligands between the cell surface and intracellular compartments is vital to many cellular operations, including communication between cells and their environment. Macropinocytosis is a regulated form of endocytosis that mediates the non-selective uptake of extracellular material. Numerous infectious pathogens exploit macropinocytosis to invade the host. Characterisation of pathogen entry pathways is essential for understanding infectious diseases but has also proven to be a powerful tool for gaining insight into normal cellular processes. We are currently investigating the molecular details of macropinocytosis and how it is modulated in response to infection with Salmonella, a leading cause of human gastroenteritis.

A major focus of the group is the characterisation of the mammalian endosomal protein complex called the retromer, which is a central regulator of early endosome protein trafficking. Retromer has recently been implicated in the progressive neurological disorders Alzheimer's and Parkinson's diseases. We are currently examining the known cellular or biochemical properties of retromer to determine the molecular mechanisms underlying these disease states.

lab members

Research Officers: Dr Markus Kerr, Dr Andrea Bugarcic, Dr Michael Hanzal-Bayer, Dr David Liebl, Dr Tim Barnett
Research Assistants: Seetha Karunaratne, John Griffin, Zhe Yang, Hadiya Agada
PhD Students: Josefine Sprenger, Jack Wang, Xiaying Qi

DIVISION OF molecular genetics & development

PETER KOOPMAN (Division Head)
MAT FRANCOIS
BEN HOGAN
MELISSA LITTLE
GEORGE MUSCAT
ANDREW PERKINS
RICK STURM
MATT SWEET
BRANDON WAINWRIGHT
CAROL WICKING
DAGMAR WILHELM

Dr Mat Francois, who established his own laboratory at the IMB in 2011, and also won a University of Queensland Research Excellence Award.

Some of the most serious pandemic diseases of the Western world are now known to have a genetic component, and for many of these, disease susceptibility is determined during fetal life.

Research groups within the division focus on how proper gene function contributes to the wellbeing of the adult organism, how genes regulate the optimal development of the embryo, and how these genetic processes can err to cause disease. We isolate and study genes from a range of species from zebrafish to mice and humans. We examine gene function at the molecular level, but also in living cells and ultimately in the entire organism. This work involves the use of new genomics tools including microarray and next-generation genome and exome sequencing, protein visualisation tools including immunofluorescence and advanced imaging methods, and gain-of-function and loss-of-function tools such as transgenesis in mice and gene knockdown in zebrafish.

Research in our division therefore involves close collaboration between research groups to generate critical mass and apply common skillsets and approaches to a broad range of biological problems. We also collaborate with members of other IMB divisions to access critical expertise in bioinformatics, cell biology and chemistry. In this way we are able to generate important insights into gene structure, function and interaction, clues to the causes of genetic disease, and new molecular approaches to the diagnosis and treatment of these diseases.

Key research areas include studies on lymphatic vessel development and its contribution to cancer metastasis (Ben Hogan), sexual development and its associated disorders (Peter Koopman, Dagmar Wilhelm), kidney development, disease and regeneration (Melissa Little), blood development and disorders (Andrew Perkins), the genetic basis of morphogenetic defects and tumorigenesis (Brandon Wainwright, Carol Wicking), and the signalling pathways and gene expression programs contributing to metabolic diseases (George Muscat), pigmentation/melanoma (Rick Sturm) and infectious and inflammatory diseases (Matt Sweet).

This year, we welcomed Dr Mat Francois as a Laboratory Head in the division. Mat, a former member of the Koopman group, gained international recognition in 2008 after publishing in *Nature* his revelation that the gene Sox18, initially discovered by the Koopman and Muscat groups in 1995, is the critical regulator of lymphatic vessel development in the embryo. ➤

DIVISION OF
molecular genetics & development

➤ Mat's work has opened up a new field of research on lymphatic vessel development and function, including the realisation that suppressing Sox18 activity may be useful in controlling cancer metastasis (see story below).

Other highlights in 2011 include the award of ARC Future Fellowships to Drs Matt Sweet and Dagmar Wilhelm, the Australia and New Zealand Society for Cell and Developmental Biology's Young Investigator Award to Dr Dagmar Wilhelm, and several Queensland Health and Medical Research Awards (see story, next page). Professor Melissa Little, Deputy Head of the Division, was appointed by the Australian Government Minister for Mental Health and Ageing, Mark Butler, to serve on a national panel to conduct an independent review on health and medical research in Australia, together with five other prominent scientific, medical, business and community leaders.

Lymphatic vessels and the spread of cancer

A project exploring how to manipulate the development of the lymphatic vascular system to block the spread of cancer cells throughout the body won a 2011 UQ Foundation Research Excellence Award. Dr Mat Francois, a researcher from the IMB's Molecular Genetics and Development Division, will use the $90,000 award to develop molecular and pharmacological tools to understand how lymphatic vessels form and spread.

"The lymphatic vessels play an important role in preventing infection and trafficking immune cells," Dr Francois said. "But they are also co-opted by cancer as a transport system for carrying tumour cells around the body. Cancer usually only becomes deadly once it spreads from its primary location, so if we can understand more about the lymphatic vascular system, we should be able to learn how to stop the spread of cancer by preventing the growth of new lymphatic vessels."

The project is based on Dr Francois' recent discovery that lymphatic vessel formation is triggered by the gene Sox18. This project will seek to find molecules that inhibit the activity of Sox18 under disease conditions. Such molecules will be used as tools to learn more about how these vessels form, as an improved knowledge of lymphatic vascular development will accelerate the development of new therapies to treat afflictions such as cancer and cardiovascular disease.

"There is a significant gap in our basic understanding of the molecular and genetic mechanisms controlling the growth and function of lymphatic vessels," Dr Francois said. "The inhibitors discovered in this project could lead to the development of new treatments designed to manage the spread of cancer via the lymphatic vasculature."

IMB scientists win Queensland medical research awards

The discovery of a new gene involved in heart development was recognised by the award of a major prize at the Queensland Health and Medical Research Awards in 2011.

Dr Kelly Smith won the Postdoctoral Researcher Award for identifying the gene *wickham*, which causes a heart valve defect. Cardiac valves play a critical role in partitioning blood inside the heart.

"Understanding how *wickham* helps the heart valves to develop and how this can go wrong may give us insights into how we can diagnose and treat congenital heart disease, the top cause of death from birth defects in infants," Dr Smith said.

Dr Smith made her discovery using zebrafish, tropical freshwater minnows that have become a model organism for researchers to use in studying development.

"Early zebrafish heart formation is similar to that in humans, but because zebrafish embryos develop outside the mother and are transparent, we can observe and study the heart as it forms," Dr Smith said.

Dr Michael Tallack, also of IMB's Molecular Genetics and Development Division, was a finalist in the Postdoctoral Researcher Award. He studies the gene Klf1, a master regulator of red blood cell production that ensures these cells are healthy and functional.

Ms Vicki Metzis, also from the division, won the Best Oral Presentation prize at the postgraduate student conference accompanying the Health and Medical Research Awards. Ms Metzis' presentation was titled, "Novel roles for Patched1 in nasal development and facial clefting disorders".

peter koopman

GENETIC REGULATION OF EMBRYO DEVELOPMENT AND HUMAN DISEASE

Our group focuses on genes that regulate sex development and fertility in the mammalian embryo, and the genetic causes of testicular cancer. Our main interest is striving to understand the events that determine whether an organism develops as a male or a female. We are studying the gene SRY, the Y-chromosome maleness gene, and how it controls the genetic and cellular events leading to testis development and male sex determination. We also use molecular genetics tools to identify other sex development genes and to study how these affect sex development, using transgenic and gene-knockout mice to answer questions about gene function. Ultimately we hope to better understand the causes of human disorders of sex development.

We are also interested in how germ cells – the embryonic precursor cells that become sperm in males or eggs in females – receive molecular signals from the testis or ovary in order to choose the corresponding path of sperm or egg development. We have discovered several signalling proteins that direct this decision, and are discovering how these signals act. This work is helping us understand the causes of infertility and of germ cell tumours such as testicular cancer, since inappropriate signalling to germ cells during fetal stages is thought to be the genetic basis of these disorders.

More broadly, the study of embryo development provides insight into mechanisms of disease and cancer, and provides a molecular and cellular basis for diagnostic and therapeutic approaches, including stem cell therapies.

lab members

Senior Research Officers: Dr Josephine Bowles
Research Officers: Dr Terje Svingen, Dr Liang Zhao, Dr Alex Quinn, Dr Cassy Spiller, Dr Simon Cridland
Research Assistants: Tara Davidson, Ee Ting Ng
Admin Assistant: Barbara Feenstra
PhD Students: Kathryn McClelland, Allen Feng, Clarissa Rios, Christian Larney

mat francois

TRANSCRIPTIONAL REGULATION OF BLOOD AND LYMPHATIC VESSELS IN HEALTH AND DISEASE

Lymphatic vessels are a vital component of the cardiovascular system and are essential for immune surveillance and maintaining fluid balance. In the adult, aberrant formation of lymphatic vessels is associated with a wide range of diseases that include chronic inflammatory disorder (rheumatoid arthritis), cancer (the spread of solid tumours) and lymphedema. Under these pathological conditions, the developmental programs that drive lymphangiogenesis become dysregulated. Hence, understanding the molecular basis that governs normal lymphatic vessel development in the embryo is a prerequisite to further identify novel target genes and develop potential new therapeutic avenues to prevent aberrant development in the adult.

Our research program is designed to identify and characterise key genetic pathways that influence lymphatic vascular development in the mouse embryo. We are using pre-clinical mouse models of cancer or lymphedema in order to validate the central role of developmental programs that are reactivated in these diseases. Ultimately we aim to develop a new class of compounds that will enable the pharmacological management of the lymphatic network, with the view to probe vascular development and set up the basis for drug development.

The experimental strategies we have developed to perform this translational research program rely on a range of tests and involve close collaborations with other IMB scientists and international research groups with experts in zebrafish biology, medicinal chemistry and live imaging.

lab members

Research Officers: Dr Melanie Murrell
Research Assistants: Vy Truong, Emmanuelle Frampton, Renae Skoczylas
PhD Students: Tam Duong, Jeroen Overman

ben hogan

MOLECULAR GENETICS OF VASCULAR DEVELOPMENT

The distribution of blood cells, hormones and essential nutrients throughout our bodies is dependent on the function of a healthy circulatory system. Blood and lymphatic vessels compose an organ network that distributes blood and also drains waste and fluid that accumulates in our tissues. We are particularly interested in the development and function of lymphatic vessels, which play a critical role in human diseases including lymphoedema, inflammatory disorders, and the spread of cancer, known as metastasis. Importantly, the inhibition of lymphatic vessel growth has been identified to be a valid approach for inhibiting the metastatic spread of several types of cancer.

We study how lymphatic vessels form from pre-existing vasculature (a process called lymphangiogenesis) in the context of embryonic development. Our work is currently focused on identifying the genes that regulate the earliest steps in the process of lymphangiogenesis. We primarily use the zebrafish embryo as a model system as it offers a unique combination of direct imaging techniques, embryological tools and genetic tools for the study of developmental processes. In the first years of the laboratory, we have used novel zebrafish mutants to identify several key genes that act as regulators of lymphatic vessel development in the embryo. The identification and study of these genes in mammals, in both health and in disease scenarios, is ongoing and should serve to identify targets for the treatment of vascular diseases and the inhibition of cancer metastasis.

group members

Research Officers: Dr Neil Bower, Dr Ludovic Le Guen, Dr Kaska Koltowska
Research Assistants: Christine Neyt, Scott Paterson
PhD Students: Joelle Kartopawiro, Baptiste Coxam

melissa little

KIDNEY DEVELOPMENT, DAMAGE, REPAIR AND REGENERATION

Chronic kidney disease (CKD) is devastating and expensive to treat. Once it has reached end-stage renal failure, CKD can only be treated with dialysis or transplantation. More than 4000 Australian adults will be diagnosed with CKD each year, costing in excess of $2 billion per annum. There is an urgent need to develop novel therapies as the rate of CKD is rising at 6-8 per cent per annum, primarily due to increasing rates of Type II diabetes and obesity. Sadly, only one in four patients will receive a transplant.

The risk of kidney failure during our lives is now known to be linked to kidney development. In particular, the number of nephrons, the 'filters' of the kidney, seem to play an important role in determining the health of the adult kidney. Our laboratory is known internationally for defining the genes involved in normal kidney development and integrating this information with an understanding of how the adult kidney responds to damage. We hope to develop novel approaches to the diagnosis and treatment of both acute and chronic kidney disease. Such therapies will grow out of our understanding of the processes involved in normal kidney development.

In 2011 we identified genes that may be able to 'recreate' a kidney stem cell state in another cell type. We have also isolated a mesenchymal stem cell population from the adult kidney itself and shown that these cells are better able to integrate back into kidney than other stem cells. We hope to ultimately move these findings closer to an outcome.

lab members

Research Officers: Dr Lorine Wilkinson, Dr Joan Li, Dr Minoru Takasato, Dr Alex Combes, Dr Jessica Vanslambrouck
Research Assistants: Kylie Georgas, Melissa Becroft, Norseha Mohammed Suhaimi, Adler Ju, Calida Neal, Nick Martel, Pei Er
PhD Students: Caroline Hendry, Yu Leng Phua
Undergraduate Students: Rory Reardon, Usukhbayar Ariunbold, Brandon Binnie

george muscat

NUCLEAR HORMONE RECEPTORS AND METABOLIC DISEASE

Nuclear hormone receptors (NRs) are proteins that translate endocrine, metabolic and pathophysiological signals into gene regulation. My group's research continues to focus on understanding the molecular role of nuclear hormone receptors (NRs) in the regulation of metabolism and body composition in transgenic mouse models. In addition, we collaboratively examine the molecular role of NRs in melanoma and breast cancer. We exploit these animal models and studies to gain insights into dyslipidemia, obesity, type II diabetes and cancer. The insights obtained from studies in animal models will be utilised to understand human health and disease.

We have previously shown that mice with decreased and dysfunctional expression of an NR called *Ror alpha* are resistant to (high-fat) diet-induced obesity. Additional studies exploring the regulation of glucose metabolism have indicated *Ror*α plays an important role in controlling insulin sensitivity and glucose tolerance in skeletal muscle.

Our studies have produced transgenic mouse lines with muscle-specific expression of an activated form of the nuclear receptor, NOR-1 (a member of the NR4A subgroup of NRs). These investigations have demonstrated that NOR-1 signalling controls muscle fibre type, oxidative metabolism, and exercise capacity. Also, the insights obtained from the studies in lean, obese and diabetic murine models are being utilised to profile the expression of the NRs, NR-associated cofactors and metabolic genes in overweight and obese children before and after the implementation of a nutrition and lifestyle program. This will enable the translation of this basic research into outcomes for human health.

lab members

Research Adjunct: Dr Gary Leong
Research Officers: Dr Patrick Lau, Dr Mary Wang, Dr Michael Pearen, Dr Rebecca Fitzsimmons, Dr Dennis Dowhan
Research Assistants: Joel Goode, Fenny Chong, Akira Ichino
PhD Students: Natalie Eriksson, Shaffinaz Abdrahman
Masters Student: Thi Nguyen
Honours Students: John Roberts-Thomson, Yii Huan Eng
Undergraduate Student: Emily Shao

andrew perkins

GENETICS OF BLOOD CELL PRODUCTION IN HEALTH AND DISEASE

Our laboratory is interested in the gene activity behind blood formation. How do the proteins that control gene activity work with one another? How do they work within biochemical and genetic pathways and how does deregulation of such programs lead to cancer? We focus on four primary areas to seek answers to these questions:

1. Protein networks that are active during embryonic stem (ES) cell specialisation into tissues derived from the middle layer of the developing embryo. We use a variety of methodologies to study these networks.

2 Gene activity of red blood cell production. Mutations in the globin gene family, which includes the protein responsible for transporting iron around the body, haemoglobin, are the most common genetic mutations worldwide. These mutations are responsible for thalassaemia and sickle cell disease, which cause serious morbidity and mortality. We are interested in trying to decipher the complex process of haemoglobin switching at a molecular level. Babies produce a different type of haemoglobin from adults, one which allows more oxygen to bind to the protein. They switch to producing adult haemoglobin at around six months old. The long-term goal is to design new drugs that target key regulators of this process and thereby reactivate fetal haemoglobin in adults to replace diseased adult haemoglobin.

3 The role played by the Kruppel-like factor (KLF) family of genes in normal cell specialisation and human skin, colon and blood cancers. We are focused particularly on myelodysplastic syndromes, a group of blood disorders where the myeloid class of cells isn't properly produced, which can lead to leukaemia in some cases, and myeloproliferative disorders, where too many bone marrow cells are produced.

4. The genetics underpinning gastrulation, the stage of development when the embryo forms three distinct cell layers, and the subsequent generation of blood stem cells within the mammalian embryo.

group members

Research Officer: Dr Michael Tallack
Research Assistant: Graham Magor
PhD Student: Paulo Amaral
Masters Students: Anton Karlsbeek, Pierre Tangermann
Honours Student: Jessica Fittock

rick sturm

MELANOGENIX

The Melanogenix laboratory is studying the biology of melanocytes, the cells that produce melanin, a pigment that determines, skin, hair and eye colour, and the genes responsible for normal human variation in these traits. In collaborative efforts we are also studying genes invovled in mole shape, size and colour. We are investigating skin and hair colour genetic associations in Europeans, focusing on known (TYR, TYRP1, OCA2, SLC45A2, SLC24A5, MC1R, ASIP, KITLG) and previously unknown (SLC24A4, IRF4, TPCN2, RAB17) candidate genes. Examining the subtle changes in these human pigmentation genes that occur between people will ultimately provide a full appreciation linking genes with physical traits. In the case of melanocytes, this is related to a person's risk of suffering from skin cancer, in particular melanoma.

Of major interest to our laboratory is the role of the protein MC1R, which is active on the surface of melanocyte cells and plays a role in stimulating melanin production. MC1R gene variants are common in the Australian population and these determine a person's skin phototype and response to UV-induced MC1R receptor activation. In addition, the group is studying how melanocytes develop into specialised cells within the skin, and the interaction of melanocytes with keratinocytes, the cells found in the outermost layer of skin. Ultimately, information we gain will allow the genes and processes involved in melanoma tumour formation and spread to be examined.

lab members

Senior Research Officer: Dr Aaron Smith
Research Officers: Dr Kimberley Beaumont, Dr Shu Shyan Wong, Dr Matthew Harrison
Research Assistants: Adam Dinsdale, Kasturee Jagirdar, Wen Lim, Darren Smit, Caroline Sturm
PhD Student: Stephen Ainger
MSc Students: Sefetogi Ramaologa, Kai Zhang
Honours Students: Alex Metcalf, Kelvin Yin

matt sweet

INNATE IMMUNITY

Our bodies have an immune system that protects us from many potentially harmful microbes, but agents that cause infectious diseases are able to overcome this defence system. Macrophages, a type of white blood cell found in all tissues of our bodies, trigger inflammation to contain and destroy infections, but many important human pathogens (e.g. HIV, TB) actually live within macrophages to avoid the immune response. We study how important human pathogens subvert normal macrophage functions required for effective host defence. In 2011, we discovered that certain clinical isolates of uropathogenic *E. coli*, the major cause of urinary tract infections, are also able to survive in macrophages. We also discovered a mechanism by which *Salmonella typhimurium*, a pathogen that causes gastrointestinal disease leading to high mortality rates in low- to middle-income countries, evades macrophage-killing responses. Such findings may ultimately lead to new strategies to treat infectious diseases caused by these bacteria and others.

In addition to providing protection against infectious diseases, inappropriate inflammation triggered by the innate immune system, including macrophages, contributes to an array of very serious chronic diseases. Our laboratory also studies the genes and pathways that lead to inappropriate inflammatory responses in macrophages. In 2011, we discovered two proteins that promote excessive macrophage inflammatory responses. Inhibitors that block the activity of these proteins may provide new avenues for anti-inflammatory drugs.

lab members

CJ Martin Fellow: Dr Kate Schroder
Research Officers: Dr Steve Broomfield, Dr Kolja Schaale
Research Assistants: Greg Kelly, Nabilah Ahmad Kamal, Kelly-Anne Masterman, Alina Zamoshnikova
PhD Students: Melanie Shakespear, Dr Nilesh Bokil, Divya Ramnath, Juliana Ariffin, Kaiwen Chen
Honours Students: Daniel Hohenhaus, Tam Nguyen

brandon wainwright

TISSUE REPAIR AND CANCER

Our laboratory mapped and isolated the Naevoid Basal Cell Carcinoma Syndrome (NBCCS) gene, "patched", and identified that it controls a molecular signalling pathway, which appears to be mutated in a wide range of tumour types. The two cancer types that are most often found in NBCCS patients are basal cell carcinoma of the skin (the most common type of skin cancer) and medulloblastom (a brain tumour that occurs predominantly in children). In both cancer types, we are examining what the cell of origin is and how activation of this pathway, known as the hedgehog pathway, causes these tumours. As we discover more about the interaction of the hedgehog pathway with other genetic pathways, we gain a better understanding of the normal development of the skin and cerebellum, and through these insights, we hope the therapeutic strategies available to treat patients with these tumours will be improved.

lab members

Research Officers: Dr Christelle Adolphe, Dr Jonathan Robson, Dr Richa Dave, Dr Lena Constantin, Dr Elaine Julian, Dr Laura Genovesi
Research Assistants: Elizabeth O'Brien, Paul Joosa
PhD Students: Rhonda Kan, Peter Yee
Honours Student: Eriza Secondes
Undergraduate Students: Hyun Lee, Tina Lin

carol wicking

DEVELOPMENTAL GENES AND HUMAN DISEASE

Defects arising from abnormal development of an embryo *in utero* are a major cause of infant mortality and childhood disability. My lab is interested in understanding these congenital diseases, with a particular focus on an expanding class of disorders known as ciliopathies. These diseases are characterised by a broad range of features including cystic kidneys, extra fingers and toes, skeletal and facial defects, obesity and diabetes. Ciliopathies arise from abnormal functioning of the primary cilium, a structure in each cell of the body that is essential for the correct development of many of our organs. In particular, the primary cilium regulates the hedgehog signalling pathway, a pivotal signalling cascade in embryo and tumour development. My lab has been studying hedgehog signalling for a number of years, primarily with respect to its role in development of the limb and face, both of which are commonly affected in people with birth defects.

We primarily use the mouse as a model system and have a number of mouse mutants under study in the lab. These mutants have allowed us to uncover novel defects arising from misregulation of hedgehog signalling in the limb and face. More recently we have shown that the defects in these mice arise from aberrant cilia function, and one of these mutants acts as a model for a subset of ciliopathies characterised by skeletal dysplasia. Further characterisation of these mouse mutants is allowing us to understand the role cilia plays in disease, with a view to enhanced diagnosis and treatment of ciliopathies.

In parallel studies, Dr Kelly Smith has introduced the zebrafish model to the lab. Kelly is continuing her own projects on characterisation of early heart development. This is based on mutants identified in a forward genetic screen and has implications for human congenital heart disease.

lab members

Research Officers: Dr Kelly Smith, Dr Fredrik Olsson
Research Assistants: Andrew Courtney, Ashley Cooper, Maria Rondon, Huijin Chen
PhD Students: Vicki Metzis, Geraldine Kaeslin, Claudio Cortes

dagmar wilhelm

TOWARDS A NEW UNDERSTANDING OF THE REPRODUCTIVE SYSTEM: FROM NON-CODING RNAS TO DISEASE

Sexual reproduction is the primary method of reproduction for the vast majority of larger organisms, including almost all animals and plants. It is the creation of a new organism by combining the genetic material of the parents, involving three main processes: first, the production of the gametes (eggs and sperm), from primordial germ cells (PGCs) through a process called meiosis; second, the fusion of two gametes during fertilisation; and third, sex determination, the decision to develop into either male or female. Gaining insights into sexual reproduction is not only essential for the understanding of medical problems such as disorders of sex development (DSDs), but also has implications for the food industries as well as the eradication of pest species.

These processes are controlled by a delicate network of gene regulation and interaction. Disturbance of this network by gene mutation or misexpression during development results in malformation and malfunction of organs, diseases such as ovarian and testicular cancer, and in most cases infertility. Therefore, each of these processes must involve a large number of regulatory mechanisms. We are investigating a new regulator of gene expression, non-coding RNAs (ncRNAs), and its role in sexual reproduction. Our research uses mouse and zebrafish as model systems and integrates molecular and developmental biology to study mechanisms of gene regulation during embryonic development, concentrating on sex determination and gonad development but extending to other developmental systems such as cartilage.

lab members

Research Officer: Dr James Palmer
PhD Students: Lindsey McFarlane, Elanor Wainwright
Occupational Trainee: Kevin van der Graaf
Honours Student: Hao Ming, Mark Cheong

Professor Alpha Yap, whose research is delivering new pathways to understanding cancer – (see story next page).

DIVISION OF molecular cell biology

ALPHA YAP
(Division Head)
KIRILL ALEXANDROV
BRETT COLLINS
BRAD MARSH
ROB PARTON
JENNIFER STOW
MIKE WATERS

Cell biology seeks to understand the molecular workings of the cell, the building blocks of our bodies.

This is fundamental for a full understanding of how our bodies work when healthy, and to understand the molecular basis of disease. The research groups of the Division of Molecular Cell Biology are tackling individual problems central to key issues in cell biology and also building essential technologies to tackle broader research challenges. The research problems include the trafficking of cytokines in inflammation (Stow); the biogenesis of membrane organisation (Parton); cell-cell adhesion and the cytoskeleton (Yap); the role of membrane trafficking in host-pathogen interactions (Teasdale, joint appointment with GCB); structural biology of membrane transport (Collins); high-resolution electron microscopy of insulin-secreting pancreatic cells (Marsh); and cell biology of growth hormone (Waters). Our efforts to develop new technologies encompass high-throughput computational analysis of cellular imaging (Hamilton, joint appointment with GCB); and new technologies for protein engineering, analysis and the development of synthetic receptors (Alexandrov).

All the individual groups of the division are supported by external research funding. These include project grants from the National Health and Medical Research Council (NHMRC), Australian Research Council (ARC), Cancer Council, and Human Frontiers Science Program and ARC Linkage grants. Members of the division are also supported by two Program Grants. Stow and Teasdale are chief investigators on the NHMRC Program Grant 'Fighting infection: exploiting host-pathogen interactions', and in 2011 Parton, Yap and Alexandrov were awarded a Program Grant to commence in 2013. Many group leaders in the division are also supported by fellowships from the NHMRC and ARC.

Members of the division maintained extensive engagement in the scientific community both nationally and internationally. Jennifer Stow is a member of the Medical Advisory Board of the Australian Cancer Research Foundation and on the Research Grants committee of the HFSP; Rob Parton serves as a senior member of the editorial boards for both *The Journal of Cell Biology* and *Molecular Biology of the Cell*; and Alpha Yap serves on the editorial boards of *Current Biology* and *Molecular Biology of the Cell*. Yap also was Chair of the 2011 Gordon Conference on Cell Contact & Adhesion. The presence of the Division was also apparent at many major national and international conferences in 2011. These include ComBio2011 (Parton, Stow, Teasdale, Yap), Hunter Cellular Biology Meeting (Parton, Stow, Collins), FASEB meetings (Parton), Gordon Research Conferences (Yap) and Keystone Meetings (Yap).

DIVISION OF
molecular
cell biology

Cell 'glue' opens new pathways to understanding cancer

Divisional researchers have found a novel way in which the proteins that 'glue' cells together to form healthy tissues can come unstuck, opening new avenues to understanding how these proteins are disturbed in diseases such as cancer.

Professor Alpha Yap and Sabine Mangold from UQ's Institute for Molecular Bioscience have been studying how cells stick together and the diseases that occur when cells detach when they should not. In particular, the progression of tumours to advanced stages commonly occurs when cancer cells separate from their tissue of origin.

"We examined a protein called HGF that is often found in cancer," Ms Mangold said. "HGF regulates cell growth, shape and movement and aids cancer cells in migrating to other tissues and spreading through the body."

"Scientists have long known that HGF disrupts the junctions where cells join together, but the exact mechanism of how this occurs hasn't been understood until now."

The team made by their discovery by examining the molecular machinery that binds cells. One key component is a protein called E-cadherin, which forms the adhesive to hold cells together.

E-cadherin associates with a scaffold found inside the cells, made of a protein called actin. Normally, actin links into a meshwork with cadherin to make strong contacts between cells.

Ms Mangold and Professor Yap found that the actin scaffolding seemed to be lost just as the cell contacts became disrupted. They discovered this occurred because HGF caused another protein, Myosin VI – which normally acts to link cadherin and actin together – to be lost from cadherin.

"So HGF was causing this interlinked meshwork of proteins to come apart, breaking up the system and causing cells to drift apart," Professor Yap said.

"The discovery of this pathway may open new avenues to understand exactly how proteins that bind cells together are affected in disease, which could lead to new targets for treatments of such disease, including cancer."

The study was published in the latest edition of the international journal *Current Biology.* It was funded by the National Health and Medical Research Council of Australia. Confocal imaging was performed at the Australian Cancer Research Foundation (ACRF) Cancer Biology Imaging Centre at the IMB, established with the generous support of the ACRF.

Research to stop cancer receives funding

Cutting-edge research that aims to stop the transformation of healthy cells into cancerous cells will be funded at IMB after an announcement by Health Minister Tanya Plibersek.

The projects form part of $8.3 million awarded to UQ from the National Health and Medical Research Council (NHMRC) to conduct world-leading medical research.

An IMB team led by Professor Robert Parton, that includes Professors Alpha Yap and Kirill Alexandrov, was awarded $7.1 million for research into cell surface changes in cancer, immunity, and muscular dystrophy.

Their research will study how the cell surface is organised into domains such as caveolae, and how junctions between cells form and function.

"The cell surface is organised into domains with distinct functions," Professor Parton said. "Caveolae, which are shaped like flasks, are thought to help transmit signals to the cell interior and protect the cells against stress."

"Defective caveolae are associated with cancer, muscular dystrophy and cardiac disease. Other specialised domains hold cells together and contribute to immunity, and defects in these domains occur in cancer and inflammation.

"Our goal is to study these domains, identify their important components, and understand how they form and function, which will have huge importance for therapeutic strategies."

UQ Deputy Vice-Chancellor (Research) Professor Max Lu congratulated all the UQ recipients of the NHMRC grants.

"UQ has some of the most innovative and successful health and medical researchers in the world, and today's announcement is acknowledgement of the high quality and vital work they are doing to further human health," Professor Lu said.

alpha yap

CADHERIN ADHESION AND TISSUE ORGANISATION IN HEALTH AND DISEASE

Cells are the building blocks of our bodies. Interactions between different cells are important to shape our developing bodies and maintain the healthy organisation of our tissues. Importantly, those interactions are disturbed in many diseases, including cancer and inflammation. My laboratory studies one set of cell-to-cell interactions, those that occur when cells attach to one another. We focus on the cadherin family of cell-cell adhesion receptors. These critically determine the ability of cells to recognise one another and organise into coherent tissues. The importance of these receptors is emphasised by the fact that loss of cadherin function promotes cancer progression in epithelial tissues (such as the breast and colon) – the commonest form of human cancers. Cadherin dysfunction also contributes to the breakdown of epithelial barriers during inflammation, notably in chronic disease of the intestine. By understanding the basic biological mechanisms of cadherin-mediated cell recognition, we aim to provide vital insights into the basis of development and common human diseases.

Currently we focus on understanding how cadherins cooperate with the actin cytoskeleton, the cellular structure that allows the cells to move and which has long been believed to be central to cadherin function. Our research indicates multiple regulators are coordinated in cadherin adhesion to maintain the integrity of cell-cell junctions. This carries the challenge of understanding how these many proteins are coordinated to work together at the right time and place in the cell. A significant breakthrough came with our recent discoveries, published in the scientific journal *Nature Cell Biology,* that these cell signals and effectors function in modules that make specific contributions to junction integrity.

lab members

Senior Research Officer: Dr Eva Kovacs
Research Officers: Dr Guillermo Gomez, Dr Aparna Ratheesh, Dr Robert McLachlan, Dr Siew Ping Han
Research Assistants: Suzie Verma, Hayley Cox
PhD Students: Sabine Mangold, Joanne Leerberg, Selwin Wu, Rashmi Priya

kirill alexandrov

NEXT-GENERATION TECHNOLOGIES FOR PROTEIN RESEARCH

Advances in life sciences and biotechnology are driven by our ability to replicate the building blocks of life in organisms, modify them, and use them in academic and industrial applications. Much of the biotechnological progress in the last forty years has stemmed from advances in analysis and synthesis technologies for DNA and proteins. However, while orders-of-magnitude cost reduction was achieved in DNA sequencing and synthesis, the protein technologies have changed comparatively little.

Our laboratory is focusing on the filling this technological gap by developing new methods for rapid in vitro synthesis of proteins and analysis of their structure and function. We have developed a novel cell-free protein expression system based on the single-celled organism *Leishmania tarentolae*. We have demonstrated that, using this technology, large sets of genes can be converted into proteins within hours. We combine this technology with another, called single molecule spectroscopy, to quantitatively analyse protein-protein interactions in multiprotein assemblies. We use this approach to study multisubunit complexes controlling the transport of molecules through the cell membrane.

lab members

Research Officers: Dr. Yann Gambin, Dr Sergey Mureev, Dr Viktor Stein, Dr Wayne Johnston, Dr Zhong Guo
Research Assistants: Veronika Schreiber, Regina Hartmann, Nichole Giles, WooRam Jung
PhD Students: Dejan Gagoski, Oleksiy Kovtun, Zakir Tnimov, Marta Kubala, Monika Koenke

brett collins

MOLECULAR TRAFFICKING LABORATORY

Each cell in our body must communicate with its surrounding environment using cell surface molecules. This communication is controlled by cellular organelles called endosomes. Not only are endosomes critical for normal cell function, their disruption is linked to many different diseases including cancer, inflammatory disorders and pathogen infection. Because neurons are especially dependant on endosomal membrane communication (consider the typical neuron can be hundreds of times the length of most other cells in our bodies!), defects in endosome function are very commonly implicated in neurological disorders including Alzheimer's and Parkinson's disease.

Our laboratory is investigating several related families of proteins with important roles in endosome biology. We combine different approaches to understand the function of endosome-associated proteins and their role in disease, and to determine their functions right down to the atomic level. The roles of these endosomal proteins are extremely varied. Many control the formation of membrane structures such as vesicles (fluid-filled cavities) and tubules. Such structures are the sites of protein trafficking – selective regions of the endosome that package and transport "cargo". A prime example is the amyloid precursor protein (APP), the breakdown of which leads to the formation of the amyloid peptides believed to cause Alzheimer's. The trafficking and breakdown of APP is of particular interest in our lab. Endosome-associated proteins control many other cellular processes including signal transduction (often perturbed in cancer), fat metabolism, movement of organelles around the cell, viral and bacterial invasion, processing of immune responses and communication between neurons to name but a few.

lab members

Research Officer: Dr Suzanne Norwood
PhD Students: Daniel Shaw, Rajesh Ghai

brad marsh

STRUCTURE-FUNCTION STUDIES OF THE PANCREATIC BETA-CELL

Our research focuses on understanding the key structure-function relationships that underpin the biosynthesis, trafficking and secretion of the hormone insulin in mammalian cells – namely, the pancreatic beta-cell. Specifically, we use a method called 'cellular electron tomography' (ET) to quantitatively map and model the organisation of beta-cells under different physiological and disease conditions. ET relies on advanced mathematical and computing techniques to generate 3D image volumes at the nanoscale from sets of 2D images taken at different angles, similar to the way in which diagnostic imaging methods like computed tomography (CT), magnetic resonance imaging (MRI) and positron electron tomography (PET) computationally reconstruct 3D image volumes for different parts (or even all) of the body. In our case, we computationally reconstruct 3D images for different parts (or even all) of the cell at nanometre resolution. This has allowed us to visualise the machinery needed to make and transport insulin within beta-cells (and release it into the bloodstream) with unprecedented accuracy and reliability. Moreover, these detailed 3D cell "atlases" are helping us to identify when and where defects occur in the 'insulin factory' that lead to beta-cell malfunction and ultimately death (broadly referred to as diabetes). Crucially, type 1 diabetes represents one of Australia's fastest-growing chronic diseases of childhood. At present, the onset of type 1 diabetes in children or adults cannot be prevented and a cure remains to be found.

lab members

Research Officers: Dr Massimo Micaroni
PhD Students: Alex Foo, Peter van der Heide, Timothy Pan, Nur Intan Ruhaiyem

rob parton

THE CELL SURFACE IN HEALTH AND DISEASE

Each of the cells that make up our organs is enclosed in a plasma membrane, a complex sheet made up of fats and proteins that plays a crucial role in detecting growth signals or taking nutrients up into the cell. At the same time, the plasma membrane protects the cell against unwanted invaders.

The properties of the plasma membrane rely on its specialisation into regions of specific function. We are studying caveolae, a specialised domain of the cell surface with a distinct structure. Caveolae have been implicated in regulation of cell growth and in maintaining the balance of fats in the cell. Defective caveolae in human patients are associated with cancer, lipodystrophies (lack of fat tissue), muscular dystrophy, and cardiac disease. To study caveolae function, we are studying cells and animals that lack caveolae or have defective caveolae. We have discovered new proteins needed for caveolar formation and their function and shown that caveolae can respond to forces on the plasma membrane by releasing signals into the cell, which allow the cell to detect and respond to stresses on the cell surface. We propose that loss of this specialised detection system causes some forms of muscular dystrophy.

We are also developing novel drug encapsulation systems with potential therapeutic applications for targeted drug delivery.

lab members

Senior Research Officer: Dr Susan Nixon, Dr Kerrie-Ann McMahon
Research Officers: Dr Manuel Fernandez-Rojo, Dr Harriet Lo, Dr Mark Howes, Dr Michele Bastiani
Research Assistants: Robert Luetterforst*, Rachel Hancock*, Charles Ferguson, James Rae, Nicole Schieber, Satomi Okano
PhD Students: Samantha Murphy, Carol Kistler, Nick Ariotti, Natalya Leneva, Natasha Chaudhary

* part-time

jennifer stow

PROTEIN TRAFFICKING IN HUMAN DISEASE

The way molecules are 'trafficked' or moved within our cells is a fundamental process that impacts on all human diseases. Our studies in cells of the immune system relate to infectious disease and inflammatory diseases and our work in epithelial cells, which cover the internal surfaces of the body, investigates their transition to cancer cells.

In cells of the immune system, the trafficking and release of chemical messengers is critical for immunity, but it can also cause inflammatory diseases like rheumatoid arthritis and inflammatory bowel disease. Our laboratory aims to find the genes and proteins responsible, and develop new strategies and new drugs to control inflammation.

Immune cells also normally protect us from infectious diseases by 'phagocytosing', or eating and killing invading bacteria and other microbes; however, some bacteria avoid these defenses and result in disease. As part of a national research program, we are working to investigate and document the many bacterial and host genes that regulate the interactions of bacteria with the cells of our immune system. This research aims to prevent and develop new vaccines, antibiotics and other treatments for infectious diseases.

lab members

Research Officers: Dr Amanda Stanley, Dr Adam Wall, Dr Lin Luo, Dr Nathan King
Research Assistants: Darren Brown, Dr Fiona Wylie, Juliana Venturato, Tatiana Khromykh, Nicholas Condon
PhD Students: Marga Gual Soler, Jeremy Yeo, Pei Ching Low, Carolin Offenhauser
Honours Student: Xuan Fei Wong
Undergraduate Student: Natalie Lansdaal

mike waters

ROLE OF GROWTH HORMONE IN GROWTH, STEM CELL ACTIVATION, CANCER, DIABETES, OBESITY AND LONGEVITY

Adult height is determined by the actions of growth hormone (GH) during childhood and adolescence. In the adult, growth hormone is an important metabolic agent, burning fat and opposing the actions of insulin. In old age, growth hormone shortens lifespan, at least in animal models. We have shown that it can regenerate stem cells in the brain of aged mice, and is needed for the increase in neural stem cells seen following exercise. We study the molecular means used by growth hormone to achieve these changes, using a variety of approaches.

The GH receptor determines the degree of the cell response to GH. Through various techniques, we have developed an understanding of how the GH receptor is activated by growth hormone. We also described how a rearrangement of an extracellular loop of GH activates a different signalling pathway that is essential for expression of a powerful immunotolerance molecule that allows mice to survive after partial liver removal, and correlates with success of liver and kidney transplants in man.

We have shown in mice that enhancement of postnatal growth by GH is dependent on its ability to activate the protein Stat5. Because these mice become strikingly obese after 6 months of age, we studied the role of Stat5a/b in controlling lipid and carbohydrate metabolism. We found insulin secretion and action are altered in these mice, and their livers are grossly fatty. Importantly, we find that GH acts in normally fed mice to burn fat, so as to maintain a normal amount of subcutaneous fat.

Finally, the striking resistance of GH-deficient and GH-receptor mutant mice and humans to cancer has led us to elucidate the pathways involved, and to seek to develop small molecule GH antagonists of therapeutic value in cancer treatment.

lab members

Research Officers: Drs Andrew Brooks, Dan Blackmore, Baogang Xie
Research Assistants: Kathryn Tunny, Tania Brooks
PhD Students: Caroline Nelson, Yash Chhabra
Honours Student: Ho Yi Wong
Occupational Trainees: Manon Vullings, Noortje van de Weem

DIVISION OF chemistry & structural biology

DAVID FAIRLIE (Division Head)
PAUL ALEWOOD
ROB CAPON
MATT COOPER
DAVID CRAIK
BEN HANKAMER
GLENN KING
RICHARD LEWIS
JENNY MARTIN
MARK SMYTHE

Affiliates:
KIRILL ALEXANDROV
BOSTJAN KOBE
ALAN MARK
ISTVAN TOTH
PAUL YOUNG

Professor David Craik receiving the American Chemical Society's Ralph F. Hirschmann Award for Peptide Chemistry from Nancy Jackson (President, American Chemical Society) and Ian Bell (Merck Laboratories).

The CASB (Chemistry and Structural Biology) Division conducts pure, strategic and applied research programs in chemistry, structural biology, biochemistry, pharmacology, virology, bacteriology and biofuels.

Researchers discover, design and synthesise new compounds; investigate the molecular and structural basis of physiology and disease; and invent new approaches and new treatments for combating disease. The division is making important contributions to understanding how to fight inflammatory diseases, cancer, diabetes and obesity, viral and bacterial infections, and chronic pain.

The division is also inventing and developing new biological and chemical technologies for translation into industrial applications.

Fellowships & Awards

Professor Craik (Principal Research Fellow to Senior Principal Research Fellow) and Professor Lewis (Senior Research Fellow to Principal Research Fellow) received prestigious promotions within the National Health and Medical Research Council (NHMRC) Fellowship scheme. Professor Fairlie changed from Australian Research Council (ARC) Federation Fellow to NHMRC Senior Principal Research Fellow. Professor Martin was awarded the 2011 Women in Biotechnology Outstanding Biotechnology Achievement in Queensland. NHMRC Training/Early Career Fellowships were awarded to Drs Julia Archbold, David Jacques and Linlin Ma, and ARC DECRA was awarded to Dr Sonia Henriques.

Research Grants

Division Laboratory Heads were lead investigators on 12 new NHMRC- and 8 new ARC-funded project and fellowship grants totalling $9M. These included new research on angiogenesis inhibitors (Craik, Daly), inhibitors of metabolism and obesity (Fairlie), antibiotics and drug resistance (Cooper, Mark), analgesics for chronic pain (King, Mobli), antiviral drugs for dengue infections (Fairlie, Young), enzyme inhibitors as antinflammatory drugs (Smythe), new antibiotics (Capon), new drugs from natural products (Capon), norepinethrine transporters (Lewis), drugs from sunflower seeds (Mylne), diagnostics for dengue infection (Cooper, Young), membrane proteins (Martin, Alexandrov, Kobe), and advanced solar-powered hydrogen production systems based on green algal cells (Hankamer). ➤

DIVISION OF
chemistry & structural biology

➤ Other new project highlights included $6 million to Professors Craik and Fairlie from Pfizer Australia, ARC Linkage and UQ for orally bioavailable drugs for diabetes; $5 million to Professors Cooper, Paterson and colleagues from the Wellcome Trust UK for re-engineering current antibiotics to make them more drug resistant; and $3.5 million to Associate Professor Hankamer from the National and International Research Alliances Program for building high efficiency microalgal biofuel systems.

Publications

The division published more than 130 papers in international scientific journals including original research articles in top chemistry journals (e.g. *Journal of the American Chemical Society*, *Angewandte Chemie International Edition*, *Organic Letters*, *Journal of Medicinal Chemistry*) and biology journals (e.g. *Nature Nanotechnology*, *Nature Chemical Biology*, *Proceedings of the National Academy of Sciences USA*, *Blood*). Some highlights included five publications by Professor Alewood and colleagues in *J Am Chem Soc*, *Angew Chem Int Edit* and *PNAS* on protein and peptide chemistry; two papers from Professor Martin and colleagues in *PNAS* on SNARE and TLR adaptor proteins. All division researchers were very active in presenting their research at conferences in North and South America, Europe, South East Asia and Australia.

Colleagues share the latest research discoveries

From the 8th to the 11th of November, division members coordinated five one-day meetings, including the Industry Affiliates Program (*Translational Research: Lessons and Challenges),* the CASB Division Symposium, and three satellite meetings on Metabolic Syndrome, Biofuels and Anti-Infectives. These involved ninety-six oral and ninety-eight poster presentations featuring visitors from overseas (Pfizer, Merck, Novartis, Genentech, Merlion, Boeing, and many others), interstate and Queensland. Laboratory Heads, researchers, students, visitors and industry affiliates shared their latest research discoveries in structural biology, chemistry, biochemistry, pharmacology and drug discovery.

(http://casb2011.imb.uq.edu.au/index.php)

david fairlie

CHEMISTRY AND HUMAN THERAPEUTICS

Our group works at the interface of chemistry, biology and disease to better understand molecular mechanisms of life, ageing, disease and death.

Our chemists discover new drugs; develop expertise in medicinal chemistry, organic synthesis, computer-aided drug design; NMR-based structure determination; and learn how small molecules interact with each other, proteins, RNA or DNA. Outcomes are new compound structures, chemical reactions and mechanisms, enzyme inhibitors, agonists/antagonists, and mimics of protein surfaces.

Our biologists use our novel compounds to elucidate functions of human proteins, human cells and animal models of human diseases. They study mechanisms of protein and cell activation, biological processes, disease development, and drug action. Researchers gain insights to human physiology, disease pathology, and develop skills in pharmacology, virology, immunology, oncology, neurobiology or biochemistry.

lab members

Senior Researchers: Dr Kalyana Akondi, Dr Jade Blakeney, Dr Aline Dantas de Araujo, Dr Frederik Diness, Dr Russell Driver, Dr Tim Hill, Dr Huy Hoang, Dr Abishek Iyer, Dr Fredrik Lindahl, Dr Ligong Liu, Dr Rink-Jan Lohman, Dr Andrew Lucke, Dr Robert Reid, Dr Conor Scully, Dr Martin Stoermer, Dr Jacky Suen
Postgraduate Students: Sheila Barbero, Shaio Chow, Anh Do, Lena Goedecke, Praveer Gupta, Johan Hamidon, Anders Larsen, Junxian Lim, Daniel Nielsen, Ranee Singh, Vernon Seow, Annika Yau
Undergraduate Students: Jessica Lewis, Laura Litten, Sing Ngooi, Alex Raven
Office Manager: Lyn Fairlie

paul alewood

DESIGN AND DISCOVERY OF BIOACTIVE PEPTIDES AND PROTEINS

The overall focus of our laboratory *(www.uq.edu.au/alewood/)* is the identification of biologically active molecules that have the potential to play important roles in human health and wellbeing. Some specific interests include: the discovery and total synthesis of potent and selective toxins from Australia's venomous creatures; the chemical synthesis of proteins and biologically active peptides (small proteins); the development of new synthetic and analytical chemistry; understanding protein structure and function. Special emphasis is placed on determining the structure-function relationships of natural and designed molecules. Current research programs involve: the discovery, isolation and description of toxins from snakes, spiders, cone snails, platypus, ticks and scorpions; studying HIV-1 Proteinase, the enzyme that makes the HIV virus infectious; the chemical engineering of molecules with the potential to perform a range of important roles in the body; and uncovering new pain pathways in chronic pain syndromes.

lab members

Senior Research Officers: Dr John Holland, Dr Lachlan Rash, Dr Andreas Brust
Research Officers: Dr Aline Dantas, Dr Tom Durek, Dr Jean Jin, Dr Markus Muttenthaler
Research Assistant: Zoltan Dekan
PhD Students: Jen Smith, Kalyani Akondi, Simone Vink, Vincent Lavergne, Tim Reeks, Jingjing Wan
Visiting Students: Anders Ruskov-Nielsen (University of Copenhagen), Anne Callesen (University of Copenhagen), Claudia Hjørringgård (Aarhus University, Denmark)

rob capon

BIODISCOVERY: LEARNING FROM NATURE

Australia is rich in plant, animal and microbial biodiversity, which inhabit ecosystems ranging from the northern tropics to as far south as Antarctica. These regions are geographically diverse, featuring deserts, mountains and rainforests, rivers, wetlands and estuaries, as well as beaches, coral reefs and deep-sea mounts. Our research mission is to explore this remarkable living resource to discover new knowledge that will inspire the development of new and improved pharmaceuticals, chemicals for use in agriculture, and research tools. Human diseases that we target include neurodegenerative diseases (i.e. Alzheimer's, Parkinson's), multi-drug resistant cancers and infectious diseases, acute and chronic inflammatory pain, diabetes and obesity. Our studies also extend to new anti-parasitic agents to treat highly drug-resistant gastrointestinal parasites in livestock, as well as "natural" strategies to control the devastating "toxic" impact of cane toads on Australian native predators. To achieve these goals we have assembled core expertise and infrastructure in organic chemistry, including sophisticated technologies and methodologies in analytical, chromatographic, spectroscopic and synthetic chemistry. Strategic alliances and collaborations across academia, industry and government further extend our capability into the disciplines of zoology, ecology and microbiology, as well as cell and molecular biology, pharmacology and biochemistry.

lab members

Personal Assistant: Naomi Epstein
Research Officers: Dr Angela Salim, Dr Andrew Piggott, Dr Hua Zhang, Dr Xue Xiao
Research Assistant: Jill Robb
PhD Students: Walter Balansa, Raju Ritesh, Soumini Vijayasarathy, Fabien Plisson, Zeinab Khalil, Xiao-Cong Huang, Venkat Kamalakkannan, Rakesh Damodar, Michelle Quezada
Undergraduate Students: Nicole Silajew, Azzah Suboh
International Visiting Scientists: Dr Fuhang Song (China), Dr Zhan-Lin Li (China)

matt cooper

DRUGS AND DIAGNOSTICS FOR SUPERBUGS, VIRUSES AND CANCER

We believe that we can more effectively treat patients by improving the way we diagnose disease. Our research is aimed at discovering new ways of treating viral and bacterial infections and cancer. We are designing and developing novel antibiotics active against drug-resistant bacteria, known as superbugs. The alarming growth of superbugs, coupled with the paucity of companies working in this area, gives impetus to this research and our efforts communicating these issues in the media, including SBS's *Insight*. We also work on tuberculosis and dengue fever, diseases responsible for millions of deaths in the developing world. Our research is leading to new ways to diagnose infections caused by bacteria and viruses, and a deeper understanding of the molecular mechanisms that lead to the evolution and spread of drug resistance. Many of the research team have significant experience in both academia and industry, with past projects leading to products on the market today. We collaborate with government agencies, pharmaceutical, biotechnology and medical device companies in Australia, Asia, UK, US. We have a strong translational focus and aim to deliver innovative solutions for unmet medical needs in the community. The Cooper Laboratory has received funding from the IMB, UQ, industry, ARC, NHMRC, philanthropists, and international organisations, including generous support from the Wellcome Trust.

lab members

PA/Group Coordinator: Jan Pinder
Administration Assistant: Chris Steel
Research Officers: Dr Bernd Becker, Dr Mark Blaskovich, Dr Tanya Bradford, Dr Mark Butler, Dr Frank Fontaine, Dr Reena Halai, Dr Karl Hansford, Dr Xiao Huang, Dr Tomislav Karoli, Dr Zyta Ziora, Dr Sreeman Mamidyala, Dr Craig Muldoon, Dr Rajaratnam Premraj, Dr Avril Robertson, Dr Alberto Silva, Dr Johannes Zuegg
Research Assistants: Angela BadilloVega, Gayathri Jayaraman, Ruby Pelingon, Soumya Ramu, Max Ranall
PhD Students: Mu Cheng, Daniel Croker, David Thomson, Megha Bajaj
Masters Student: Tran Thi Dat Nguyen
Summer Students: Azzah Suboh, Xuyu Liu, Natalia Brodaczewska, Alvin He, Lu Xiaohua, Kate Bastick

david craik

NMR AND PROTEIN STRUCTURE IN DRUG DESIGN

Our laboratory determines the structures of proteins that are important in drug design and agriculture, and uses this information to design new drugs and crop protection agents. We undertake studies in which we modify proteins by "grafting" new biologically active sections onto them, or by stabilising them by cyclisation. We have molecules under development for the treatment of multiple sclerosis, cardiovascular disease, cancer and chronic pain. We also undertake fieldwork in Australia and overseas for the collection of plant species so we can explore the diversity and evolution of the cyclotide family of plant proteins. We study the structures of a range of toxins from cone snails, spiders and snakes and use this information to understand their mode of action against ion channels and other receptors.

lab members

Research Officers: Dr Norelle Daly, Dr Richard Clark, Dr Masa Cemazar, Dr Joshua Mylne, Dr Quentin Kaas, Dr Sonia Henriques, Dr Karl Johan Rosengren, Dr Joakim Swedberg, Dr Tina Schroeder, Dr Xinying Jia
Research Assistants: Dr David Wilson, Chia-Chia Tan, Ashley Cooper, Aurelie Chanson, Amy Argyros, Uru Malik, Phillip Walsh, Philip Sunderland, Olivier Cheneval, Dr Peta Harvey, Dr Yen-Hua (Crystal) Huang, Soohyun Kwon, Anjaneya Ravipati (Swami), Husen Jia (Ari)
PhD Students: Laura Cascales, Philip Nguyencong, Crystal Yen-Hua Huang, Louise Thorstholm, Phillippa Smith, Basar Oku, Muharrem Akcan, Angeline Chan, Aaron Poth, Rilei Yu, Alysha Elliot, Bodil Carstens, Tunjung Mahatmanto, Uru Malik, Anne Conibear, Paola Ojeda, Charlotte Dsouza
Occupational Trainees/Visiting Students: Elizabetha de Souza, Philipp Cromm, Marcus Gerlach, Iselin Elvheim, Stijn Agten, Ludovico Migliolo
Undergraduate Students: Johanna Coyle, Joseph O'Neill, Joel Herring
Sabbatical Visitors: Dr Octavio Franco, Dr Chongxu Fan, Dr Christian Gruber
Honours Students: Kate Martinac, Christina Delay

ben hankamer

ALGAL BIOFUELS

The development of CO_2-neutral fuels for the future is one of the most urgent challenges facing our society for three reasons: to minimise the effects of climate change, ensure fuel security and provide a secure basis for sustainable economic growth. Currently, most global energy is used in the form of fuel (e.g. coal, gas, oil), with only 17% used as electricity. Yet, almost all clean energy systems being developed, such as wind, wave and solar technologies, are focused on electricity generation. We are targeting the larger fuel market by developing microalgae systems that capture solar energy and convert it into fuels (e.g. biodiesel, methane, ethanol or hydrogen). A major advantage of this technology is that it can be located on non-arable land and use waste and saline water sources, essentially eliminating the *food vs. fuel* concerns of earlier biofuel systems (e.g. corn ethanol). Microalgae could also produce a wide range of high-value products, such as medically active peptides, at agricultural scale. This has the potential to couple to medical research at the IMB to novel scale-up production systems. To maximise the speed of development the Solar Biofuels Consortium (www.solarbiofuels.org) was established in 2007. It now includes seven international teams of ~100 researchers and approximately 10 industry partners who together are conducting all aspects of research from bio-discovery through to bioreactor scale-up. At IMB, we have conducted extensive economic modelling that guides the development of profitable systems. These economic models help identify key factors for optimisation. A major focus of the lab is the structural biology of membrane proteins and macromolecular assemblies, in particular those of the photosynthetic machinery, which drives the first step in biofuel production.

lab members

Research Officers: Dr Michael Landsberg, Dr Ian Ross, Dr Melanie Oey
Research Assistant: Rosalba Rothnagel
PhD Students: Juliane Wolf, Evan Stephens, Khairul Radzun, Erin Ahern, Tony Bui, Emily Knauth, Anne Sawyer, Winnie Waudo, Maurizio Chioccioli, Eugene Zhang, Andrew Ringsmuth, Rubbiya Ali, Gisela Jakob, Jennifer Yarnold

glenn king

BUGS AND DRUGS: rational development of novel antibiotics, analgesics, and environmentally-friendly insecticides

Research in my laboratory is aimed at the development of novel pharmaceuticals and environmentally-friendly insecticides by harnessing the remarkable chemical diversity encoded in the venoms of spiders, scorpions, and centipedes. We also study signalling by bacterial proteins in order to establish a platform for the development of novel antimicrobial agents. Expertise is available in the group to take a molecule all the way from discovery to preclinical studies. Most research projects are highly interdisciplinary and the experimental techniques employed range from molecular biology through protein chemistry to structure determination using NMR spectroscopy and X-ray crystallography. Research in the lab is currently funded by grants from the Australian Research Council, National Health and Medical Research Council, and Grain Research & Development Corporation.

lab members

Senior Research Officers: Dr Susan L. Rowland, Dr Mehdi Mobli
Research Officers: Dr Raveendra Anangi, Dr Kathryn Greenwood, Dr Volker Herzig, Dr Rikki Hvorup, Dr Brit Winnen
Research Assistant: Radha Seshadri
PhD Students: Margaret Hardy, Sandy Gonzalez, Jonas Jensen, David Morgenstern, Natalie Saez, Darshani Rapasinghe
MSc Students: Sing Yan Er, Xiao Zhen Lin, Sebastian Senff, Nga Pham

richard lewis

PHARMACOLOGY OF MARINE TOXINS

Peptides are small proteins that can be used in research or new therapeutics. Much of my team's research focuses on the conotoxins, small peptides from predatory marine snails, many of which have potential in pain management. These mini-proteins act selectively at a wide range of ion channels, receptors and transporters found in the membranes of cells. This research starts with the discovery of new venom peptides, the synthesis of these peptides, studying their effect on tissues and receptors, cellular imaging of functional effects through to finally co-crystal structures and docking models revealing how the peptide binds to its target. Several conotoxins discovered in my group have been taken into the clinic, including Xen2174 for severe pain. In addition, we are studying how another class of marine toxins, the ciguatoxins, produces the debilitating disease known as ciguatera.

Highlights for 2011 include patenting a new assay allowing the rapid discovery of new inhibitors of sodium channels that are critical to the transmission of pain signals. Our research is supported by a National Health and Medical Research Council Program (2010-2014) and Project (2011-2013) grants, two Australian Research Council Discovery grants (2012-2014), and Fellowships to key personnel.

lab members

Research Officers: Dr Irina Vetter (NHMRC Training Fellowship), Dr Anderson Wang, Dr Sebastien Dutertre (UQ Fellowship), Dr Lotten Ragnarsson-McGrath
Research Assistant: Asa Anderson, Marco Inserra
PhD Students: Marco Inserra, Josh Wingerd, Silmara Rodrigues de Sousa, Prerna Jha
MSc Students: Prerna Jha, Mriga Dutt, Nikita Abraham, Prasanth Jutty Rajan
Program Grant Administration Officer: Thea Monks
International Visiting Scientists: Dr Katharina Zimmermann (Germany), Dr Cheryl de Valliere (Switzerland), Sergio Agustín Román González (Mexico)

jenny martin

PROTEIN STRUCTURE AND DRUG DESIGN

Our goal is to better understand how proteins cause disease and to develop novel drugs targeting disease-causing proteins, especially those involved in inflammation, diabetes and infection. For example, macrophages are cells that represent the body's first line of defence against infection, but they can cause inflammation. In 2011, we defined the structures of three proteins present in high levels in macrophages.

Insulin stimulates glucose uptake into fat and muscle cells, a process affected in Type II Diabetes. With David James (Garvan), we are investigating the molecular mechanisms behind this function. We have shown that the protein Munc18c stimulates delivery of glucose transporters to the surface of fat cells and provided an explanation for how this is regulated.

We have also begun developing inhibitors of bacterial DSB proteins as potential drugs that may overcome antibiotic resistance. DSB proteins catalyse the reactions that enable bacteria to cause disease. We have identified chemicals that bind to target DSB proteins that we are now optimising for potency and efficacy. We are also establishing a DSB structural library to underpin future drug design efforts on important human pathogens. This year we have solved the structures of two DSB proteins.

lab members

Senior Research Officers: Dr Begoña Heras, Dr Shu-Hong Hu, Dr Premkumar Lakshmanane
Research Officers: Dr Andrew Whitten (NHMRC Fellow), Dr Gordon King, Dr Maria Halili, Dr Karl-Fredrik Lindahl, Dr Michelle Christie, Dr Mathieu Coincon, Dr Roisin McMahon, Dr Julia Archbold (NHMRC Fellow), Dr Kevin Chen
UQ ROCX Facility Manager: Karl Byriel
Research Assistants: Russell Jarrott, Stephanie Tay
PhD Students: Kevin Chen, Patricia Walden, Asma Rehman, Wilko Duprez, Fabian Kurth
Honours Student: Heather Nutt
Visiting Scientist: Sofia Caria (Monash)
Visiting Student: Reinhard Zech (U Bremen, Germany)

mark smythe

COMBINATORIAL CHEMISTRY AND MOLECULAR DESIGN

Our research focuses on advancing drug design and synthetic, organic and peptide chemistry to discover novel drug candidates. We apply these design and discovery methodologies to discover new drugs to treat unmet medical needs or provide better therapeutic solutions to existing marketed drugs.

Our projects are multidisciplinary and focus on achieving medical outcomes. They range from technology development and early drug discovery to preclinical candidate selection. Using a combination of mathematics, software development, drug design, medicinal chemistry and phage display, we are developing new approaches to treat asthma, leukaemia and inflammatory bowel disease.

In addition, we have designed and synthesised a new spin label to accurately determine distances in biological systems, capitalising on rapid advances in biological techniques. Determining distance is a vital step in understanding a molecule's structure, which is integrally linked to its function.

lab members

Senior Research Officers: Dr Craig Murphy, Dr Greg Bourne, Dr Sonya Scott,
Research Officers: Dr Jenny Zhang, Dr Fernanda Cardoso, Dr Rayma Mandyam, Dr Woan Mei Kok
Research Assistants: Jaimee McMahon, Eva Mowe, Angelika Christ
PhD Student: Christina Kulis

joint appointments & affiliates

Joint appointments and affiliates exist to foster research collaborations between IMB and other institutes and schools at The University of Queensland. They are actively involved in our labs and facilities, share supervision of students, and attend IMB events.

Joint appointments

Professor Philip Hugenholtz
School of Chemistry and Molecular Biosciences

Professor Geoff McLachlan
School of Mathematics and Physics

Professor Scott O'Neill
Monash University

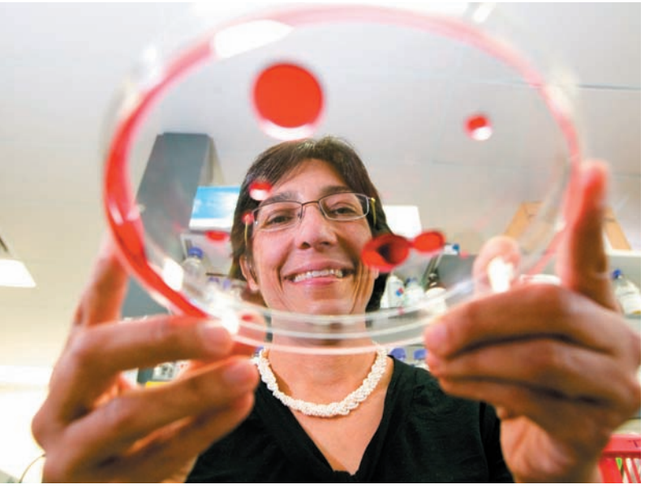
Affiliates

Mikael Boden
School of Chemistry and Molecular Biosciences

Professor Matt Brown
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

Dr Richard Clark
School of Biomedical Sciences

IMB Affiliate Professor Ranjeny Thomas, Diamantina Institute for Cancer, Immunology and Metabolic Medicine



Professor Nicholas Fisk
Faculty of Health Sciences

Professor Ian Frazer
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

Professor Jane Hunter
School of Information Technology and Electrical Engineering

Associate Professor Stuart Kellie
School of Chemistry and Molecular Biosciences

Professor Bostjan Kobe
School of Chemistry and Molecular Biosciences

Professor Daniel Markovich
School of Biomedical Sciences

Professor Alan Mark
School of Chemistry and Molecular Biosciences

Associate Professor Fred Meunier
Queensland Brain Institute

Dr David Pennisi
School of Biomedical Sciences

Dr Allison Pettit
UQ Centre for Clinical Research

Dr Liza Raggatt
UQ Centre for Clinical Research

Dr Johan Rosengren
School of Biomedical Sciences

Associate Professor Joe Rothnagel
School of Chemistry and Molecular Biosciences

Dr Kate Stacey
School of Chemistry and Molecular Biosciences

Professor Ranjeny Thomas
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

Associate Professor Peter Thorn
School of Biomedical Sciences

Professor Istvan Toth
School of Chemistry and Molecular Biosciences

Associate Professor Christine Wells
Australian Institute of Bioengineering and Nanotechnology

Professor Paul Young
School of Chemistry and Molecular Biosciences

core research facilities

1 Australian Cancer Research Foundation (ACRF) Cancer Biology Imaging Facility and ACRF Dynamic Imaging Facility

Located on Level 6 of the IMB, the ACRF Cancer Biology Imaging Facility was founded with a $2.5 million ACRF grant. The ACRF Dynamic Imaging Facility on Level 2 was established with a $1.2 million ACRF grant some years earlier. Both facilities allow the advanced imaging of cancer cells using different techniques.

2 UQROCX – Crystallisation Facility

The UQ Remote Operation Crystallisation and X-ray Diffraction Facility, on Level 2 of IMB, is a crystallisation and crystallography facility funded by the Australian Research Council and UQ.

3 Protein Expression Facility (PEF)

PEF, located at UQ's Australian Institute of Bioengineering and Nanotechnology, provides the complete infrastructure and training needed for recombinant protein expression, thus enabling research that is otherwise too costly and laborious for individual laboratories.

4 Australian Zebrafish Phenomics Facility (AZPF)

The AZPF, on Level 1 of IMB, assists Australian scientists to continue high-quality, world-class research by providing support for zebrafish facilities and/or activities to enhance the national health and medical research effort.

Dr Frank Fontaine using the ACRF Cancer Biology Imaging Facility.

5 Molecular and Cellular Proteomics Mass Spectrometry Facility (MCPMSF)

Located on Level 7 of IMB, the MCPMSF houses a complement of state-of-the-art mass spectrometric, high-performance liquid chromatographic and robotic instrumentation.

6 Nuclear Magnetic Resonance (NMR)Facility

The NMR Facility, with equipment on Levels 2 and 7 of IMB, makes the powerful technique of nuclear magnetic resonance spectrometry accessible to research groups and industry clients.

7 Facility for Life Science Automation (LISA)

LISA, on Level 6 of IMB, uses its robotic equipment and expertise to assist both internal and external clients in performing cell-based RNA interference screens in tissue culture.

occupational health & safety

The University of Queensland and IMB emergency response systems were tested early in the year by the Brisbane floods in January. Extensive damage was recorded in some areas of the St Lucia and Gatton campuses, but the IMB was not significantly affected. After a difficult start to the year, the IMB continued to produce high-quality research and maintain a high standard of workplace safety and regulatory compliance.

Significant events in 2011

- IMB personnel took the opportunity in the months after the flood crisis to review our emergency response systems and infrastructure, and update our procedures manual.
- IMB passed all mandatory Australian Quarantine and Inspection Service (AQIS) and Office of Gene Technology Regulation (OGTR) compliance audits and audits by the Brisbane City Council for compliance with license requirements for bulk storage of flammable liquids.
- As indicated in the 2010 OH&S report, the IMB responded to significant changes in the AS2243 (2010) series with some new policies, including a requirement for mandatory eye protection in all laboratories.
- The 2010 OH&S report goal of a significant decrease in the number of needlestick injuries was achieved, with none reported in 2011.
- The Cairns branch of the *Eliminate Dengue* project led by Professor Scott O'Neill was visited and the safety systems were audited by IMB Safety Manager Dr Paul Lovelock. The group has now implemented most of the suggested improvements.
- One of our floor managers, Anne Tobin, was temporarily seconded to the UQ OH&S Unit to assist with biosafety work; Dr Paul Lovelock, Floor Manager Jill Bradley and Anne Tobin continued to assist the Unit in carrying out campus biosafety and general safety audits in other areas of the St Lucia campus.

Challenges for the IMB's safety infrastructure in 2012 include:

- Modifying and updating policies and procedures to ensure compliance with new nationally harmonised OH&S legislation effective as of January 1, 2012, and communicating these changes to all IMB personnel.
- Retraining all current Workplace Health and Safety Officers (WHSOs) to act as Workplace Health and Safety Co-ordinators (WHSC).
- Maintaining IMB's high compliance rate for online training for Fire Safety and Workplace Safety units, and improving Laboratory Safety compliance rates.
- Maintaining compliance with UQ OH&S Goals for 2012 and continuing to actively audit IMB and UQ safety systems.
- Develop the IMB induction system further to provide detailed safety information in languages other than English.

commercialisation

IMBcom Pty Ltd has been The University of Queensland's company for commercialisation of valuable discovery research of the IMB, responsible for the protection and development of the University's IMB intellectual property portfolio. Established in 2000, the company operated as a separate commercial entity, but with a charter of service to the University's commercialisation objectives.

In November 2011 the board of IMBcom noted the forecast presented by management for the next two to three years showing declining opportunities for R&D contract revenues for the company, the uncertainty of securing services agreements with other clients, and the lack of prospects of early returns from commercialisation of IMB's IP portfolio. To preserve the company's current valuable IP and cash assets, the board of IMBcom, in consultation with its shareholder UQ Holdings, resolved to restructure the company's operations from 31 December 2011 to become a holding company for its assets. Following the restructure decision, the company made offers of redundancy to all staff.

In January 2012 the University will transfer the commercialisation functions of IMBcom to UniQuest, the largest of UQ's commercialisation companies. By mid 2012, IMBcom will have completed arrangements with its business partners and licencees to affect the seamless transfer of IMBcom's commercialisation functions, including the management of its intellectual property pipeline, to UniQuest.

In IMBcom's eleven-year existence, the company created 12 biotech start-up companies which have sourced investments of more than $100M, and contracted $25M in research funding into the IMB laboratories. These companies have raised more than $100 million through private sector investment, $25 million in federal and state government commercial grants and currently employ or contract over 50 individuals in R&D and commercialisation. These spinouts have gone on to develop strategic relationships in their own right with many other Australian and international biotechnology and pharmaceutical companies, and have encouraged the growth and establishment of service providers, adding to the fabric and critical mass of the industry in Queensland. The companies continue to mature under their own management once substantial investment is raised.

In 2011, IMBcom negotiated several significant biotechnology deals, including contracts for collaborative research, partnering and licences. The company also helped secure more than $4M in industry research grants for the IMB.

The IMB has a commitment to the training of high-quality graduate students in molecular bioscience and provides a more holistic training that includes commercial dimensions. In 2011, IMBcom continued to deliver this objective through the provision of special workshops. These "bootcamps", or BioBusiness Retreats, incorporate elements of career preparation, understanding and working in a commercial environment, and working in teams to produce valuable outcomes. The training engages experienced professionals from the pharmaceutical, biotechnology, investment and research industries, and has provided one of the building blocks of the commercial culture emerging in the IMB. These programs have provided commercial, project and team management skills to over 1000 individuals to date, some of whom have adopted careers in the industry, being placed in Queensland biotechnology companies and IMBcom itself. The IMBcom model is now widely offered by organisations that recognise that the preservation of value in intellectual property is the key to building assets upon which industry develops. Importantly, IMBcom has "incubated" more than 40 trained professionals who have entered the biotechnology industry in technical, administrative and commercial roles.

research training

IMB is home to 155 postgraduate students from more than 40 countries worldwide. The majority of the Institute's students are PhD candidates, but there are also graduates studying MPhil and coursework Masters degrees. The student cohort at IMB has been overseen by Professor Rob Capon and managed by Dr Amanda Carozzi, with Cody Mudgway as a part-time assistant. In 2011, the team grew in response to UQ's strategic plan for 2020, which involves increasing the ratio of postgraduate to undergraduate students at the university from 1:4 to 2:3 in order to supply students with extra skills for obtaining jobs in the coming decade and beyond. In order for IMB to respond to this challenge, Olga Chaourova, formerly Manager of International Development and Strategy at the Faculty of Arts, was appointed as a Recruitment and Engagement Officer, while Robyn Evans from the Faculty of Science lent her expertise one day a week on engaging science students, as well as helping with other postgraduate matters. Cody Mudgway also began to work full-time for the postgraduate office.

The team surveyed the laboratory heads to determine which labs had the capacity to take on more students, however the Institute is limited somewhat by space constraints. In order to help the university achieve its target, the IMB has been examining alternative ways of delivering quality education and training without taking on large numbers of extra research students. Professor Mark Ragan helped establish a Master of Bioinformatics, which will be run through the School of Chemistry & Molecular Biosciences. The development of new masters programs will cater for the needs of the modern workforce; for example, there is a worldwide shortage of bioinformaticians, who use computational disciplines to solve complex biological problems.

Under the guidance of Professor Capon, the team also began developing a new postgraduate website, which will launch in conjunction with the new IMB website in 2012. This will provide prospective students with a streamlined process for applying for postgraduate programs, which should save time for both laboratory heads and students. The new website will also contain more information for lab heads and currently enrolled postgraduates on milestones and processes such as nominating assessors.

The University of Queensland announced two major initiatives in 2011 aimed at improving the PhD student experience. The first of these was the Visit UQ program, which allows prospective research students from interstate the opportunity to be flown to Brisbane and meet with potential advisors and tour the facilities. The Graduate School also announced the UQ Career Advantage PhD Program, for students commencing in 2012. Students enrolled in this program will receive extra training and development opportunities in one of three areas: Higher Education Practice and Leadership; Research Innovation, Translation and Commercialisation; and Global Collaborations. Whichever program a student chooses, they will benefit from more chances to collaborate with industry and potential employers, and an extra skill set that will be applicable in a wide variety of fields.

(L-R): Cody Mudgway, Olga Chaourova, Professor Rob Capon, Dr Amanda Carozzi and Robyn Evans

Many of our students won prizes and received awards during the year, a full list of which can be found on the IMB website (www.imb.uq.edu.au). Some highlights included Ernest Tee winning the Amgen Award for best Honours student and Dean's Awards to Drs Kylie Alexander (Sweet lab), Mark Howes (Parton lab) and Yen-Hua (Crystal) Huang (Craik lab) for being in the top 10% of PhD graduates at the university in 2011.

The IMB postgraduate office is looking forward to the challenges and opportunities of 2012 as they seek to provide a high level of support for the Institute's students.

alumni conferrals 2011

NAME	SUPERVISOR	THESIS TOPIC	DESTINATION
Angela Jeanes	Yap	PI3K signalling in the maintenance of epithelial cell structure: Analysis of E-cadherin-based adhesion and cell height	School of Biomedical Sciences, UQ
Philip Nguyencong	Craik	The Discovery, Isolation and Characterisation of Cyclic Trypsin Inhibitors from Momordica cochinchinensis and other Cyclotides	AlphaPharm, Brisbane
Lisa Crowther	Muscat	Elucidating the Role of Chicken Ovalbumin Upstream Promoter-Transcription Factor II (COUP-TFII) in Skeletal Muscle: Implications for Metabolism	Queensland Children's Medical Research Institute, Brisbane
Caroline Hendry	Little	Reprogramming adult kidney epithelial cells to induced nephron progenitors	Mt Sinai Medical Center, New York, USA
Sabine Mangold	Yap	Characterizing the role of Myosin VI at E-cadherin cell-cell adhesions	Eskitis Institute, Griffith University, Gold Coast
Samantha Murphy	Parton	Characterisation of Lipid Droplet Metabolism	Monash University, Melbourne, Victoria
Pei Low	Stow	Investigating the Role of Phosphoinositide 3-Kinase in Cytokine Trafficking and Secretion	Barts Cancer Institute, London, UK
Joao Marcal Fidalgo	Cassady	Characterisation of the role of PPAR-delta in Osteoclast Biology	QML Brisbane
Rodrigo Morales	Alewood	Chemical synthesis and pharmacological characterization of the frog Prokineticin Bv8 and study of the mechanism of chemical defence of cane toads (Rhinella marina)	Monash Institute of Pharmaceutical Sciences, Melbourne, Victoria
Jonathan Robson	Wainwright	The role of Patched1 during development of the mouse cerebellum and regulation of neural stem cells in medulloblastoma	Institute for Molecular Bioscience
Alhadi Bustamam	Burrage	Modelling statics networks in bioinformatics applications using advanced computing.	Uni. of Indonesia, Depok, West Java
Kai-En Chen	Martin	A structural genomics approach to the structure determination of macrophage proteins	Academia Sinica, Taiwan
Evan Stephens	Hankamer	Commercialisation and Development of Integrated Microalgal Production Systems	Institute for Molecular Bioscience
Joo Young Choi (MPhil)	Ragan	Exploring small molecules and their drug-like properties using Semantic Web technologies	Korean Institute of Criminology, Seoul, Korea
Paulo Amaral	Mattick	Expression and chromatin association of noncoding RNAs	University of Cambridge, UK
Thomas Whitington	Bailey	Using ChIP-seq technology to understand transcription factor biology	Karolinska Institute, Stockholm, Sweden
Ritesh Raju	Capon	Exploring the Chemical Diversity of Australian and Fijian Marine Microbes	Helmholtz Centre for Infection Research, Saarbrücken, Germany
Laura Cascales Bolano	Daly	MCoTI-II Biosynthesis and Applications	University of Zurich, Switzerland
Margaret Hardy	King	Isolation and characterization of orally active insecticidal peptides from spider venoms	Institute for Molecular Bioscience
Muharrem Akcan	Craik	Design and discovery of cyclic peptides with applications in drug development	Institute for Molecular Bioscience
Nurul Mohamad (MPhil)	Boden	The collection and data-driven analyses of proteins localized to nuclear compartments	Malaysian Biotechnology Corporation, Kuala Lumpur
Daniel Shaw	Collins	Structural Basis for Assembly and Membrane Modulating Properties of the Retromer Protein Coat Complex	Hastings Deering, Brisbane

support staff

Executive Assistant Sue Allen

Finance Manager Angela Gardner

Principal Finance Officer Scott Aldridge

Finance Officers Jackie Gidley, Louise Hendriks, Danielle Rodgers, Sanjay Sundarlal, Fiona Zhang

Purchasing Officers Robyn Craik, Beverley Forrest, Thi Lu, Rosanna Quinlivan

Grants Officer Michelle Foley

Office Manager Lucinda Essery

Receptionists Gail Howard, Patricia Howarth, Desla Shand, Erin Shand

Mail Clerk Margarette Elsmore

Infrastructure Manager Chris Barnett

Floor Managers Jill Bradley, Charles Ferguson, Christine Fraser, Jacky Hung, Ian Lane, Miki Miyagi, Jodie Robinson, Anne Tobin

Workshop Manager Mick Thwaite

Workshop & Maintenance Gary Carloss, Rene Croisier, Jason Hurst, Leigh Rose, John Srnka, Mark Ziza

Store Manager Barry Pitt

Storemen Bob Allen, Jeremy Mead

Central Sterilising Facility Manager Dawn Walsh

Central Sterilising Facility Marie Campbell, Linda Molloy

Safety Manager Dr Paul Lovelock

HR Consultants Joanne French, Caraine Gomez, Felicity Ray, Samantha Dyson

HR Officer Natasha Crocker

IT Manager Rowan Gronlund

IT Staff Derek Benson, Damien Beverley, Matthew Bryant, Christian De Marco, Brett Dunsmore, Calvin Evans, Chris Hunt, Nelson Marques, Scott Martin, Lance Rathbone, Marcus Schull, Jimmy Wu

Communications Officer Bronwyn Adams

Advancement Assistant Emma Lee

Postgraduate Administrative Officer Dr Amanda Carozzi

Postgraduate Recruitment Robyn Evans

Postgraduate Assistant Cody Mudgway

engagement

With the support of the University's senior management, and in response to a new ten-year strategy at UQ, IMB engagement took a new direction in 2011 with the appointment of a Deputy Director (Advancement) to oversee alumni and community engagement, communications and philanthropic giving in late June. Amanda Whelan worked as a lobbyist for one of the U.S.'s highest-ranking environmental law firms, before joining the Florida Association of Counties as a Senior Adviser and Advocate. Ms Whelan is committed to growing the philanthropic support IMB currently receives as well as raising the Institute's overall profile.

Left to right: UQ Chancellor John Story, Dr Rosamond Siemon, Amanda Whelan, Andrew Stallman and Jill Stallman at UQ's Celebration of Giving, hosted by IMB.

IMB's team of volunteer Science Ambassadors are a group Ms Whelan hopes to further engage in the future. Science Ambassadors are researchers at IMB who are passionate and committed to sharing their work and love for science with the community at-large. In 2011, there were a total of 23 Ambassadors, and together they provided tours, visited local schools and hosted numerous local, national and international visitors at the IMB, including delegates and politicians. This year's program was overseen by a committee including Ambassadors Dr Richa Dave (Co-ordinator), Dr Elaine Julian (Material Manager), Phillippa Smith and Dr Margaret Hardy (past Co-ordinators and Advisers), Dr Michael Tallack, and administrative staff Dr Amanda Carozzi (Student Administrative Officer), Jenny Greder (Marketing Manager) and Bronwyn Adams (Communications Officer). Ambassadors in 2011 were: Dr Guy Barry, Dr Nilesh Bokil, Dr Andrew Brooks, Natasha Chaudhary, Dr Nicole Cloonan, Baptiste Coxam, Dr Marcel Dinger, Wilko Duprez, Dr Guillermo Gomez, Marga Gual Soler, Dr Michael Hanzal-Bayer, Julie Klint, Tunjung Mahatmanto, Uru Malik, Kelly-Anne Masterman, Nur Intan Ruhaiyem, Anne Sawyer, Evan Stephens and Brit Winnen.

In November, IMB hosted the University's largest annual donor event, *Celebration of Giving*. More than 240 donors and supporters of UQ attended the reception, including Andrew Brice, Patricia Byrne, Lesley Bryant, Dr Rosamond Siemon, Dr Donald Tugby, Ms Jessie Yeowart, Dr Felice Zaccari and Mrs Margredel Zaccari. Guests received guided tours of the Institute from IMB Laboratory Heads and Science Ambassadors, were briefed on the research currently underway across the University and were thanked for their generous donations to UQ over the past year.

Engaging with the community can take many forms. Researchers Darren Brown and Dr Michael Landsberg, the winner and runner-up of 2010's Ångström Art competition, had already proven their talent at producing stunning images. In 2011, they reinforced this by having images selected for *Incredible Inner Space*, an exhibition of scientific art displayed at Questacon. The images can be viewed at www.ammrf.org.au/innerspace

Dr Nick Hamilton and artist Joannah Underhill also began exploring the nexus of art and science in a collaboration that was named one of the 10 most innovative in the country by *The Australian* newspaper. Ms Underhill is a cancer survivor who is using the imaging and microscopy equipment of the Australian Cancer Research Foundation Cancer Biology Imaging Facility and the expertise of Dr Hamilton and researcher John Griffin to view and paint her cancerous cells. She will be exhibiting this work in 2012 at venues including the Royal Brisbane and Women's Hospital where she received treatment. Ms Underhill will be blogging about her residency at IMB at: http://envisagingtheinvisible.blogspot.com.au/, and one of her works features on the front of this report.

financials

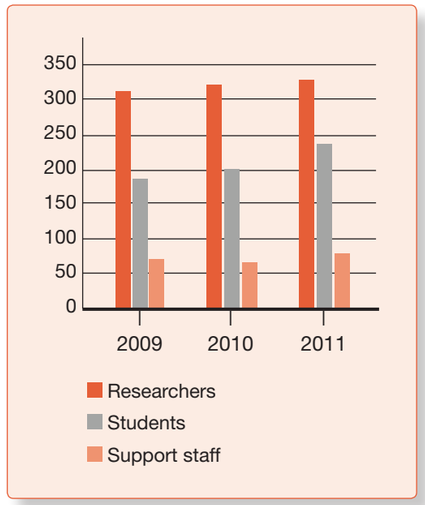
INCOME STATEMENT

INCOME	2009 $'000	2010 $'000	2011 $'000
PEER REVIEWED INCOME			
ARC Grants	7,257	8,086	7,500
NHMRC Grants	15,488	19,865	20,866
State Government Grants	4,896	826	1,663
Other Peer Reviewed Grants – Domestic	3,157	6,051	5,157
Other Peer Reviewed Grants – International	1,037	713	2,794
OPERATING INCOME			
UQ Awarded Grants	5,701	4,137	4,769
UQ Operating Funding	6,114	6,321	6,539
State Government Grants	10,000	10,000	10,000
Sales and Services Revenue	1,760	1,252	951
OTHER INCOME			
Philanthropy	2,216	1,882	1,136
Commercialisation	3,006	3,226	3,242
Other Income & Recoveries	141	107	57
TOTAL INCOME	**60,774**	**62,465**	**64,674**
EXPENDITURE			
SALARIES			
Researchers	25,101	29,890	31,206
Infrastructure	2,619	2,656	2,752
Administrative	1,637	1,865	2,002
RESEARCH EXPENDITURE			
Research Services	14,533	17,027	16,371
Commercialisation*	1,200	1,200	1,200
Research Higher Degree Support	1,199	1,253	1,384
UQ Internal Collaborations and Agreements	807	683	810
OPERATING EXPENSE			
Capital Equipment	4,868	5,928	5,530
Information Technology	879	745	674
Administration and Support	326	330	359
Infastructure and Development	1,332	1,071	1,010
TOTAL OPERATING EXPENDITURE	**54,503**	**62,649**	**63,298**
NET INCOME	**6,271**	**(184)**	**1,375**

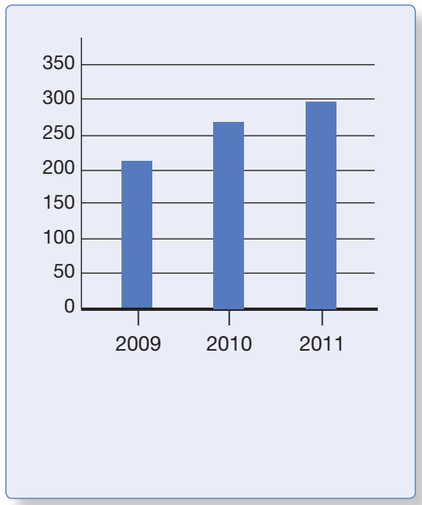
* IMBCom service agreement

The IMB financial figures have been presented in a simplified manner compared to previous annual reports.
For more information, please email finance-manager@imb.uq.edu.au

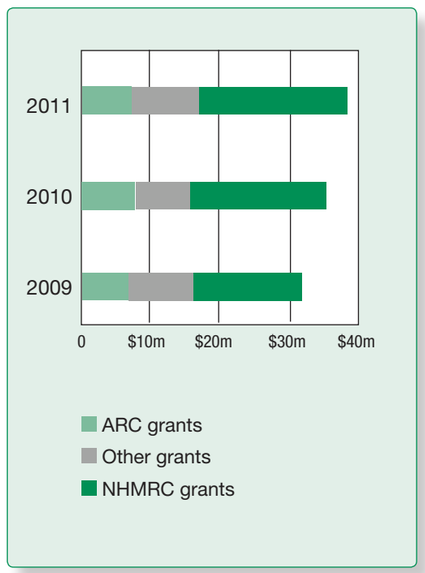
STAFF AND STUDENTS



SCIENTIFIC PUBLICATIONS



PEER REVIEWED GRANT INCOME



DISTRIBUTION OF EXPENDITURE

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History boosts future of kidney research

Kidney research at IMB is progressing well thanks to a generous donation from a historian with an eye on the future.

For the past several years, Dr Rosamond Siemon, an author and UQ alumnus with a PhD in history, has fully funded a PhD scholarship for kidney research to Professor Melissa Little's laboratory at IMB. The first recipient of the scholarship, Caroline Hendry, graduated from UQ in July 2011.

Dr Hendry's dissertation involved forcing adult kidney cells to turn back into kidney stem cells, which may one day hold the key to repairing the kidney without dialysis or a transplant.

"The project was a huge risk, it was never going to attract formal government funding until I could provide preliminary data proving it was theoretically possible," Dr Hendry said. "Having the scholarship allowed me to pursue that data, and Professor Little won a $600,000 government grant purely based on results from the first year of my PhD, as well as honours. We've now been able to push the adult kidney cells to a place where they do behave a lot like kidney stem cells."

The success of the project is partly due to the travel funding that came with the scholarship, which allowed Dr Hendry to attend international meetings with others in the field who were attempting similar feats.

"Absolutely no one else in Australia was working in that space and to be able to talk with people about what was happening in their labs right that minute and how they dealt with roadblocks was priceless. Once I got back, having spoken to all of those people and soaked up their ideas, the project just went into overdrive and everything was happening."

Dr Siemon decided to donate funding for the scholarship after her son-in-law died from polycystic kidney disease, an inherited disorder for which there is currently no cure.

"I never heard of the disease before my son-in-law fell ill with it," Dr Siemon said. "He suffered for twenty years before his death. I don't want my descendants, or anyone else, to suffer like that, so I thought I would do what I could to find a solution. I would like to think others are doing whatever they can to find solutions to the diseases they know about. We will never find answers without research."

(L-R): Professor Melissa Little, Dr Rosamond Siemon and Dr Caroline Hendry at Dr Hendry's graduation

"It's meant an awful lot for me," Dr Hendry said of the scholarship. "I feel a lot more responsibility and commitment because I know this is somebody's personal wish to bestow this money and see something good come out of it. I thought about it when I was in the lab on Saturday night instead of going out. It was good to know someone was backing me."

Dr Hendry is now working as a researcher at the Mt Sinai Medical Center. Barbara Maier has been selected as the next scholarship recipient, and will begin her project in Professor Little's laboratory in 2012.

Make a difference today, contact the IMB Advancement Office to learn how you can donate a research scholarship: (+61) 7 3346 2132 or advancement@imb.uq.edu.au

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