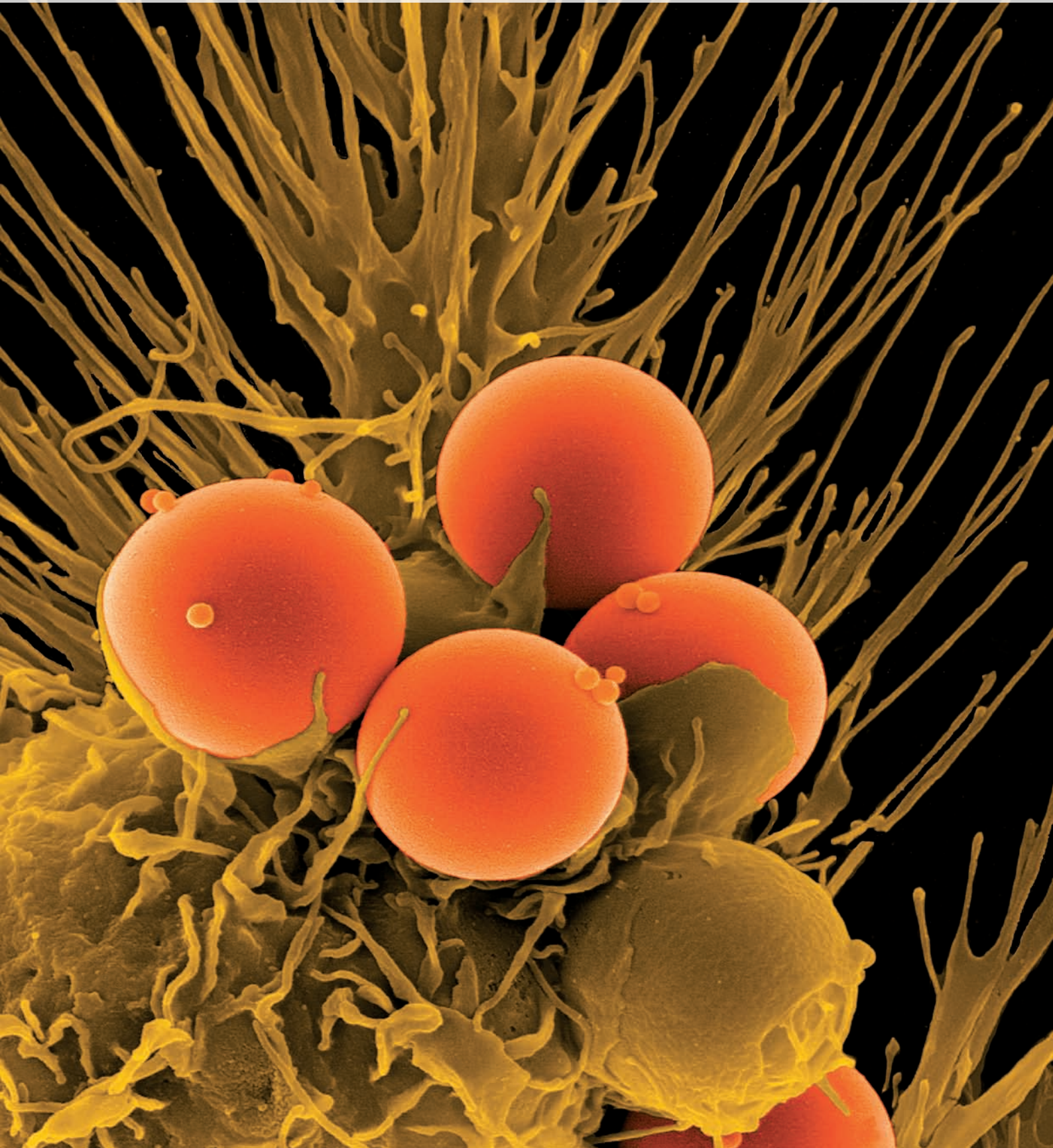
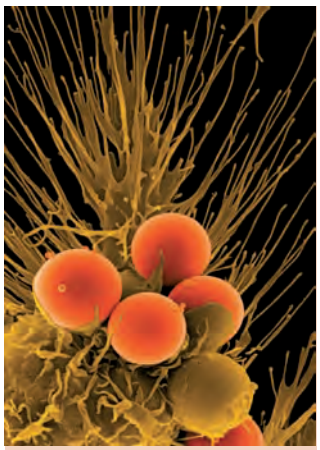
THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

IMB Institute for Molecular Bioscience

ANNUAL REPORT 2010



COVER IMAGE: WINNER OF THE 2010 IMB ÅNGSTRÖM ART COMPETITION



DARREN BROWN: MACBEADS

A merged image of two scanning electron microscope images of macrophages ingesting latex beads (dark orange) as part of the phagocytic process during the immune response. The macrophage is an immune cell that fights invading pathogens by 'eating' them – surrounding them and engulfing them.

INSTITUTE FOR MOLECULAR BIOSCIENCE ÅNGSTRÖM ART CENTENARY COLLECTION

As part of our contribution to UQ's Centenary in 2010, the Institute held an art competition. IMB researchers were invited to submit scientific images, and our judging panel selected a winner and two runners-up (see page 81 for more details).

Part of the winner's prize was having his or her image featured on the front cover of the 2010 annual report. Darren Brown, from the Stow group, was awarded this honour for his image 'MacBeads'. Altogether, 62 images were submitted, a selection of which makes up the artwork for this report. The image titles, authors and a brief description can be found alongside each.

To view the entire Centenary Collection, please visit *www.angstrom-art.com*

IMB Annual Report 2010
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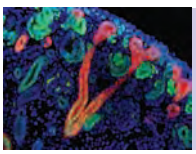


JESS INESON: TREE OF LIFE

Microscopic snapshot of a developing kidney

IMB VISION STATEMENT

CREATIVITY, MOTIVATION AND INTELLECTUAL FREEDOM are the vital components of scientific discovery and technological process, and underpin the research philosophy of the Institute for Molecular Bioscience.

Our research mission is to understand the information contained in our genes and proteins – the very foundation of our existence and health.

By understanding how and why humans and animals develop the way they do, we will be better equipped to understand the basis of our differences and how and why things go wrong in disease states like cancer.

In time, our collaborative research will lead to improved therapies and diagnostics, enhancing our ability to combat common diseases and genetic disorders.

It will also give rise to new ideas, technologies and knowledge-based industries to improve the health and quality of life of future generations.

CHAIR'S MESSAGE

2010 WAS SIGNIFICANT FOR BOTH The University of Queensland and the Institute for Molecular Bioscience. UQ celebrated its Centenary, and January 1 marked ten years since the IMB was officially established. Ninety years after its birth, UQ had its first institute.

Since 2000, the IMB has been joined by seven other UQ institutes and its budget has grown from $19.5 million to almost $90 million.

Its second quinquennial review, covering the institute's performance from 2005-2009, was conducted by a distinguished panel led by an eminent financial expert, Henry Smerdon. The review demonstrates that the IMB has emerged, in one decade, as equal in output to Australia's long-established leaders in biomedical discovery.

The review process included an assessment by the Allen Consulting Group of the IMB's economic impact. This demonstrates that the Institute generated $220 (directly and indirectly) from a Queensland Government investment of $50 million.

Further, the investment is forecast to have a significant expansionary effect, boosting Gross State Product by between $450 million and $650 million by 2029.

In other words, every $1 the Queensland Government invested in IMB will return between $4.50 and $6.50 to the state.

The advantage conferred by this public funding is reflected in human capital. The IMB has directly created 350 jobs since 2000, and Allen Consulting Group projects that employment in Queensland will increase by between 800 and 1,100 jobs by 2029, thanks to the Institute.

These impressive numbers attest to the sustained impact of strategic government support for research.

The IMB's vigour is linked to successful leveraging of seminal funds from government, The Atlantic Philanthropies and UQ, and to networks of outstanding partners in research, industry, philanthropy and not for profit organisations.

Fundamentally, the source of its strength is outstanding people – staff, students, the board, the scientific advisory committee and directors. It has been my pleasure to interact with these people during 2010, as chair of the IMB board and Vice-Chancellor of the University.

The outcomes of the first 10 years vindicate the calculated risks taken by the founders and early funders of the IMB, who foresaw that it could influence a new direction in research and innovation for UQ – and for Queensland.

The Institute for Molecular Bioscience has been instrumental to the growth in global esteem for bioscience discovery conducted in Queensland and nationally, and has established its own credentials to address complex and urgent global challenges.

Professor Paul Greenfield, AO
Vice-Chancellor
The University of Queensland

> **"...every dollar the Queensland Government invested in IMB will return between $4.50 and $6.50 to the State"**

JOHN GRIFFIN: HOOP PINE POLLEN

Hoop pines (Araucaria cunninghamii) are a species of tree endemic to eastern Australia. They produce prodigious amounts of pollen, making samples easy to obtain.

DIRECTOR'S REPORT

2010 WAS A BIG YEAR AT THE Institute for Molecular Bioscience. The University celebrated its centenary during 2010 and we marked our tenth year as an institute, joining in with major university events and running some of our own. The most significant of these was a competition for images from scientific research that formed the Centenary Collection of the IMB Ångström Art initiative. The entire collection of 62 entries was on display for The University of Queensland Centenary Community Day on the 18th of April, 2010, after which 25 of the images were selected for reproduction on iPhone skins, which have been given away at a number of university and industry events throughout the year.

The early part of the year saw us focused on preparations for the July 2010 Quinquennial Review of our State Government funding. This Review, chaired by Mr Henry Smerdon, AM, former Under-Treasurer of the State Government, was critical in determining future funding arrangements with the State Government after 2014. In addition to a submission prepared by the IMB, the Allen Consulting Group was engaged to provide an assessment of our economic and social contributions to the State.

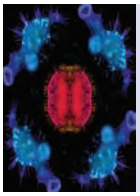
The IMB submission tracked the performance of the Institute between 2005 and 2009 across a range of measures including competitive grant income, publication output, postgraduate student graduations and commercialisation of research. Across all of these measures we performed at a comparable level to three other significant Australian biomedical science institutes – the WEHI, QIMR and the Garvan Institute. This was particularly pleasing when the relative age of each of the benchmarking institutes was taken into account, with IMB being by far the youngest. In a short ten-year period, IMB has made a significant contribution to scientific enquiry at a national and international level through publication in high-impact journals, graduation of over 180 PhD students with specialised skills in molecular bioscience, bioinformatics and chemistry, and the spinning out of 14 companies from research and discovery. From a State Government investment of $82.5 million (to the end of 2009), a total of $211.30 million in additional income has been leveraged.

At the time of going to press, the report from the Quinquennial Review Team had been presented to the State Government and preliminary discussion about future State Government funding of the IMB and other UQ research institutes, including the Queensland Brain Institute and the Australian Institute for Bioengineering and Nanotechnology, is now underway.

“In a short ten-year period IMB has made a significant contribution to scientific enquiry at a national and international level through publication in high-impact journals, graduation of over 180 PhD students with specialised skills in molecular bioscience, bioinformatics and chemistry, and the spinning out of 14 companies from research and discovery”

CANCER BIOLOGY IMAGING FACILITY OPENING

Our first major activity for 2010 was the opening of the ACRF Cancer Biology Imaging Facility by the Governor of Queensland, Her Excellency Dr Penelope Wensley, AO, in February of this year. Funded with a $2.5 million grant from the Australian Cancer Research Foundation, the new Facility combines with the existing ACRF Dynamic Imaging Facility at the IMB to provide the most sophisticated research facility in Australia for fluorescence imaging of cancer cells. The advanced laser microscopes in the facility will be used by researchers at the IMB and throughout Queensland to research the origins of cancer, develop new drugs and create prevention strategies for risk groups.



DARREN BROWN: SEADRAGONS

A fluorescence microscope image of macrophages labelled with antibodies

QUEENSLAND CENTRE FOR MEDICAL GENOMICS OPENING

The Premier the Honourable Anna Bligh, MP, performed the honours at the opening of the Queensland Centre for Medical Genomics, located within the Institute, on June 16th. This facility has been funded by the largest-ever NHMRC grant, a State Government NIRAP grant and cash and in-kind support from a number of sources including the Cancer Council of NSW, Applied Biosystems and The University of Queensland. It was a pleasure to welcome the Premier to the Institute and to showcase the new facility that will give researchers a better understanding of pancreatic and ovarian cancer, with a view to developing better treatments for these diseases. Since the Centre's opening, work has been progressing well on the sequencing of 500 different pancreatic and ovarian cancer genomes and data has been released to the research and general community through the auspices of the International Cancer Genome Consortium.

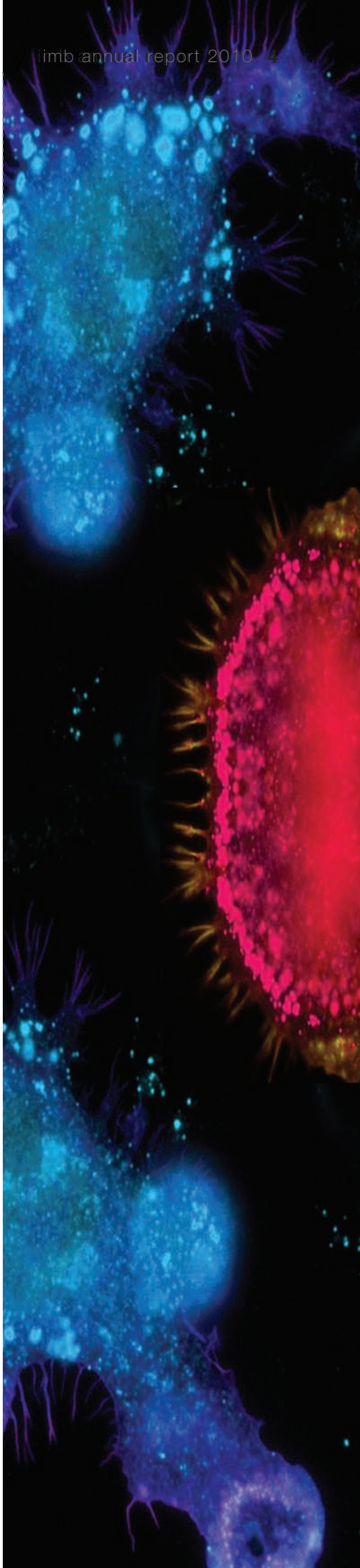
It is a mark of the excellence of the IMB that each year our researchers pick up awards from within the University and from external professional societies for outstanding contributions to science. 2010 has been no exception and my congratulations go to Professor David Craik who was awarded the Ralph F. Hirschmann Award in Peptide Chemistry from the American Chemical Society, Dr Ben Hogan who received a UQ Research Excellence Award for his research into the human lymphatic system, Dr Ryan Taft who was a finalist in the People's Choice Eureka Awards and Dr Richard Clark, who received a Queensland Health and Medical Research Senior Researcher award.

Other outstanding efforts during the year included Professor John Mattick, AO, who successfully applied for an NHRMC Australia Fellowship to follow on from his ARC Federation Fellowship, Professor Jenny Stow and Associate Professor Rohan Teasdale, who were successful in an $8.9 million NHMRC program grant application to examine cell biology and inflammation and Professor Rob Parton, who received a Best and Brightest Achievement Award from the NHMRC in March for the highest-ranked project grant nationally.

Overall our success in the major domestic grant schemes for projects commencing in 2011 was a little down on last year's success rates. We were, however, coming off a very high base, including a 59% success rate in the NHMRC schemes, and an adjustment down in our overall success rate was inevitable. This slight downward shift in the amount of domestic competitive research funding coming in for 2011 is offset, however, by the success of Professor Matt Cooper in obtaining a UK Wellcome grant for his research into new therapies for antibiotic-resistant infections. The amount of money being invested by the Wellcome Trust in Matt's research is significant and will enable him to make major strides in understanding and treating antibiotic-resistant infections.

2011 is shaping up to be a busy year. Our first UQ Academic Board Review occurs in April 2011. This Review will examine our contributions to the University, particularly in the teaching and collaborative research areas, as well as taking into account the performance metrics already submitted to the State Government. With a staff cohort committed to excellence across all areas of our operations I am confident that we will come through this second review with flying colours. I look forward to rising to the challenges of 2011.

Professor Brandon Wainwright
IMB Director



DEPUTY DIRECTORS' REPORT

RESEARCH

The end of 2009 marked the close of IMB's first decade of existence and meant it was time for our second quinquennial review. This document contained some very pleasing statistics that demonstrated how we have grown and strengthened as an organisation. For example, in the five years from 2005 to 2009, our competitive grant income from national and international sources grew to over $160m, which represented an increase of 87 percent from the first five years. Two thirds of our group leaders now support their own salaries with senior research fellowships, an increase of 50 percent in the number of fellowships since 2005. We have published over 1050 papers in the last five years, a 60 percent increase in output. Many of these papers were accepted in top-rank international journals such as *Science*, *Nature* and *Cell*, and in leading disciplinary journals. These publications were cited, on average, more than 3000 times per year, an increase of 74 percent from 2000-2004. Our success rates in NHMRC and ARC funding schemes are consistently higher than national and Queensland averages; particularly notable is our 90 percent success rate for ARC Linkage grants.

We aim to continue improving in the future. Our achievements from the first year of our second decade, outlined below, show that we are on track to achieve this aim.

Professor Sean Grimmond was part of a worldwide collaboration that published a paper in *Nature* in April. The International Cancer Genome Consortium is working to map the genomes of 50 different types and subtypes of cancer. Professor Grimmond leads Australia's research effort, which involves sequencing 500 pancreatic and ovarian tumours in collaboration with Professor Andrew Biankin from the Garvan Institute and Professor David Bowtell from the Peter MacCallum Cancer Centre.

As Professor Wainwright noted in his report, our grant results for 2010 were not as spectacular as 2009 but we still performed well. The IMB received nearly $10 million for projects and equipment from the NHMRC and the ARC, and six IMB researchers were offered a total of seven fellowships from the two funding bodies. More details of these grants and fellowships can be found in the Highlights section beginning on page 10, however I would like to make particular mention of Dr Matt Sweet, who had the opportunity to take up both an ARC Future Fellowship and an NHMRC Research Fellowship. Dr Sweet was appointed as a group leader at IMB in 2007, and his excellent results in these fellowship rounds are a testament to his leadership and the quality of his research.

Professor John Mattick's Australia Fellowship (see Professor Wainwright's report, preceding page, or Highlights section on page 10, for more details) means the IMB is now home to four recipients of this highly regarded award for medical research, and we are the only research institute in Australia to have received an Australia Fellowship every year since the program's inception.

While we rightly recognise our winners of national fellowships, the IMB is also committed to providing opportunities to support the work of outstanding early-career researchers to facilitate their move towards independent researcher status. With this in mind, the institute's executive committee decided in 2010 to create the IMB Fellowship scheme. Exceptional researchers from among our postdoctoral scientists would be selected to receive financial support for their projects, with up to four 'IMB Fellows' resident at the Institute at any one time.

Dr Joshua Mylne from the Craik group was chosen as the inaugural IMB Fellow. Dr Mylne was originally a botanist who studied vernalisation – the process by which plants sense cold and alter their flowering time. Within the Craik group, which has a strong focus on developing improved protein frameworks for drugs, Dr Mylne has been examining the potential of a mechanism within sunflower seeds to manufacture peptide drugs cheaply and quickly. This project would allow the efficient production of drugs, particularly in third-world

"We aim to continue improving in the future. Our achievements from the first year of our second decade, outlined here, show that we are on track to achieve this aim"

– Professor Jenny Stow
Deputy Director (Research)

countries. Dr Mylne's fellowship was named the John S. Mattick Fellowship after group leader Professor John Mattick, who was both the co-founder and inaugural Director of the IMB.

Many of our other researchers received recognition through prizes and awards. Professor Wainwright has already made mention of many of the most significant for 2010, however I would like to highlight an award presented to one of our Joint Appointees, Professor Geoffrey McLachlan. The Statistical Society of Australia acknowledged Professor McLachlan with the Pitman Medal, its highest honour, which recognises 'outstanding achievement in, and contribution to, the discipline of Statistics'. The gold medal is awarded annually at most, and since its inception 32 years ago has only been bestowed 18 times. In his role as a Joint Appointee, Professor McLachlan works closely with researchers from the Division of Genomics and Computational Biology, and you can read more about his research on page 64.

We had 27 students graduate in 2010, and I am pleased to report all of these students have found employment, with some remaining at IMB to continue working on projects they began in their PhDs, while a few have commenced positions in different departments of UQ or other organisations in Brisbane. One-third of the group have chosen to start their postdoctoral careers overseas, with positions in Indonesia, the USA (California and Florida), Singapore, Germany and Switzerland. While family and other circumstances can prevent some postdoctoral students from taking up work outside of Australia, the fact that so many of our students have found employment in international laboratories speaks to the world-quality training they receive at IMB. This is further demonstrated by the number of our students who receive a Dean's Commendation for Outstanding Research Higher Degree Thesis. The results for the 2009 graduates were released in 2010, and we were very pleased to see that five IMB students were recognised. This award is given to students who receive unanimous commendations from their examiners, and who make a significant contribution to their field of research. No more than 10 percent of research higher degree graduates are on this list every year, and the fact that well over 10 percent of our students were named is a credit to the students, their supervisors and the IMB graduate program.

ADMINISTRATION AND INFRASTRUCTURE

Our systems and administration staff work 'behind the scenes' to allow IMB scientists to perform our core business of research. The non-research tasks, such as delivering mail, equipment maintenance, grant administration, reception, sterilisation, receiving deliveries, purchasing and managing accounts, recruitment, communications, IT and other administrative functions are all performed by these staff, and I thank them for contributing to the IMB's success.

One staff member who deserves special recognition is our Infrastructure Manager, Chris Barnett. In 2010, Chris recorded his 25th year of employment at The University of Queensland and was recognised at a ceremony for long-serving staff. Chris began with UQ in 1985 in the department of Physiology and Pharmacology, working on developing drugs for asthma. He moved to the centre that preceded the IMB five years later. His first job at the institute was as a research assistant, looking at the molecular biology of intracellular infection. Chris has since risen through the ranks and now manages our laboratory support systems and liaises with UQ's Properties and Facilities staff to ensure the smooth running of the IMB building and facilities.

There were some senior staff movement during the year. Jeremy Kroes, IMB's Workshop Manager, left and was replaced by Michael Thwaite. Jane Weber, the Level 6 Floor Manager, moved to Melbourne and Jacky Hung took the position.

IMB hosted 5000 visitors in 2010, with visitors from universities in 27 other countries, a demonstration of the strength of our reputation and collaborations with other institutions.

"IMB hosted 5000 visitors in 2010, with visitors from universities in 27 other countries, a demonstration of the strength of our reputation and collaborations with other institutions"

– Dr Ian Taylor
Deputy Director
(Systems and Administration)

Dr Richard Clark with cyclotide-containing African plants and cone snail shells

2010 feature

PAIN RELIEF IN A CONE SNAIL SHELL

Most people wouldn't turn to a deadly marine creature for pain relief, but that's exactly what scientists at the IMB are doing, with promising results.

The cone snail, found in the waters of the Great Barrier Reef and tropical regions worldwide, has very toxic venom that can kill a person in less than 30 minutes. This venom is delivered through a barb sharp enough to pierce a diver's wetsuit. Researchers became interested in the cocktail of toxins that make up the venom when they realised that survivors of cone snail stings reported feeling no pain. Investigations into the venom revealed it contained a powerful analgesic.

The applications to human health were immediately apparent. Chronic pain occurs when the nerves themselves are damaged and is caused by a range of conditions including diabetes, stroke, cancer and nerve damage from surgery. It can be a debilitating disease, and current treatments have significant drawbacks. For a start, they are ineffective on some patients. Even when treatments do relieve pain, they have other problems. Morphine is often used in pain relief, but sufferers become used to the drug and, over time, need increasing amounts. It is also addictive and has side effects such as nausea and vomiting. Clearly, improved treatments are needed.

Enter the cone snail. Professors Richard Lewis and Paul Alewood isolated a number of molecules from cone snail venom that have the potential to relieve pain. These molecules are peptides, small proteins. The cone snail peptides, known as conopeptides, have a high specificity, meaning they hit only their target and not any other receptors. This is a sought-after attribute for drug candidates, as it lessens or eliminates side effects. The drawback to peptides? They have trouble surviving in the body, and if administered orally, are broken down by digestive enzymes before they can reach their target. Injecting a peptide drug straight to the spinal cord can ensure delivery, but increases the risk of infection. But research from another IMB laboratory is overcoming even this disadvantage.

Professor David Craik is a world expert on circular peptides, known as cyclotides. He described the first cyclotide, kalata B1, which is found in the African plant *Oldenlandia affinis*. African women use a tea made from the leaves of this plant to stimulate childbirth, which caught the attention of a Red Cross doctor in the 1960s. Some kind of protein had to be present in the tea to have an effect on the uterus, but what type of protein could survive the boiling that is part of the tea-making process? When Professor Craik determined the structure of kalata B1 in the 1990s, this question was answered: a circular protein.

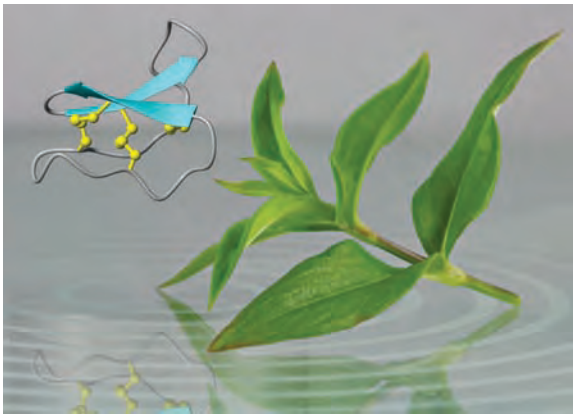
Digestive enzymes attack the ends of proteins, but circular proteins have no ends, meaning they can survive the maelstrom of the body's digestive system and travel to their target, making them an ideal template for drugs. So the IMB researchers had the two ingredients necessary: the protein that relieved pain, and the protein that could survive in the body and be delivered to the correct site for pain relief. The trick would be putting them together.

Professor Craik and Dr Richard Clark have been working on this challenge for a number of years. In 2010, they published the results of their work in the journal *Angewandte Chemie*.

> **"The cone snail peptides, known as conopeptides, have a high specificity, meaning they hit only their target and not any other receptors"**

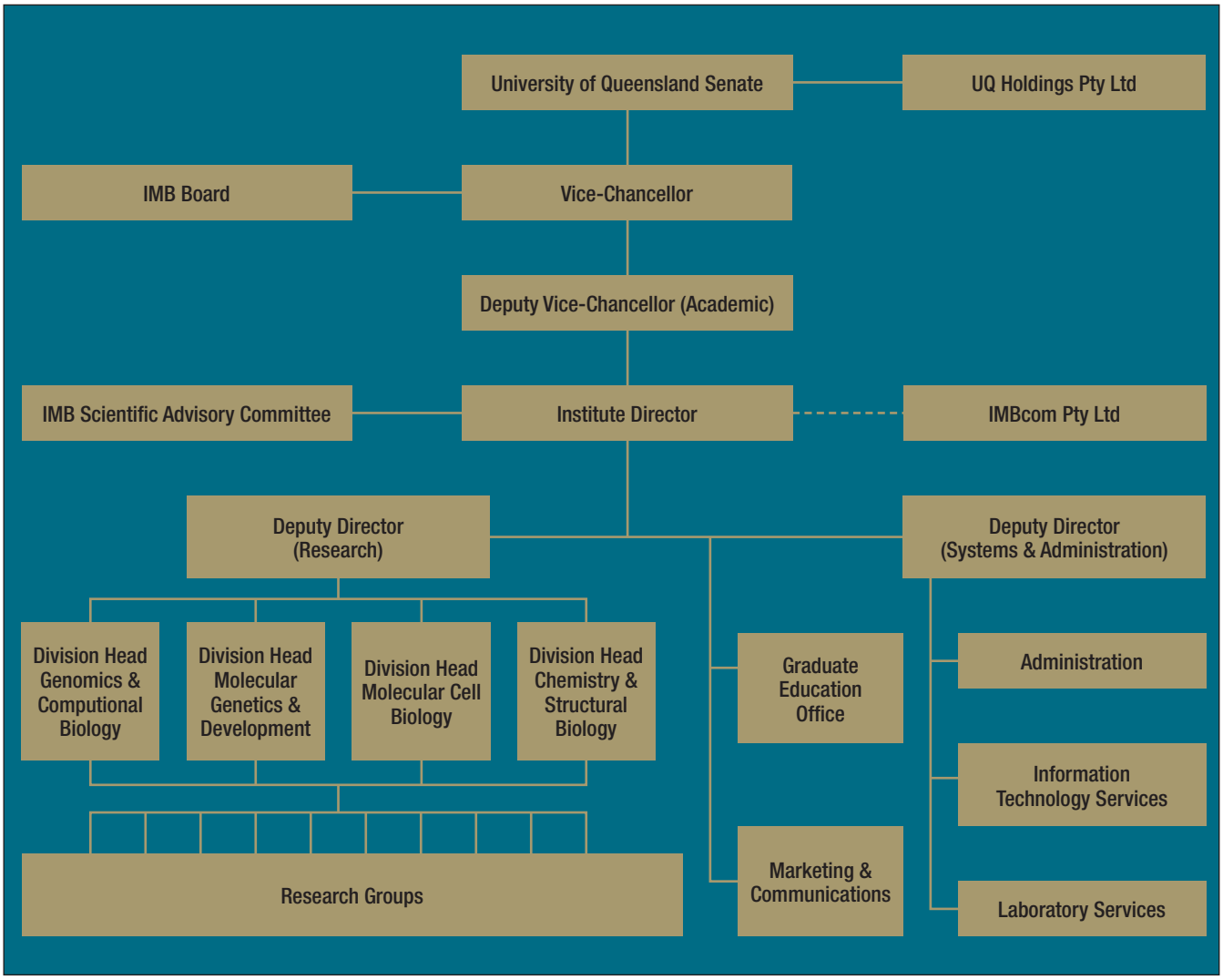
The team successfully engineered a synthetic version of a conopeptide and used amino acids to link the two ends of the peptide, forming a circle. Testing on this synthetic cyclotide proved that it retained the biological activity it demonstrated while it was a straight peptide, i.e., it relieves pain. It is also very potent, meaning a drug made from this circular peptide could likely be administered in small doses, decreasing the risk of addiction.

The next step in the process is human trials, assessing the drug candidate for its safety and analysing the effect it has on the human body and the effect the human body has on it. The researchers hope the molecule will pass muster and go on to be a safe, low-dose, effective treatment for chronic pain. The very fact it has made it this far is testament to two IMB discoveries, one from animals and one from plants, that have been brought together to create a promising new drug candidate. Watch this space.



Photograph of the plant Oldenlandia affinis *with the structure of the prototypic cyclotide kalata B1.*

2010 IMB ORGANISATIONAL CHART



IMB HIGHLIGHTS 2010

RESEARCHERS DELVE INTO GENETIC CODE OF TUMOURS IN HUNT FOR CANCER THERAPIES

Australian scientists are playing a vital role in a worldwide search for cancer therapies, described in top scientific journal *Nature*. The scientists are part of the International Cancer Genome Consortium (ICGC), a group of researchers from 22 countries who are conducting large-scale studies on the genomes of different tumour types.

The ICGC members will together sequence the genetic codes of 25,000 tumours from 50 different types of cancer over five years. Professor Sean Grimmond is leading the Australian team, responsible for sequencing pancreatic and ovarian tumours.

"We have identified changes in the genetic code from normal tissues to tumours, but we don't yet know if these changes are responsible for disease," Professor Grimmond said. "Our next step is running tests in the lab to determine if these genetic changes have a biological effect. We will do this for every tumour we sequence over the five-year project."

SOWING THE SEEDS OF MALE FERTILITY

Australian scientists have discovered the chemical signals that ensure men produce sperm instead of eggs. Dr Josephine Bowles and Professor Peter Koopman led a team that found that a protein called FGF9 promotes the production of sperm in males while suppressing the development of eggs.

"It sounds obvious, that men produce sperm and women produce eggs," Dr Bowles said. "But sperm and eggs start out as identical cells, and it's only through a complex process of signals that these cells end up as sperm in men and eggs in women."

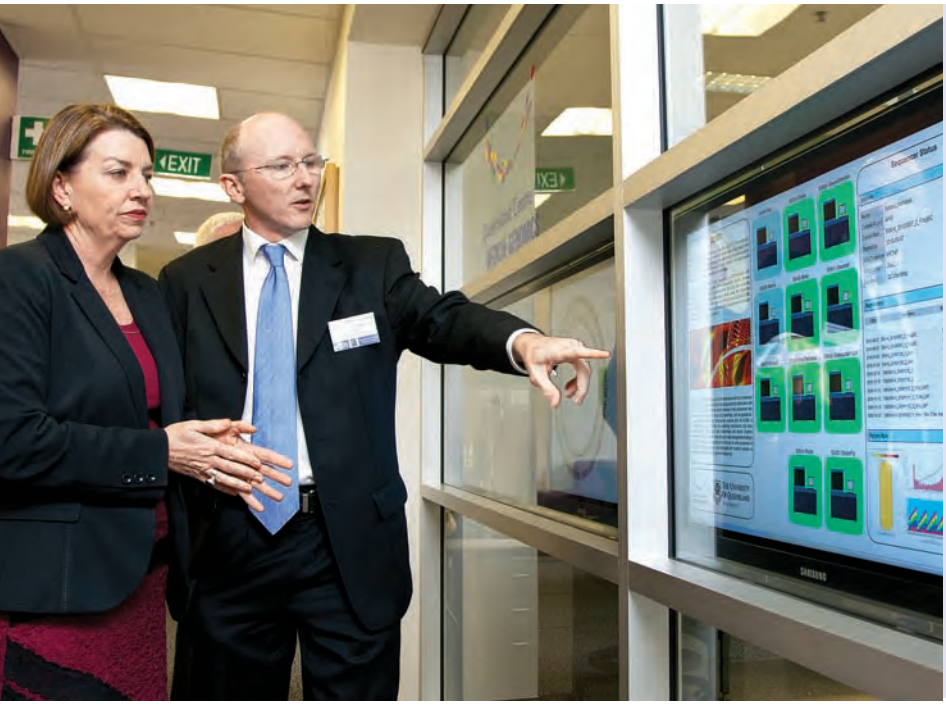
GENOME EXPLORATION FINDS KEYS TO GENE REGULATION AND DISEASE

A deep genome exploration has found tens of thousands of tiny pieces of genetic material, less that one percent of the length of the average gene, that may regulate gene expression and disease.

Professor John Mattick and Dr Ryan Taft (*pictured*) from IMB, and Dr Cas Simons from the Queensland Facility for Advanced Bioinformatics, showed that these 'tiny' RNA molecules are abundant at the start of genes and discovered they are also found at gene splice sites, where genes are turned on or off.

The work was published in the premier scientific journal *Nature Structural and Molecular Biology*, and led to Dr Taft being named a finalist in the Eureka Prizes Early Career Research and People's Choice Awards.

IMB HIGHLIGHTS 2010



QCMG Director Professor Sean Grimmond and Premier the Hon. Anna Bligh at the opening of the Queensland Centre for Medical Genomics

WORLD-CLASS GENOME CENTRE OPENS AT IMB

Premier Anna Bligh opened a multi-million dollar genome research facility on June 16, 2010 that will help pave the way for personalised genetic treatment.

The Queensland Centre for Medical Genomics was established with a $5 million grant from the Queensland Government and contains 11 next-generation sequencing machines that will allow researchers to compare the genomes of people with genetic diseases and determine which changes have occurred to cause the disease.

"This will lead to the development of more accurate therapies as well as a better understanding of genetic diseases, QCMG Director Professor Sean Grimmond said. "We are moving rapidly towards a future in which individuals are diagnosed and treated according to their genetic code."

PROBING THE MACHINERY BEHIND TISSUE HEALTH

PROBING THE MACHINERY BEHIND TISSUE HEALTH

A team of researchers has uncovered several key molecules that control the health of a major tissue in the body, the site of inflammation and 80 percent of cancers, in work published in *Nature Chemical Biology*.

Professor Alpha Yap led the researchers, from the IMB and the National Institutes of Health in the U.S.A., who probed the molecular machinery of epithelial tissues, which cover the internal and external surfaces of the body. They identified two of the key molecules that keep the epithelium healthy, as well as the signalling pathways that control these molecules.

"Understanding these signalling pathways will give us a better insight into how these diseases are caused, information that could lead to improved treatments," Professor Yap said.

'STEM CELL DETECTIVES' UNCOVER POTENTIAL CANCER CAUSE

Australian researchers have uncovered a new mutation in stem cells that may be linked to the development of leukaemia, breast and colon cancer.

A team led by Dr Peter Papathanasiou from the John Curtin School of Medical Research at the Australian National University and IMB's Associate Professor Andrew Perkins have completed a three-year screening project to find the genes that control the development and turnover of stem cells.

A major finding of the new study was the discovery of a novel DNA mutation in the c-Myb gene, which has previously been linked to a number of different cancer types. The project was the first in the world to mutate the mammalian genome in a specific search for novel genetic regulators of stem cells, and the findings were published in the journal *Blood*.

SCIENTIFIC IMAGES GO FROM LAB TO LIMELIGHT

IMB researchers were given the chance to display their artistic skills in the revamped Ångström Art competition, which aims to showcase stunning scientific images. Entries were open to all IMB researchers and the organisers received 62 images altogether.

Judges Professor Stephen Walker, Executive Dean of the Faculty of Science; Nick Mitzevich, Director of the UQ Art Museum; and Mrs Beverley Trivett, Director of the John Trivett Foundation; chose the winner and two runners-up.

Mr Darren Brown, a research assistant from the Stow group, contributed both the winning image, "MacBeads", and one of the runner-up images, "RealMacAlien". Dr Michael Landsberg, a Research Officer from the Hankamer group, rounded out the runners-up with his image, "Insect Assassin". The winning image can be viewed on the front cover of this report, while the full collection can be seen at www.angstrom-art.com

From left: Mr Tom Dery, Chair of ACRF; Professor Brandon Wainwright, Director of IMB; Her Excellency Dr Penelope Wensley AO, Governor of Queensland; and Professor Paul Greenfield AO, Vice-Chancellor of UQ at the official opening of the ACRF Cancer Biology Imaging Facility.

ADVANCED CANCER RESEARCH CENTRE OPENS AT UQ

IMB researchers now have access to some of the world's leading cancer imaging equipment with the opening of a $2.5 million facility funded by the Australian Cancer Research Foundation (ACRF).

The ACRF Cancer Biology Imaging Facility, the most advanced of its kind in the Southern Hemisphere, was officially opened in February by the Governor of Queensland, Her Excellency Dr Penelope Wensley AO.

The facility is an expansion of a $1.2 million facility at IMB funded by ACRF in 2003. The new facility has three advanced imaging microscopes to conduct fluorescence imaging, which will allow researchers to unravel the molecular reasons why healthy cells turn cancerous and spread through the body.

grants

HEALTHY BOOST FOR MEDICAL RESEARCH

The health industry of the future could involve growing therapeutic drugs in seeds and fighting tumours with scorpion venom after these and other projects from the IMB were funded by the National Health and Medical Research Council (NHMRC).

IMB researchers received over $6 million in NHMRC grants, more than a fifth of UQ's total of around $29 million. Professor Melissa Little and Dr Nick Hamilton received $691,310 to study kidney development to improve our understanding of chronic kidney disease, while $689,784 went to Professor Matt Cooper to develop new antibiotics to treat resistant bacteria.

IMB RESEARCH GETS $4.6 MILLION FUNDING BOOST

IMB received $4.6 million from the NHMRC in January 2010, including a $4 million Australia Fellowship awarded to Professor John Mattick, AO. This is Australia's most prestigious Fellowship in the fields of health and medical research.

Professor Mattick will use the fellowship to further explore his theory that so-called 'junk' DNA actually specifies a hidden layer of regulatory information essential to human development, brain function and gene-environment interactions. If Professor Mattick is correct, the project will transform our understanding of human biology and intelligence and create an enlightened framework for future research into human health and disease.

Professor David Fairlie also received a $610,500 Development Grant to commercialise drugs for inflammatory diseases. The grant will allow him to test molecules he has designed to determine if they have the right pharmacological properties to provide therapeutic effects.

MILLION-DOLLAR FUNDING FOR IMB RESEARCH

Researchers from the IMB will be leading projects such as improving pain treatments and developing clean fuels after receiving nearly $3.5 million in funding from the Australian Research Council (ARC).

Professor Glenn King received $550,000 to develop drugs for chronic pain based on compounds from spider venom, while Associate Professor Ben Hankamer was awarded $375,000 to improve the ability of microalgae to produce hydrogen. $660,000 went to Professor Peter Koopman and Dr Jo Bowles to study how sperm and egg production begins in the foetus.

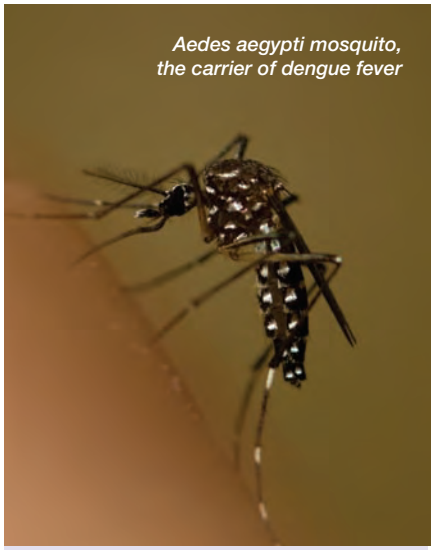
TALENTED HEALTH AND MEDICAL RESEARCHERS WIN FUNDING

Six IMB researchers were offered seven fellowships from the NHMRC and the ARC.

Professor Jenny Stow and Dr Matt Sweet were offered NHMRC Research Fellowships, while Dr Mathias Francois from the Koopman group received a Career Development Award and Dr Richard Allen from the King group was awarded a Postdoctoral Training Fellowship. These four fellowships represent a quarter of the NHMRC fellowships awarded to The University of Queensland.

Dr Matt Sweet, Dr Brett Collins and Dr Ben Hogan were all offered ARC Future Fellowships, which are aimed at mid-career researchers and academics.

IMB HIGHLIGHTS 2010



Aedes aegypti mosquito, the carrier of dengue fever

RESEARCHERS LINK UP TO DEVELOP DENGUE TEST

Professor Matt Cooper and his group will team with Alere Australia to develop a cheap, simple test for diagnosing dengue fever in its early stages. The project received $225,000 from the ARC's Linkage program, which links university researchers with industry partners.

Dengue virus is re-emerging as a global health problem, with over 2.5 billion people in 100 countries at risk. Early, accurate detection is vital both for limiting transmission and treating the patient so the disease doesn't progress to dengue haemorrhagic fever. Globally, only about three percent of people infected with the virus are currently being accurate diagnosed.

"A low-cost device able to diagnose dengue in the field will be of major benefit in controlling a disease that predominantly affects developing countries where ready access to high-level medical facilities is limited," Professor Cooper said. "The proposed device would remove subjectivity from the interpretation of the test results and provide accurate early diagnoses, which will lead to improved strategic containment of outbreaks and better treatments to avoid serious secondary dengue infections."

QUEENSLAND GOVERNMENT BOOST FOR CLEAN FUELS RESEARCH

Queensland Premier Anna Bligh announced nearly $1.5 million in funding to Associate Professor Ben Hankamer and collaborators for the development of low-cost, high-productivity microalgal photo-bioreactors.

A photo-bioreactor is basically a sealed aquaculture system that brings in sunlight to provide the energy the algae need to grow and produce biofuels such as biodiesel and hydrogen.

The Queensland Government investment will enable the researchers to test the economic feasibility of scaled-up, new-generation algal energy systems and has attracted a further $2 million in support from industry and UQ.

RESEARCH INFRASTRUCTURE GIVEN HALF-MILLION DOLLAR BOOST

A team of scientists in Brisbane and Cairns, led by Professor Paul Alewood, received a half-million dollar grant to explore Queensland's flora and fauna for useful molecules.

The $550,000 Australian Research Council Linkage Infrastructure, Equipment and Facilities grant, awarded to a team of UQ and James Cook University (JCU) researchers, will be used to establish a facility for identifying molecules that can act as markers and treatments for disease.

"This new facility will markedly accelerate the discovery and development of molecules from Queensland organisms with the potential to lead to new therapies for a range of difficult-to-treat diseases including pain, cancer, autoimmunity, allergies, obesity and infection," Professor Alewood said.

$5 MILLION FOR RESEARCH INTO BREAST CANCER RECURRENCE

An IMB researcher is part of a team that received a $5 million National Breast Cancer Foundation grant to develop treatments to target the recurrence of breast cancer.

Professor Alpha Yap is one of eight chief investigators on the project, led by Professor Erik Thompson from St Vincent's Institute and the University of Melbourne. The team will focus on a series of cellular changes that make cells more mobile and more likely to survive in new environments.

Cells that have undergone this process can move away from the primary tumour and plant themselves in a new part of the body, remaining dormant until they arise in the future as a secondary tumour. Most fatalities in breast cancer are due to secondary tumours, hence the importance of studying this process.

IMB RESEARCHERS BUILD LINKS WITH THE WORLD

Two researchers from the IMB will collaborate with international experts to overcome obstacles to algal biofuel production and the development of drugs to treat antibiotic-resistant infections.

Professor Jenny Martin and Evan Stephens were both awarded Queensland International Fellowships, which give researchers the opportunity to travel overseas for at least 12 weeks to undertake a high-quality, technically feasible and strategically valuable project with a leading international knowledge partner.

The applications from both IMB researchers were selected as the best in their category, with Professor Martin's in the Biotechnology category and Mr Stephens' falling under Renewable Energies. Professor Martin travelled to the UK to work with leading membrane protein expert Professor So Iwata in Cambridge for four months; Mr Stephens visited collaborators in Germany, with whom he has been developing methods to increase and harvest fuel production from microalgae.

IMB FELLOWSHIP FOR PLANT BIOLOGIST

Research into using plant seeds to produce otherwise costly drugs has snagged Dr Joshua Mylne the inaugural IMB Fellowship, the Professor John S. Mattick Fellowship.

The IMB Fellows program was established by the Institute in 2010 and aims to provide support for outstanding senior postdoctoral scientists to transition to independent researchers. The fellowship was named after Professor John Mattick, co-founder and inaugural Director of the IMB.

Dr Mylne will use the $90,000 fellowship to help support his research into the way sunflower seeds manufacture proteins, a process he believes could be modified to produce protein drugs.

Professor John Mattick presents Dr Joshua Mylne with his John S. Mattick Fellowship certificate.

awards

WORLD'S LARGEST SCIENTIFIC SOCIETY AWARDS IMB RESEARCHER

An IMB researcher developing a drug for pain from cone snail venom has been awarded a prestigious prize from the world's largest scientific society. Professor David Craik won the Ralph F. Hirschmann Award in Peptide Chemistry from the American Chemical Society.

Peptides are small proteins that play a number of important roles in the body. Professor Craik was recognised for his work with circular peptides, known as cyclotides. He described the first cyclotide and has been a major contributor to the field ever since.

One of his most significant achievements is the engineering of a new circular peptide to treat pain. Normal peptides can relieve pain but are unstable, while the circular version created by Professor Craik has proven effective at treating pain in early trials.

FIVE IMB GRADUATES' THESES IN TOP TEN PERCENT

Five IMB students made the Dean's Awards List for Outstanding Research Higher Degree Theses: Dr Ming Chang (Sweet group), Dr Conan Wang (Craik group), Dr Markus Muttenthaler (Alewood group), Dr Ryan Taft and Dr Tim Mercer (Mattick group).

IMB RESEARCHER ONE OF HIGHEST-RANKED IN NATION

Professor Rob Parton was recognised as being one of the best and brightest in the country at the NHMRC awards, held in March. Professor Parton received the Achievement Award for having the Highest-Ranked Project Grant.

These grants are awarded by the council to fund specific projects, and each application is individually ranked. Out of the 683 grants awarded across Australia in 2009, Professor Parton's application was ranked the highest.

His project will investigate ways of treating prostate cancer through suppressing the secretion of a protein called caveolin. This protein is normally embedded in the cell surface but in aggressive forms of prostate cancer it is secreted from cancerous cells and promotes the progression of the disease.

IMB RESEARCHERS TOP STATE WITH PAIN AND IMMUNE RESEARCH

IMB researchers took out half of the awards on offer at the 2010 Queensland Health and Medical Research Awards. Dr Richard Clark won Senior Researcher of the Year for his work on developing a medication for chronic pain using cone snail venom, while Dr Kate Schroder won Postdoctoral Researcher of the Year for completing the first comparison of mice and human innate immune systems.

TOP HONOURS STUDENTS AWARDED

The best IMB honours students of the past two years were recognised with an awards presentation in late March. The Amgen Award is given to the overall best IMB honours student in a particular year, with the winner being decided based on grades for the honours thesis and the overall honours mark.

The 2008 winner was Elanor Wainwright, who completed her thesis in the Koopman/Wilhelm laboratories. Ms Wainwright's project explored the role of Mir-202, a type of RNA, in gonad development.

Sheila Barbero and Anne Sawyer shared the award in 2009. Ms Barbero, from the Fairlie group, studied a type of enzyme that has potential therapeutic benefits if used after a stroke. Ms Sawyer investigated the purification and characterisation of a protein from a species of green algae, which the Hankamer group are genetically modifying to produce commercial quantities of hydrogen and other biofuels. All three women have gone on to PhD study within the IMB.

STUDENT PRIZES

For a detailed list of other student prizes in 2010, please turn to page 69.

IMB HIGHLIGHTS 2010

TINY FISH MAY HOLD KEY TO CANCER AND LYMPHATIC DISEASE BREAKTHROUGHS

An IMB researcher is using small transparent fish as a weapon in the battle against cancer and lymphatic disease. Dr Ben Hogan won a $70,000 UQ Foundation Research Excellence Award to advance his work using zebrafish to study the development of the lymphatic system.

Lymphatic vessels form a network similar to that of blood vessels to transport fluid, immune cells and fats around the body, and are also the route through which cancer spreads.

“Despite these major functions, the lymphatic system remains one of the most understudied organ systems in terms of its development,” Dr Hogan said. “We have identified several zebrafish mutants that develop without lymphatic vessels, and will genetically map four of these mutants and identify genes essential for lymphatic vessel development.”

Dr Ben Hogan in the zebrafish facility.

Ernest Tee, Bachelor of Science Valedictorian and IMB honours student

PERFECT SCORE FOR IMB HONOURS STUDENT

Ernest Tee, an honours student from the Cooper group, was named the Valedictorian of the UQ Bachelor of Science, coming first in his graduating class of 332 Bachelor of Science and 162 Bachelor of Science (Honours) students with a grade point average of 7.0 – a perfect score.

Mr Tee’s honours project involved synthesising a chemical compound called essramycin that supposedly demonstrated antibacterial activity.

Mr Tee successfully manufactured an artificial version of essramycin and also confirmed its chemical structure. However, he found that the synthetic essramycin was inactive against all major bacterial strains that were tested.

“This was in direct contrast to its reported antibacterial activity,” Mr Tee said. “My project confirmed that essramycin is not a suitable molecule for treating antibiotic-resistant bacteria.”

commercialisation

BIOTECH BOSS APPOINTED TO NATIONAL BOARD

An IMBcom executive will have a hand in driving the nation’s biotechnology agenda with his appointment to the Ausbiotech board.

Dr Peter Isdale, AM, CEO of IMBcom, the commercialisation company for the IMB, was appointed to the board in August 2010 to replace retiring member Dr Simon Carroll. AusBiotech is the industry organisation for Australia’s biotechnology sector, representing over 3000 members.

“I welcome the opportunity to contribute to the progress of the industry through the governance system of a very effective advocate for its members,” Dr Isdale said. “We are in exciting and prospective times where the life sciences-based industries are providing responses to global challenges.”

IMB ADVISORY BOARD









Left column, from top:
Prof. Paul Greenfield, Prof. Brandon Wainwright, Prof. Frank Gannon, Dr Russell Howard, Dr Peter Isdale

Right column, from top:
Prof. Nicos Nicola, Prof. Deborah Terry, Prof. Stephen Walker, Dr Jane Wilson

PROFESSOR PAUL GREENFIELD AO (CHAIR)

Professor Paul Greenfield, AO, is Vice-Chancellor of The University of Queensland. Professor Greenfield graduated with first-class honours in Chemical Engineering from the University of New South Wales (UNSW) and worked in the private sector before completing a PhD at UNSW. He then worked at CSIRO before winning a three-year fellowship to the U.S.

In 1975 Professor Greenfield joined The University of Queensland as a lecturer in chemical engineering, and a decade later became Head of Department and then Pro-Vice-Chancellor (Physical Sciences and Engineering) before being appointed an inaugural Executive Dean. In 1997 he was appointed as Deputy Vice-Chancellor and from 2002 to 2007 served as UQ Senior Deputy Vice-Chancellor, before becoming Vice-Chancellor in 2008.

Professor Greenfield has extensive experience as a Board Director and is currently Director on a number of company boards. He has consulted and worked widely with industry on a range of projects, as well as on the economic evaluation of projects. His interests lie in biotechnology, environmental management, and R & D management and commercialisation.

Professor Greenfield chairs the Group of Eight, a network of research-intensive Australian universities, and the Australian Nuclear Science and Technology Organisation. He is also Chair of the Scientific Advisory Group of the South East Queensland Healthy Waterways Partnership, the Expert Panel on Purified Recycled Water, the Riversymposium Strategic Planning Committee, the Thiess International Riverprize Committee and the International Water Centre. Professor Greenfield is a member of the Defence Science and Technology Organisation Advisory Board, representing the academic and research community.

In 2006 he was appointed an Officer in the Order of Australia for his contribution to science and engineering through research in chemical engineering, wastewater and environmental management, biotechnology and to the tertiary education sector. Professor Greenfield won the Chemeca Medal in 1995, awarded jointly by the Institution of Chemical Engineers and the Institute of Engineers Australia for outstanding contribution to the profession.

PROFESSOR BRANDON WAINWRIGHT (IMB DIRECTOR)

Professor Brandon Wainwright was appointed Director of the Institute for Molecular Bioscience in late 2006. Previously, he was the Deputy Director (Research) of the IMB from 2002.

Professor Wainwright completed his undergraduate and postgraduate studies at the University of Adelaide, after which he took up a postdoctoral fellowship at St Mary's Medical School, the University of London. He remained at St Mary's for six years, eventually becoming a Medical Research Council Senior Research Fellow.

In 1990, he moved back to Australia, joining the Centre for Molecular and Cellular Biology (CMCB) at The University of Queensland. Professor Wainwright stayed with the CMCB when it was merged with another UQ Centre (the Drug Design and Development Centre) in 2000 to create the Institute for Molecular Bioscience.

In addition to being Director of the IMB, Professor Wainwright serves on a number of boards, including those of the Australian Genome Research Facility, the Australian Stem Cell Centre, the Mater Medical Research Institute and the Health and Medical Research Council of Queensland. He has served as assessor for both the NHMRC and ARC on a number of occasions.

Professor Wainwright's major research focus is the use of genomic approaches to dissect the basis of common genetic

IMB Advisory Board

disease. He led the team responsible for finding the origins of the often-fatal brain tumour, medulloblastoma, and he is also studying cystic fibrosis and basal cell carcinomas of the skin. Through the mapping and isolation of the genes responsible for these diseases, he has continued to follow through on each to understand how the genetic defects lead to the disease.

The ultimate aim of his work is to discover the genes which, when altered, cause the tumour cell to grow in an uncontrolled fashion. Ultimately this will provide validated targets against which potential therapeutics can be developed.

IAN FLETCHER

Ian Fletcher is the Director-General of the Queensland Government's Department of Employment, Economic Development and Innovation (DEEDI). He has served in a number of high-level public-sector roles during his 27-year career. Mr Fletcher held positions in the New Zealand diplomatic service, then joined the United Kingdom civil service in 1989. He worked for UK Trade and Investment in arranging the UK's overseas commercial network, before becoming Chief Executive and Comptroller-General of the Intellectual Property Office.

Mr Fletcher's career comprises extensive experience in trade and investment, and he has already established a substantial understanding of DEEDI'S business and the key economic drivers and challenges facing Queensland's economy.

PROFESSOR FRANK GANNON

Professor Gannon has been the Director-General of Science Foundation Ireland since mid-2007. In January 2011 he will relocate from Dublin to Brisbane to take up a role as Director of the Queensland Institute of Medical Research.

From 1994-2007, Professor Gannon was the Executive Director of the European Molecular Biology Organisation (EMBO), Secretary-General of the European Molecular Biology Council, and Senior Scientist at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany. His major research interest is the Estrogen Receptor as a Transcription Factor and epigenetics.

He has published over 200 research articles. In addition, he has been involved in the establishment of two spin-out companies and is a member of an advisory group to the European Commissioner for Research and Innovation.

DR RUSSELL HOWARD

Dr Howard is currently CEO and founder of Oakbio Inc., a cleantech company in California developing sustainable microbe-based technologies for making valuable chemicals currently made by the petrochemical industry. He is also founder and former CEO of Maxygen, a company focused on optimisation and development of significantly improved proprietary versions of marketed protein pharmaceuticals. Maxygen also created businesses in agriculture (Verdia) and chemicals manufacture (Codexis).

Originally trained in biochemistry and chemistry at the University of Melbourne, Dr Howard spent over 20 years studying infectious diseases, primarily the molecular basis for the pathology of malaria. Before joining Maxygen, Dr Howard served at research institutes, biotechnology companies and a pharmaceutical company both in Australia and overseas, particularly in the USA. In addition to numerous patents, Dr Howard has over 140 publications in peer-reviewed journals.

DR PETER ISDALE, AM

Dr Peter Isdale, AM, is the CEO of IMBcom Pty Ltd., The University of Queensland's commercialisation company for the IMB. He is a former Business Director at the Australian Institute of Marine Science (AIMS), Australia's national marine research agency. He is also a former Principal Research Scientist at AIMS, and authored or co-authored more than 30 papers in his field of marine and climate research.

He has 20 years of experience in the operation and governance of private, public and ASX-listed companies in Australia, Asia and the Pacific Rim. He is a Member of the Australian Institute of Company Directors. Dr Isdale currently holds six non-executive directorships in biotech companies, senior positions on Foundations around the world and is an Adjunct Professor at Texas A&M University.

He holds a PhD in Marine Geomorphology (1982) from James Cook University. In 2006 he was awarded an Order of Australia (AM) for service to marine science through research and as a contributor to the development and commercialisation of biotechnology.

PROFESSOR NICOS NICOLA, AO

Professor Nicos Nicola is an ex officio member of the IMB Board, as he serves as the Chair of the IMB Scientific Advisory Committee. He is Assistant Director of the Walter and Eliza Hall Institute, as well as Joint Head of their Cancer and Haemotology Division and a Research Professor of the University of Melbourne.

Professor Nicola completed both his undergraduate and postgraduate degrees at the University of Melbourne, before working for a year at Brandeis University in Massachusetts, USA. He then joined the Walter and Eliza Hall Institute in 1977.

He is responsible for major discoveries including the purification of mouse G-CSF, the definition of the human equivalent of G-CSF and the purification of Leukaemia Inhibitory Factor. Professor Nicola has published over 250 journal articles and 20 patents.

PROFESSOR DEBORAH TERRY

Professor Terry is the Deputy Vice-Chancellor (Academic) of The University of Queensland. Her role is to preserve UQ's commitment to providing high-quality university teaching.

Areas under Professor Terry's direct management include the six UQ research institutes; the UQ Graduate School; Office of Undergraduate Education; Office of Prospective Students and Scholarships; the Teaching and Education Development Institute; Centre for Educational Innovation and Technology; Centre for Innovation in Professional Learning; and the Student and Administrative Services Division.

Professor Terry completed a Bachelor of Arts and a PhD in Psychology at the Australian National University and began at The University of Queensland as a postdoctoral research fellow, then as a lecturer. She was appointed Deputy Head of the School of Psychology in 1997, then Head of School in 2000.

Professor Terry accepted the position of Executive Dean, Faculty of Social and Behavioural Sciences in 2006, before being appointed half-time as Pro-Vice-Chancellor (Teaching and Learning) in 2007and Deputy Vice-Chancellor (Teaching and Learning) in 2008.

Professor Terry's primary research interests are in the areas of attitudes, social influence, persuasion, group processes and intergroup relations. She also has applied research interests in organisational and health psychology and has published widely in these areas.

Professor Terry is a Fellow of the Academy of Social Sciences in Australia, a Fellow of the Australian Psychological Society, previous chair of the Australian Research Council's College of Experts in the social, behavioural and economic sciences, and past President of the Society for Australasian Social Psychology. She currently holds editorial positions with the *British Journal of Psychology* and the *European Journal of Social Psychology*.

PROFESSOR STEPHEN WALKER

Professor Stephen Walker is the Executive Dean of the Faculty of Science at The University of Queensland. In this role, Professor Walker is responsible for the academic leadership and management of one of the largest and most diverse science faculties in Australia.

Professor Walker was appointed as Executive Dean for Engineering, Physical Sciences and Architecture at The University of Queensland in February 2006 and then Executive Dean of the Faculty of Science from January 2009. Prior to these positions, he spent five years at the Australian Research Council (ARC), as Executive Director for Engineering and Environmental Sciences, and as Acting CEO for a substantial part of 2004. In these roles, he was responsible for competitive research funding across a range of discipline areas and schemes, including management of the ARC Linkage Projects scheme, and had substantial input to Australian Government research policy on issues such as research funding schemes, research infrastructure and research priority areas.

Professor Walker has broad research interests, including numerical modelling and development of instrumentation in areas such as atmospheric and oceanographic plume dispersion, remote sensing, coastal oceanography and eutrophication, and also in medical research (electrocardiology). He has extensive experience in collaborative research, in conjunction with Government agencies, utilities and private industry.

DR JANE WILSON

Dr Jane Wilson is a professional company director with a background in medicine, finance, banking and consulting and has over 20 years of experience in business strategy, corporate governance and the commercialisation of research in both agricultural and biotechnology sectors.

She has a Masters degree in Business Administration from the Harvard Business School where she studied agribusiness and the health sector.

Dr Wilson is the current Chair of IMBcom (The University of Queensland's commercialisation company for the Institute for Molecular Bioscience) and a Director of the General Sir John Monash Foundation, Sonic Healthcare Ltd, CathRx Ltd, UQ Holdings Ltd, Universal Biosensors Inc. and Union College. Dr Wilson is Finance Director of the Winston Churchill Memorial Trust and is a member of The University of Queensland Senate.

Dr Wilson is also a Member of the Yalari Advisory Board, a Fellow of the Australian Institute of Company Directors, past Queensland President of the AICD and National Board Director of AICD and is currently on the AICD Advisory Panel. She was the inaugural Chairman of Horticulture Australia Ltd from 2000 to 2004 and was a Director of the National Archives Advisory Council for six years from 2002 to 2008.

She is involved in a number of charitable and cultural organisations and has also served on the Premier's Smart State Council and the Queensland Government Biotechnology Taskforce and the boards of Energex Ltd, WorkCover Queensland, AGEN Biomedical Ltd and Protagonist Ltd.

IMB SCIENTIFIC ADVISORY COMMITTEE









Left column, from top: Prof. Nicos Nicola, Prof. Chris Abell, Prof. David Galas, Prof. Nancy Jenkins, Prof. Robb Krumlauf.

Right column, from top: Prof. Chris Marshall, Prof. Jill Mesirov, Prof. Greg Petsko, Prof. Marino Zerial.

PROFESSOR NICOS NICOLA (CHAIR)

Professor of Molecular Haemotology
Assistant Director
Walter and Eliza Hall Institute of Medical Research, Melbourne, Victoria

PROFESSOR CHRIS ABELL

Professor in Biological Chemistry
Department of Chemistry
University of Cambridge, UK

PROFESSOR DAVID GALAS

Vice-President
Chief Academic Officer & Norris Professor of Applied Life Sciences
Keck Graduate Institute of Applied Life Sciences, Claremont, California, USA

PROFESSOR NANCY JENKINS

Co-Director
Institute of Molecular and Cell Biology, Singapore

PROFESSOR ROBB KRUMLAUF

Director
Stowers Institute, Kansas City, Missouri, USA

PROFESSOR CHRIS MARSHALL

Centre for Cell and Molecular Biology
Institute of Cancer Research UK

PROFESSOR JILL MESIROV

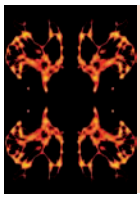
Broad Institute of MIT and Harvard, Cambridge, Massachusetts, USA

PROFESSOR GREG PETSKO

Gyula and Katica Tauber Professor of Biochemistry and Chemistry
Director, Rosenstiel Basic Medical Sciences Research Center
Brandeis University, Boston, Massachusetts, USA

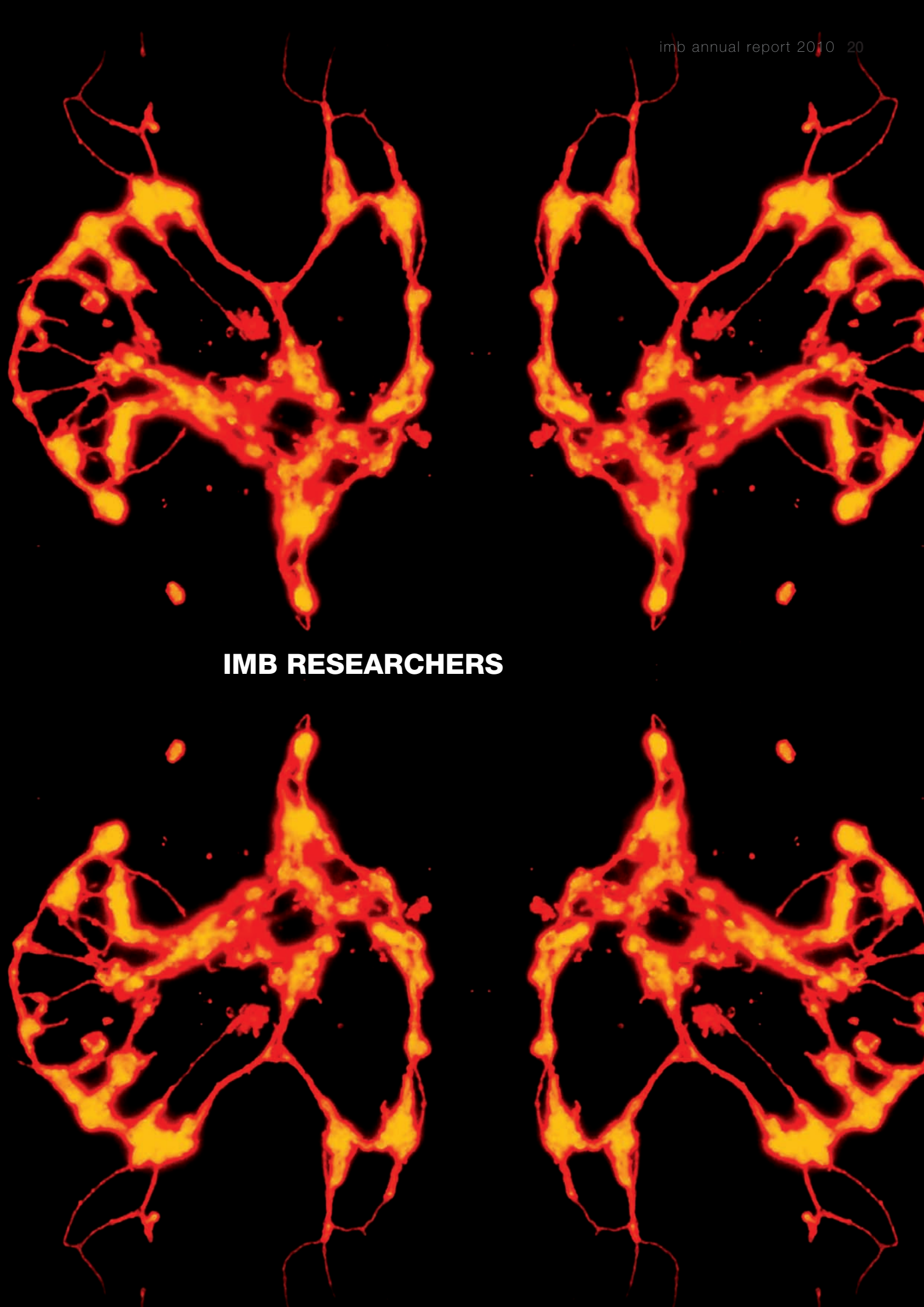
PROFESSOR MARINO ZERIAL

Max Planck Institute of Molecular Cell Biology, Dresden, Germany



SUSAN NIXON: EMBER

Mirror images of a human prostate cancer cell line (PC3) transfected with a mitochondrial marker



IMB RESEARCHERS

Division of
GENOMICS & COMPUTATIONAL BIOLOGY

In 2010 the Division's research in genomics, computational biology and bioinformatics was led by six Group Leaders (Dr Tim Bailey, Professor Sean Grimmond, Professor John Mattick, Professor Mark Ragan, Associate Professor Rohan Teasdale, Dr Nick Hamilton) one Joint Appointee (Professor Geoff McLachlan) and one Affiliate (Professor Jane Hunter).

NICOLE CLOONAN: COLOUR SPACE

This image depicts the DNA sequence of human chromosome 21 represented in colour-space, enhanced electronically to resemble an image seen in a kaleidoscope.

FELLOWSHIPS AND AWARDS

Professor John Mattick was awarded an NHMRC Australia Fellowship. This five-year fellowship, worth $4 million, is designed for leading health and medical researchers both from Australia and overseas. Professor Geoffrey McLachlan was awarded the Pitman Medal by the Statistical Society of Australia. This gold medal recognises great achievement in the field of statistics, and Professor McLachlan is only the 18th recipient since the prize was established in 1978. Dr Ryan Taft, a postdoctoral researcher in the Mattick group, was a finalist in two Eureka Prizes, the Early Career Research Award and the People's Choice Award. Dr Taft was selected for his examination of the non-coding portion of the human genome, known informally as 'junk DNA'. He discovered, in collaboration with Professor Mattick, tiny RNAs (tiRNA), the smallest-yet discovered segments of genetic material that may play a role in gene expression. Dr Taft was awarded a Dean's Commendation for an Outstanding Research Higher Degree Thesis, as was Tim Mercer, also from the Mattick group.

CENTRES AND FACILITIES

The Queensland Centre for Medical Genomics (QCMG) was officially opened in June by Queensland Premier Anna Bligh. Professor Sean Grimmond, QCMG Director, and his team continue to make rapid progress in sequencing pancreatic and ovarian tumours as part of the International Cancer Genome Consortium. At the end of 2009, the team had sequenced around 1 terabase of patient samples. One year on, they are close to achieving 10 terabases of genetic material, at a rate of roughly three tumours and three matched normals per month. The senior team expect the sequencing rate to rise in 2011, with the arrival of upgraded equipment from Applied Biosystems.

The senior team for the National Computational Infrastructure Specialised Facility in Bioinformatics, and the EMBL Australia EBI Mirror, was appointed in 2010. Dr David Green was seconded as Project Manager from his role as Manager of the high-performance computing group at UQ ITS. Dr Gerald Hartig, Gavin Graham and Peter Scott accepted roles as Senior IT Managers for development of Applications, Systems and Web Services respectively. Dr Hartig is a former IMB PhD student who has since spent time in IT management positions in telecommunications and biotechnology organisations.

The ARC Centre of Excellence in Bioinformatics marked its final year in 2010. The Centre links 16 groups of researchers at five Australian and four international institutions to develop an understanding of how genomic information is translated into structures and functions within the mammalian cell. The Centre was originally funded for five years, from 2003 until 2007, after which time the ARC conducted a review and not only extended the funding for the Centre for another three years, but also upgraded it to a Centre of Excellence. Many components of the Centre's research will continue under external grant and fellowship funding. The Centre's annual national Winter School in Mathematical and Computational Biology, which in 2010 attracted 261 registrants from 41 institutions across Australia and ten other countries, will be continued under funding from Bioplatforms Australia and EMBL Australia.

GRANT FUNDING AND RESEARCH

In 2010, group leaders in the Division held over $14 million* in competitive grants. Some of the new grants received in 2010 included a $691,310 grant from NHMRC, on which Dr Nicholas Hamilton was a Chief Investigator with Professor Melissa Little from the Molecular Genetics and Development division. The grant involves gaining a better understanding of kidney disease through studying nephron formation. Dr Hamilton will use his novel approaches to image-based modelling of cellular processes to contribute to improving our knowledge of kidney development. Professor Mark Ragan and Professor Lars Nielsen (AIBN) received a $340,000 grant from ARC to study the genetic sequences of more than 700 pancreatic tumours. He will compare the tumour genomes to those of undiseased tissue in order to identify the mutations that disrupt the process of normal development and cause cancer.

MAJOR PUBLICATIONS

The division's group leaders published in a range of high-ranking international journals throughout the year, including *Nature* (Grimmond), *Cell* (Grimmond, Teasdale), *Nature Methods* (Grimmond, Hamilton, Ragan), *Nature Structural and Molecular Biology* (Mattick), *Bioinformatics* (Bailey, Ragan) *Developmental Cell* (Mattick), *Genome Research* (Bailey, Mattick, Grimmond), and *Stem Cells* (Grimmond).

TIMOTHY L. BAILEY

PATTERN RECOGNITION AND MODELLING IN COMPUTATIONAL BIOLOGY

WE DEVELOP AND UTILISE computational methods to understand biological processes, especially the regulation of gene expression. Knowing how gene expression is regulated is essential to understanding cellular processes such as reproduction and metabolism. Currently we focus on three areas: 1) regulation of transcription, 2) the organisation and stability of nuclear proteins, and 3) the formation of nucleic acid triple helices. By studying transcription, sub-cellular protein organisation and protein stability, we focus on three key steps in gene expression. Our work on nucleic acid triple helices is partly motivated by recent evidence that suggests that these, too, may play a role in gene expression.

In 2010, we collaborated 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. Our study (in collaboration with the Perkins group at IMB) of how the transcription factor Klf1 controls the development that leads to red blood cells was made possible by the use of recently developed high-throughput DNA-sequencing technology. We developed and refined several algorithms for analysing the DNA-binding signals of transcription factors contained in this new type of data. This allowed us to map part of the genetic regulatory network controlling red blood cell development. Using more conventional computational means, we identified putative regulatory targets of NFIA, a key regulator of neural precursor cell development in certain regions of the brain. These predictions were then validated in the laboratory by the Richards group at QBI. This work illuminates a small part of the regulatory network of neural development. Similarly, in collaboration with the Little group at IMB, we made computational predictions of the binding targets of several transcription factors that guide kidney development. These predictions are currently being verified in the lab, and we hope to publish this work early in 2011.

Our continuing work on modelling transcriptional regulation in the fruit fly uncovered a possible explanation for how some transcription factors can act both as activators and repressors of transcription. The explanation lies in the ability of some transcription factors to be altered by the addition of SUMO—a covalent protein modification—possibly affecting their regulatory function. We also developed a computational model for predicting the trafficking of particular proteins to compartments within the nucleus, and a model for predicting the stability of proteins directly from their sequence.

We also continued our work on combining genomic and epigenomic data in a single model to predict where transcription factors bind in the genome in a particular tissue. This approach, pioneered by us, proved to be much more effective than previous methods. We are continuing this work, and will be incorporating it into our sequence analysis workbench (MEME SUITE), which is used by thousands of biologists. This year we published three major improvements to the algorithms in the MEME SUITE, created a mirror site at QFAB, and finalised a licensing agreement among UQ, UCSD and the University of Washington for continued commercialisation of the software.

In the coming year we will continue to develop models and predictors of transcriptional regulation and proteins. In collaboration with groups in the state of Washington and in Mexico, we will develop more sensitive ways of predicting transcription-factor binding using epigenomic data. We will also continue our work on protein stability prediction and nuclear organisation. Finally, we are about to start experimentation with a new type of microarray to study the formation of nucleic acid triple helices, which we hope will shed light on the potential *in vivo* roles of this structure.

KEY PUBLICATIONS

Bailey, T.L. *et al.* (2010). The value of position-specific priors in motif discovery using MEME. *BMC Bioinformatics* **11**: 179.

Bauer, D.C., Buske, F.A., and Bailey, T.L. (2010). Dual-functioning transcription factors in the developmental gene network of *Drosophila melanogaster*. *BMC Bioinformatics* **11**: 366.

Bauer, D.C. *et al.* (2010). Predicting SUMOylation sites in developmental transcription factors of *Drosophila melanogaster*. *Neurocomputing* **73**: 2300-2307.

Buske, F.A., Boden, M., Bauer, D.C., and Bailey, T.L. (2010). Assigning roles to DNA regulatory motifs using comparative genomics. *Bioinformatics* **26**: 860-866.

McLeay, R., and Bailey, T.L. (2010). Motif Enrichment Analysis: A unified framework and method evaluation. *BMC Bioinformatics* **11**: 165.

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Tallack, M.R. *et al.* (2010). A global role for KLF1 in erythropoiesis revealed by ChIP-seq in primary erythroid cells. *Genome Research* **20**:1052-1063.

LAB MEMBERS

Research Fellow: Dr Mikael Boden

Research Officers: Dr Chris Leat, Dr Philip Machanick, Dr Kai Willadsen

PhD Students: Denis Bauer, 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

THE QUEENSLAND CENTRE FOR Medical Genomics (QCMG) was officially opened by the Premier of Queensland, the Hon. Anna Bligh, MP, on June 16, 2010. The laboratory is focused on globally surveying genomic, transcriptomic and epigenomic information using next-generation sequencing and array-based approaches, and then integrating this data to define the underlying molecular networks controlling biological processes (such as cell division and differentiation) and pathological states (pancreatic, ovarian and breast cancer). This systems-wide approach will provide the means to identify key genes driving specific phenotypes and also the chance to model the different layers of control guiding biological states.

Defining the complete repertoire of mutations driving pancreatic and ovarian cancer development and progression

The next-generation sequencing facility at QCMG has been actively scaling the output required for the International Cancer Genome Consortium (ICGC) project with Australia's contribution covering pancreatic cancer and a smaller subset of ovarian cancer patients. The informatics pipelines needed to handle the data output have been established, with many of the tools created in house; the focus for the informatics group over the next 12 months will be on automating many of the manual steps still used which will allow the ICGC project to be scaled appropriately. The ICGC's ultimate aim is to create comprehensive genomic, transcriptomic and epigenomic atlases of the molecular changes arising in human tumours. The consortium will achieve this by characterising up to 50 different tumour types and/or subtypes from across the globe over the next five years.

Studying mammalian transcriptomes at single nucleotide resolution

We are continuing to actively survey the transcriptional complexity in specific biological states using a next-generation sequencing approach (RNAseq) in an effort to put newly discovered transcripts into a functional context. RNAseq supersedes traditional array-based expression profiling as it allows us to simultaneously monitor gene activity, study alternative splicing events, identify promoter and 3' UTR usage, and capture expressed sequence variation (SNPs and mutations). It also provides an opportunity to study novel expression events (including retrotransposon expression, the complexity in small RNAs and identification of novel non-coding RNAs). We are actively engaged in RNAseq studies to create a human and mouse tissue transcriptome atlas, study transcriptome complexity in human Embryonic Stem Cells (hESCs) and inducible Pluripotent (iPS) cells, as well as surveying transcriptome content during the cell cycle.

RESEARCH PROJECTS

- Sequencing the mammalian transcriptome in toto
- Phasevarions of pathogenic neisseria
- Predicting the function of onco-miRs through mRNA-mRNA networks
- Functionally characterising mammalian microRNA-mRNA interactions
- Defining the complete repertoire of genetic damage driving development and progression of breast cancer in a mouse model

KEY PUBLICATIONS

Chiu, H.-S. *et al.* (2010). A comprehensive catalogue of gene expression in the developing lower urinary tract and genital tubercle reveals strong links with cadherin and Wnt signaling and identifies epidermal gene networks in the developing genital tubercle. *Developmental Biology* **344**: 1071-1087.

Cloonan, N., and Grimmond, S.M. (2010). Simplifying Complexity. *Nature Methods* **7**: 793-795.

Mercer, T.R. *et al.* (2010). Regulated post-transcriptional RNA cleavage diversifies the eukaryotic transcriptome. *Genome Research* **20**: 1639-1650.

Schmeier, S., *et al.* (2010). An Atlas of Combinatorial Transcriptional Regulation in Mouse and Man. *Cell* **140**: 744-752.

Tallack, M. *et al.* (Grimmond, S.M. listed as a corresponding author) (2010). A global role for KLF1 in erythropoiesis revealed by ChIP-seq in primary erythroid cells. *Genome Research* **20**: 1052-1063.

The International Cancer Genome Consortium (Grimmond, S.M., listed as leader of the Australian project & member of the technology and scientific steering committees) (2010). International network of cancer genome projects. *Nature* **464**: 993-998.

LAB MEMBERS

Executive Officer: Dr Peter Wilson

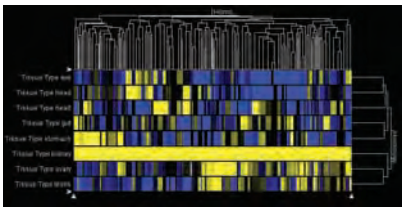
Senior Research Officers: Dr Brooke Gardiner, Dr Nicole Cloonan, Dr Nic Waddell, Dr Lynn Fink, Dr Sarah Song

Research Officers: Dr Karin Kassahn, Dr Katia Nones, Dr Craig Nourse, Dr Conrad Leonard, Dr Jason Steen, Dr Jill Shepherd

Research Assistants: Anita Steptoe, Suzanne Manning, David Miller, Milena Gongora, Shivangi Wani, Ehsan Nourbakhsh, Ivon Harliwong, Senel Idrisoglu, Scott Wood, Darrin Taylor, Oliver Holmes, Matthew Anderson, William Waterson, Qinying Xu

PhD Students: Rathi Thiagarajan, Keerthana Krishnan, Mellissa Brown, David Wood

Honours Students: Hilary Martin, Muhammad Fudlullah



Heatmap of kidney markers from a panel of embryonic tissues (12.5dpc).

NICK HAMILTON

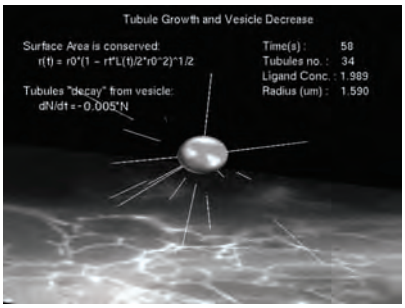
MODELLING, VISUALISATION AND CLASSIFICATION OF LIVE CELL IMAGING

HIGH-THROUGHPUT SCREENS FOR applications such as drug and genomic discovery are leading to massive image sets in need of new methods of analysis. Further, live cells may now be imaged in 3D over time with the interactions and dynamics of multiple proteins observed 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 new data sources to be realised.

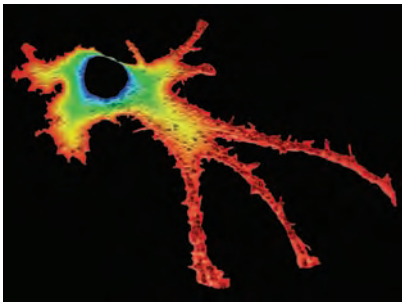
As a Strategic Partner of the ARC Centre of Excellence in Bioinformatics, I am Science Leader on The Visible Cell® project. This project integrates multi-scale 3D cellular image data and reconstructions with advanced bioinformatic methods for 3D spatial data query and annotation by incorporating an ontological foundation with novel methods for processing semantic and imaging data. The aim is to provide an environment in which multiple sources of bio-data can be easily integrated, queried, mathematically modelled and visualised to generate and test biological hypotheses. Related projects include the Automated Subcellular Phenotype Classifier (ASPiC), which combines novel image statistics with machine-learning methodologies to enable rapid near-perfect-accuracy classification of high-throughput imaging and the iCluster high-throughput bioimage visualiser.

Towards the analysis of 3D and 4D bio-imaging, the group has been developing two streams of research. The first is in quantification, to extract the key parameters that describe the systems being observed. In this area we have developed the Object Based Colocalisation (OBCoL) system to segment and quantify individual structures from 3D and 4D whole-cell imaging. This approach has enabled the detailed analysis of spatial distribution of proteins on individual subcellular structures. The second is in building mathematical models of the subcellular systems observed based on the quantification methodologies of the first stream. For instance, dynamic geometric models based on live cell imaging have provided surprisingly detailed information and insights into the systems observed and have been used to predict biologically relevant and experimentally verifiable quantities such as pH change. Other interests include modelling of recruitment and expulsion of proteins from membranes.

The group is strongly multidisciplinary and collaborative, with a focus on delivering methodologies and tools to be used by researchers.



Modelling and interference from video microscopy imaging of cells.



Visualising and quantifying protein distribution in the Visible Cell® [source data: K Beaumont].

RESEARCH PROJECTS

- Visualisation and automated classification of bio-imaging via machine learning
- The Visible Cell® software and science program
- Mathematical modelling of kidney development
- Statistical testing and content-based searching of bio-imaging
- Mathematical modelling of endosomal systems from live cell video microscopy imaging
- Segmentation and quantification of 2D, 3D and 4D live cell imaging

KEY PUBLICATIONS

Walter, T., Shattuck, D., Baldock, R., Bastin, M., Carpenter, A.E., Duce, S., Ellenberg, J., Fraser, A., Hamilton, N.A., Pieper, S., Ragan, M.A., Schneider, J., Tomancak, P., and Hériché, J.-K. (2010). Visualization of image data from cells to organisms. *Nature Methods* **7**: S26-S41.

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Hamilton, N.A., Kerr, M.C., Burrage, K., and Teasdale, R.D. (2007). The dynamics and geometry of vesicles and tubules in endocytosis. Current Protocols in Cell Biology Suppl. 35. K. Morgan, Ed. Wiley Interscience.

Hamilton, N.A., Pantelic, R.S., Hanson, K., and Teasdale, R.D. (2007). Fast automated cell phenotype image classification. *BMC Bioinformatics* **8**: 110.

LAB MEMBERS

Research Officers: Dr Daniel Marshall, Dr Oliver Caincross, Dr Matthew Moores

Co-supervised PhD Students: Alhadi Bustamam, Mitchell Stanton-Cook, Intan Ruhaiyem, Josefine Sprenger

Visiting Researcher: Dr John Belward

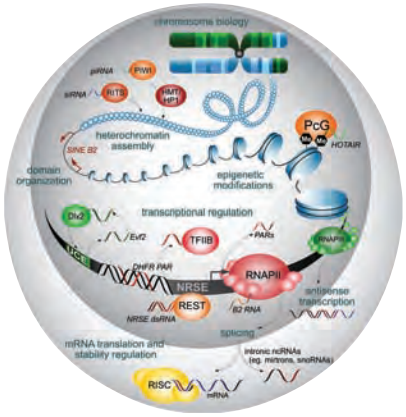
JOHN MATTICK

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 50 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 percent 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.

Using a range of experimental and bioinformatic techniques, we are working in conjunction with collaborators in the United States, Europe and Japan to characterise and understand the functions of these regulatory RNAs, and to validate our prediction that mammalian differentiation and development is primarily directed by sophisticated RNA regulatory networks that interact with generic effector complexes including transcription factors and chromatin-modifying enzymes.

We have demonstrated that the majority of long noncoding RNAs are expressed in precise cellular and subcellular locations in the brain, that a subset of noncoding RNAs are dynamically regulated during the differentiation of embryonal stem cells, neural stem cells, immune cells and muscle, as well as in cancer, and that some of these RNAs are essential components of subnuclear structures or complexed with particular types of activated chromatin. We have also identified new classes of tiny RNAs associated with transcription start and splice sites, and shown that protein-coding sequences are preferentially located in nucleosomes, which provides a platform for epigenetic control of gene expression and transcript structure. We have also found that conventional protein-coding mRNAs can also be processed to produce regulatory RNAs, and that RNA is the plastic substrate for epigenome-environment interactions. The outcomes of our research will be to expand our understanding of human evolution, development, brain function and disease.



RESEARCH PROJECTS

- Characterisation of the transcriptome and identification of new classes of regulatory RNAs by targeted deep sequencing
- Characterisation and functional analysis of regulatory RNAs in normal development and disease
- Characterisation of chromatin-associated RNAs and identification of RNA:DNA triplexes in the genome
- Characterisation of noncoding RNAs associated with subcellular organelles
- Analysis of the role of noncoding RNAs in enhancer function
- Analysis of the patterns of noncoding RNA evolution and structural parsing of the transcriptome
- Characterisation of the targets of RNA editing enzymes and the phenotypic consequences of their inactivation

KEY RECENT PUBLICATIONS

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Mercer, T.R., *et al.* (2009). Long noncoding RNAs: insights into functions. *Nature Reviews Genetics* **10**: 155-159.

Taft, R.J., *et al.* (2009). Tiny RNAs associated with transcription start sites in animals. *Nature Genetics* **41**: 572-578.

Amaral, P.P., Dinger, M.E., Mercer, T.R., and Mattick, J.S. (2008). The eukaryotic genome as an RNA machine. *Science* **319**: 1787-1789.

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Senior Research Assistant: Ke-Lin Ru

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Honours Student: Rebecca Johnston

Visiting Researchers: Anton Karlsbeek, Dr Mythily Mariasegaram, Dr Johanna Vendelin

MARK RAGAN
COMPUTATIONAL GENOMICS

WE USE ADVANCED BIOINFORMATIC and computational methods to investigate similarities and differences among genomes and the proteins they encode. Our goal is to make rigorous quantitative inferences, at both global and fine scales, about how genomes, gene and protein families, regulatory networks and cellular functions have evolved and diversified. To deal with very large quantities of data we use advanced data-management methods, implement high-throughput computational workflows, and develop new algorithms, approaches and software.

Genomes have diversified, both structurally and functionally, from shared ancestral states. We develop methods and employ analytical pipelines to reconstruct the paths of descent (phylogenomics) and to study processes of change through time (evolutionary genomics). We have characterised pathways of lateral genetic transfer where genetic information moves across, not within, genealogical lineages, and have developed statistically based approaches to discover genetically recombined regions and recombination breakpoints. We are now applying these approaches to understand genome diversification and the evolution of pathogenicity in bacteria.

Another major direction of our research is in the inference, comparison and analysis of biomolecular networks in mammalian cells in normal development and disease. We are developing scalable approaches that let us interrogate diverse data types including molecular sequences (single-nucleotide polymorphisms and copy-number variation), protein and RNA structures, metabolic and signalling pathways, regulatory and molecular interaction networks, gene expression profiles, subcellular localisation, cellular function, orthology maps and phylogenetic profiles.

For more information on our group and our research projects, please see *www.imb.uq.edu.au/index.html?page=11671*

RESEARCH PROJECTS

- Investigating the impact of lateral genetic transfer on the development of pathogenicity and virulence in bacteria
- Inferring biomolecular interaction networks in mammalian cells based on expression profiles
- Understanding how heterogeneous genotypes (SNP, CNV) interact with cellular networks to cause or maintain disease, particularly cancer
- Abstracting and analysing biomolecular control networks as graphs
- Fine-scale mapping of orthologous and paralogous regions of mammalian genomes
- Studying protein-protein interaction networks in cellular context
- Computationally discovering novel miRNA targets in mammalian genomes

KEY PUBLICATIONS

Maetschke, S.R. *et al.* (Ragan, M.A. listed as senior author) (2010). A visual framework for sequence analysis using n-grams and spectral rearrangement. *Bioinformatics* **26**: 737-744.

Davis, M.J., Sehgal, M.S., and Ragan, M.A. (2010). Automatic, context-specific generation of Gene Ontology slims. *BMC Bioinformatics* **11**: 498.

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Chan, C.X., Darling, A.E., Beiko, R.G., and Ragan, M.A. (2009). Are protein domains modules of lateral genetic transfer? *PLoS ONE* **4**: e4524.

Kassahn, K.S., Dang, V.T., Wilkins, S.J., Perkins, A.C., and Ragan, M.A. (2009). Evolution of gene function and regulatory control after whole-genome duplication: comparative analyses in vertebrates. *Genome Research* **19**: 1404-1418.

Ragan, M.A., and Beiko, R.G. (2009). Lateral genetic transfer: open issues. *Philosophical Transactions of the Royal Society of London B: Biological Sciences* **364**: 2241-2251.

Darling, A.E., Miklós, I., and Ragan, M.A. (2008). Selection on genome arrangement in circular bacterial chromosomes. *PLoS Genetics* **4**: e1000128.

LAB MEMBERS

Research Officers: Dr Melissa Davis (QFAB), Dr Stefan Maetschke, Dr Chenwei Wang

Queensland Facility for Advanced Bioinformatics Senior Team: Jeremy Barker (CEO), Dr Dominique Gorse (Technical Manager)

NCI SF Bioinformatics / EMBL Australia EBI Mirror Team: Dr David Green (Project Manager), Gavin Graham, Dr Gerald Hartig

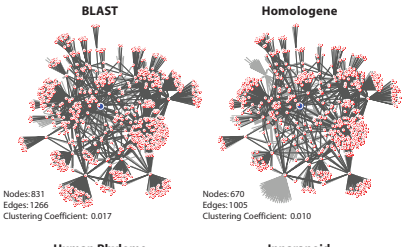
Manager, ARC Centre of Excellence in Bioinformatics: Lanna Wong

Scientific Programmer: Chikako Ragan

PhD Students: JooYoung Choi, Piyush Madhamshettiwar, Chang Jin Shin, Elizabeth Skippington

International Trainees: Alexandra Diem (Friedrich-Schiller-University Jena), Martin Simonsen (Aarhus University)

Undergraduate Research Trainee: Ann Bui



A multiple whole-genome alignment of six strains of Escherichia coli consists of 34 rearranged pieces larger than 1 kb.

ROHAN TEASDALE

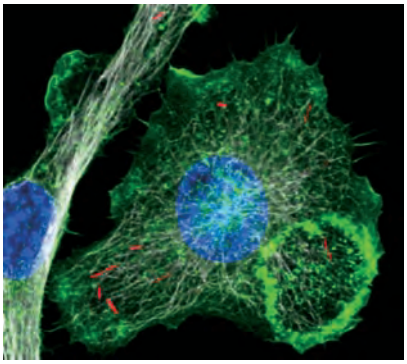
ENDOSOMAL DYNAMICS: REGULATED ENDOCYTOSIS, HOST-PATHOGEN INTERACTIONS AND PROTEIN TRAFFICKING

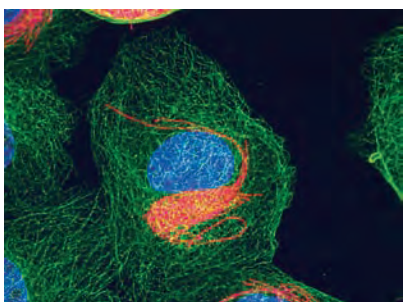
THE ENDOSOMAL/LYSOSOMAL system of mammalian cells is a highly dynamic organelle, and the trafficking pathways within the endosomal system are fundamental for a wide variety of key cellular processes. My group is developing cellular and computational approaches to identify novel mammalian proteins associated 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. A major current focus of the group is the characterisation of the mammalian retromer complex. My research into defining the composition of a mammalian endosomal protein complex, termed the retromer, has made major contributions to its recent emergence as a central critical regulator of early endosome protein trafficking. I discovered a novel core retromer complex, defined by a second VPS26 paralog, and originally discovered multiple members of the sorting nexin family that associate with retromer. Our recent work on sorting nexin 5 (SNX5) represents the first report of the association of sorting nexins and retromer proteins with macropinosomes. This study involved the application of high-quality live cell imaging to visualise the maturation process of macropinosomes. Based on our findings of a dynamic association of GFP-SNX5 with macropinosomes, we have detected a transient and very extensive tubular network that is essential to the maturation of the macropinosome in macrophages.

Macropinocytosis is a regulated form of endocytosis that mediates the non-selective uptake of extracellular material. Macropinocytosis is highly relevant to many aspects of both normal cell function and disease with particular importance in tumour progression and metastasis and in many infectious diseases. Recently I have focused on the establishment of a systems biology approach to examine the biogenesis of macropinosomes. I have established a number of functional assays to quantify the kinetics of formation and fate of individual macropinosomes.

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 these pathways and how they are modulated in response to infection with *Salmonella*, a leading cause of human gastroenteritis. Currently we have established High Content Screening (HCS) approaches, combined with high-throughput RNA.





RESEARCH PROJECTS

- Host-Pathogen interactions during Salmonella infection
- Maintaining and updating LOCATE: A Protein Subcellular Localisation Database – *http://locate.imb.uq.edu.au*
- Developing computational approaches to analyse image and real-time microscopy data
- Studying endosome dynamics, macropinocytosis and retromer
- Systems biology of the mammalian endosome
- Establishment of High Content Screening (HCS) applications including high throughput RNA-interference (RNAi) screens

KEY PUBLICATIONS

Kerr, M.C., Wang, J.T.H., Castro, N., Hamilton, N.A., Town, L., Brown, D.L., Meunier, F.A., Brown, N.F., Stow, J.L., and Teasdale, R.D. (2010). Inhibition of the PtdIns(5) kinase PIKfyve disrupts intracellular replication of *Salmonella*. *EMBO Journal* **29**: 1331-1347.

Wang, J.T., Kerr, M.C., Karunaratne, S., Jeanes, A., Yap, A.S., and Teasdale, R.D. (2010). The SNX-PX-BAR family in macropinocytosis: the regulation of macropinosome formation by SNX-PX-BAR proteins. *PLoS One* **5**: e13763.

Kerr, M.C., and Teasdale, R.D. (2009). Defining Macropinocytosis. *Traffic* **10**: 364-371.

Hamilton, N., and Teasdale, R.D. (2008). Visualizing and Clustering High Throughput Sub-cellular Localization Imaging. *BMC Bioinformatics* **9**: 81.

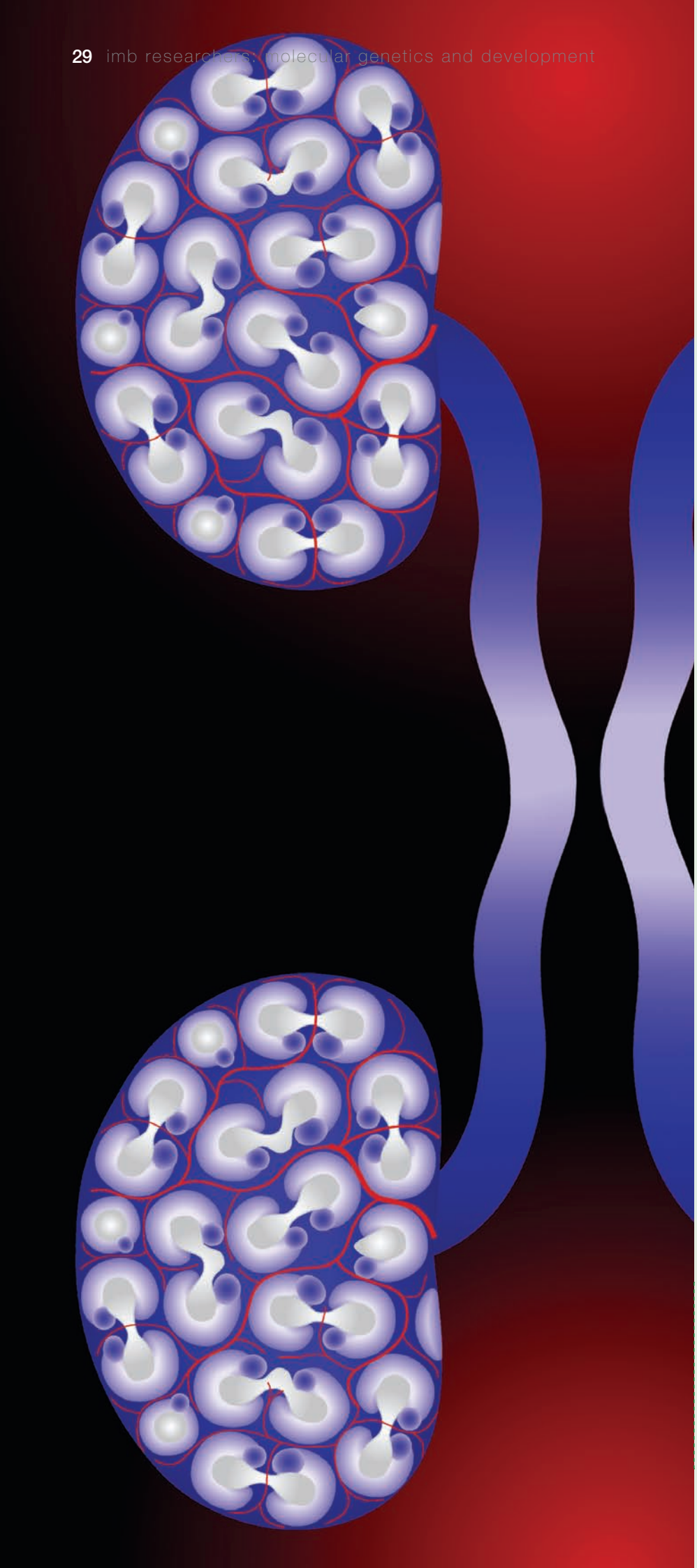
Sprenger, J., Fink, J.L., Karunaratne, S., Hanson, K., Hamilton, N., and Teasdale, R.D. (2007). LOCATE: A Mammalian Protein Subcellular Localization Database. *Nucleic Acids Research* **36**(Database issue): D230-233.

LAB MEMBERS

Research Officers: Dr Markus Kerr, Dr Andrea Bugarcic, Dr Michael Hanzal-Bayer, Dr David Liebl

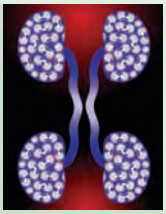
Research Assistants: Seetha Karunaratne, John Griffin, Zhe Yang, Shara Close

PhD Students: Josefine Sprenger, Jack Wang



Division of MOLECULAR GENETICS & DEVELOPMENT

This has been another outstanding year for the MGD Division, with our researchers continuing to make seminal contributions to our understanding of development, metabolism and genetic disease. A paper by Dr Josephine Bowles and Professor Peter Koopman in Developmental Cell, describing the discovery of a protein that promotes spermatogenesis while suppressing oogenesis, was an example of the high-quality research performed in the division in 2010.



KYLIE GEORGAS: KIDNEY ART

A schematic diagram of embryonic mouse kidneys. The diagram has been modified from a kidney diagram designed and drawn for the GUDMAP website.

The Molecular Genetics and Development Division currently consists of ten groups containing around 100 researchers and students in total. A detailed description of each group's research can be found in the following pages, but briefly, the research focus of each group is: the development and function of the lymphatic vessels (Dr Ben Hogan); the formation of the developing embryo, particularly the gonads and blood and lymphatic vessels (Professor Peter Koopman); the development, repair and regeneration of the kidney (Professor Melissa Little); the role of nuclear hormone receptors in metabolic disease (Professor George Muscat); blood development (Associate Professor Andrew Perkins); the genetics of human pigmentation and skin cancer risk (Associate Professor Rick Sturm); the mechanisms by which the innate immune system responds to infection (Dr Matt Sweet); the genetics of tissue repair and heritable cancers, including basal cell carcinomas and medulloblastomas (Professor Brandon Wainwright); the molecular mechanisms behind limb and craniofacial development (Associate Professor Carol Wicking) and the elucidation of the regulatory mechanisms of embryonic development (Dr Dagmar Wilhelm).

The division continues to sustain its research through success in competitive grant rounds. Our researchers received $1.5 million in project grants from the National Health and Medical Research Council and $1 million from the Australian Research Council (ARC). These included IMB's largest grant across both schemes of $691k to Professor Melissa Little. This grant will fund Professor's Little's studies on kidney development, which aims to improve our understanding of chronic kidney disease. Professor Little is also one of the investigators on another large grant, $627k, led by Professor Karen Moritz of UQ's School of Biomedical Sciences. This grant will examine the effect of lower oxygen levels on kidney development. Professor Peter Koopman and Dr Josephine Bowles received $660k from the ARC to continue the work described in their *Developmental Cell* paper (see above). The other three grants awarded to chief investigators from the division in these funding rounds went to: Dr Kelly Smith, a postdoctoral researcher from the Wicking group, Dr Ben Hogan, the institute's youngest group leader, who was awarded two, and Dr Mathias Francois, a Koopman group postdoc who shared one of Dr Hogan's grants. The latter two researchers were also successful in Fellowship funding rounds, with Dr Hogan being awarded an ARC Future Fellowship and Dr Francois receiving an NHMRC Career Development Award. Dr Matt Sweet was particularly successful in these rounds, being offered both an NHMRC Research Fellowship and an ARC Future Fellowship. As always, it is encouraging to see early- and mid-career researchers achieving success.

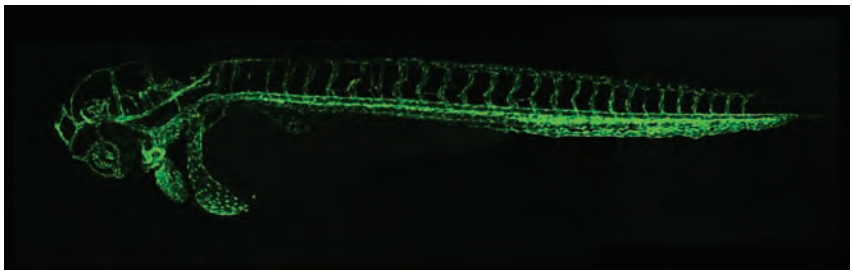
The division's researchers were not just recognised for their work through the awarding of competitive grants, but also through prizes. Dr Ben Hogan won a University of Queensland Research Excellence Award, worth $70,000, to identify genes critical to the development of the lymphatic vessels through the use of zebrafish models. Dr Kate Schroder from the Sweet group was awarded Postdoctoral Researcher of the Year at the Queensland Health and Medical Research Awards, the second year in a row this prize was won by a researcher from our division. Dr Schroder completed the first comparison of mice and human innate immune systems. In our student cohort, Dr Ming Chang, also from the Sweet group, was named on the Dean's Awards List for Outstanding Research Higher Degree Theses. Only the top ten percent of research higher degree students are recognised in this way each year. Vicki Metzis from the Wicking group won several awards in 2010, including the IMB and Inter-Institute rounds of the Three-Minute Thesis competition, and the People's Choice Award in the Inter-Institute round. For a list of the remainder of Ms Metzis's awards, and for other student awards, please see page 69.

Our researchers continued to interact with the wider scientific community, presenting at conferences and other institutes, and hosting visitors to the IMB in return. These visitors included four national and international speakers in IMB's Friday Seminar Series: Dr Stephen Cohen, Deputy Director of the Institute of Molecular and Cell Biology in Singapore; Professor Christopher Goodnow, Director of the Australian Phenomics Facility at the Australian National University in Canberra; Professor Simon Foote, Director of the Menzies Research Institute at the University of Tasmania in Hobart; and Professor Sharad Kumar from Adelaide's Institute of Medical and Veterinary Science. Dr Dagmar Wilhelm organised the Division's fortnightly seminar program, a forum for our staff and students to present their work to the rest of the division, and allow each of us a wider understanding of the research being undertaken across our ten laboratories. We continued to run the Brisbane Developmental Biology Seminar Series, a monthly seminar for all developmental biologists in Brisbane. In October, Dr Dagmar Wilhelm and Dr Kelly Smith organised the inaugural Cell and Developmental Biology Meeting. This symposium is one of the few that allows junior scientists, including postgraduate students, to share the stage with senior researchers, and was a huge success. Our division also sponsored the 6th Australian Developmental Biology Workshop in Melbourne, a training ground for the next generation of Australian developmental biologists.

Last year I reported that the Division had been reviewed by Professor Robb Krumlauf and Professor Nancy Jenkins from the IMB's Scientific Advisory Committee. As a result of feedback from that review, this year we instituted a divisional retreat aimed at improving our collective sense of belonging and gaining a better understanding the division's areas of research interest and technical approaches. The retreat was very successful, with participants emerging with an increased awareness of best practice in the field as a whole, technology, equipment and services available at IMB and emerging research trends and technologies.

BEN HOGAN

MOLECULAR GENETICS OF VASCULAR DEVELOPMENT

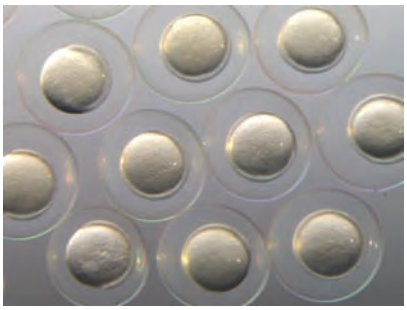


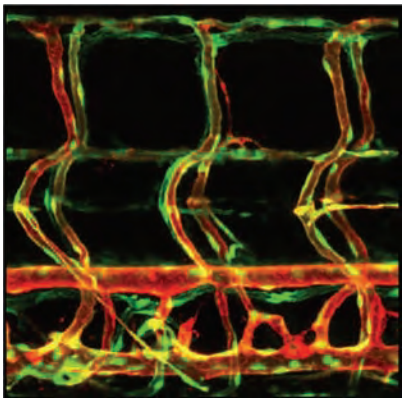
THE DISTRIBUTION OF BLOOD cells, hormones and essential nutrients throughout our bodies is dependent on the function of a healthy circulatory system. Blood and lymphatic vessels compose an organ network that distributes blood and also drains waste and fluid that accumulates in our tissues. We are particularly interested in the development and function of lymphatic vessels, which play critical roles in human diseases including lymphoedema, inflammatory disorders, and cancer 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 our inaugural year, the laboratory has begun by identifying several key new regulators of lymphatic vessel development in the zebrafish. The characterisation of these genes in mammals, in health and disease scenarios, is ongoing and should serve to identify targets for the treatment of vascular diseases and the inhibition of cancer metastasis.

RESEARCH PROJECTS

- Identification and characterisation of mutants with abnormal vasculature
- Identification and characterisation of key regulators of lymphatic vessel differentiation
- Analysis of the role of the human disease gene Ccbe1 in lymphangiogenesis
- Live imaging of vascular development





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Hogan, B.M., Herpers, R., Witte, M., Heloterä, H., Alitalo, K., Duckers, H.J., and Schulte-Merker, S. (2009). Vegfc/Flt4 signalling is suppressed by Dll4 in developing zebrafish intersegmental arteries. *Development* **136**: 4001-4009.

Hogan, B.M., Bussman, J., Wolburg, H., and Sculte-Merkers, S. (2008). ccm1 cell autonomously regulates endothelial cellular morphogenesis and vascular tubulogenesis in zebrafish. *Human Molecular Genetics* **17**: 2424-2432.

Hogan, B.M., Layton, J.E., Pyati, U.J., Nutt, S.L., Hayman, J.W., Varma, S., Heath, J.K., Kimelman, D., and Lieschke, G.J. (2006). Specification of the primitive myeloid precursor pool requires signaling through Alk8 in zebrafish. *Current Biology* **16**: 506-511.

GROUP MEMBERS

Research Officers: Dr Neil Bower, Dr Ludovic Le Guen

Research Assistants: Christine Neyt, Scott Paterson, Emmanuelle Frampton (née Lesieur)

PhD Students: Joelle Kartopawiro, Baptiste Coxam

PETER KOOPMAN

GENETIC REGULATION OF EMBRYO DEVELOPMENT AND HUMAN DISEASE

OUR GROUP FOCUSES ON GENES controlling the formation of various organs in the developing embryo.

Our main interest is striving to understand the events that determine whether an embryo 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 specialise in the identification and characterisation of other sex development genes using techniques such as microarray screening and transgenic mouse models, and studying how these affect sex development. Ultimately we hope to better understand the causes of human disorders of sex development.

We are also interested in how an embryonic cell type known as germ cells comes to eventually develop as sperm in males or eggs in females. We have discovered several molecular signals 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.

A third major focus in our group includes investigating the role of Sox18, a gene we discovered and have shown triggers the formation of the lymphatic system. This discovery is expected to lead to better ways of controlling lymphatic development and function in diseases such as lymphedema and cancer metastasis. We are developing anti-Sox18 drugs as potential adjunct treatments for cancer.

In summary, 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.

RESEARCH PROJECTS

- Sex determination and gonadal development
- Development of male germ cells
- Sox gene function and evolution
- Molecular genetics of lymphatic development

KEY PUBLICATIONS

Bowles, J., Feng, C.-W., Spiller, C., Davidson, T.-L., Jackson, A., and Koopman, P. (2010). FGF9 suppresses meiosis and promotes male germ cell fate in mice. *Developmental Cell* **19***:* 440-449.

François, M., Caprini, A., Hosking, B., Orsenigo, F., Wilhelm, D., Browne, C., Paavonen, K., Karnezis, T., Shayan, R., Downes, M., Davidson, T., Tutt, D., Cheah, K.S.E., Chan, M., Stacker, S.A., Muscat, G.E.O., Achen, M.G., Dejana, E., and Koopman, P. (2008). SOX18 induces development of the lymphatic vasculature in mice. *Nature* **456**: 643-647.

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LAB MEMBERS

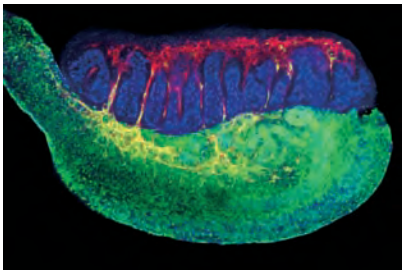
Senior Research Officer: Dr Josephine Bowles

Research Officers: Dr Mathias Francois, Dr Terje Svingen, Dr Kallayanee Chawengsaksophak, Dr Kenichi Kashimada, Dr Cassy Spiller, Dr Antoine Rolland

Research Assistants: Tara Davidson, Allen Feng, Ee Ting Ng, Danielle Wilson, Cameron Curtis

Admin Assistant: Barbara Feenstra

PhD Student: Tam Duong



Recombinant organ culture with GFP expressing mesonephros (green) and wild type testis allows analysis of cell migration into the testis during development. Migrating endothelial cells integrate with endogenous vasculature (yellow and red respectively) which separate forming testis cords (blue).

MELISSA LITTLE

KIDNEY DEVELOPMENT, DAMAGE, REPAIR AND REGENERATION

EACH OF US HAS A PAIR OF KIDNEYS that plays an important role in maintaining fluid balance, blood volume and electrolyte balance. On top of this, they regulate blood pressure, bone density and number of red blood cells via the production of specific growth factors. As a result of the many complex roles played by the kidneys, kidney disease has a profound effect on the patient.

Chronic kidney disease (CKD) is a devastating disease and an expensive one to treat. Once this condition has reached end-stage renal failure, it can only be treated with dialysis or transplantation. Each year, more than 4000 Australian adults will be diagnosed with CKD, which costs the health system 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 percent per annum, primarily due to increasing rates of Type II diabetes and obesity. Sadly, only one in four patients will be lucky enough to receive a kidney transplant.

As for other organs, there are many conditions, both experimental and genetic, that result in impaired kidney function. Perhaps more surprising is the fact that the risk of kidney failure during our lives is now known to be linked to what happens during the development of our kidneys. Our laboratory is acknowledged internationally for our work in defining the genes involved in normal kidney development and in integrating this understanding with an understanding of how the adult kidney responds to damage. In this way, 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.

RESEARCH PROJECTS

- Modelling kidney development in 3D
- Investigating the specification and turnover of the nephron progenitor population during kidney development
- Determining the basis of cessation of nephron formation and how nephron number is varied genetically and environmentally
- Dissecting the nephron progenitor niche so as to find ways to expand this population
- Reinitiating kidney development to repair an adult kidney
- Characterising stem cells in the adult kidney
- Dissecting the basis of progression to chronic renal disease

KEY PUBLICATIONS

Chiu, H.S. *et al.* (Little, M.H. listed as senior author) (2010). Comparative gene expression analysis of genital tubercle development reveals a putative appendicular Wnt7 network for epidermal differentiation. *Developmental Biology* **344**: 1071-1087.

Lin, S.A. *et al.* (2010). Subfractionation of differentiating hES populations allows the isolation of a mesodermal population enriched for intermediate mesoderm and renal progenitors. *Stem Cells and Development* **19**: 1637-1648.

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Lusis, M., Li, J., Ineson, J., Li, J., and Little, M.H. (2010). Isolation and culture of metanephric mesenchyme-derived nephrospheres reinforces evidence that embryonic renal progenitors are multipotent and exhaust during cessation of nephron formation. *Stem Cell Research* **5**: 23-39. (Editorial comment on this article published in same issue)

Rumballe, B., Georgas, K., Wilkinson, L., and Little, M.H. (2010). Molecular anatomy of the kidney: what have we learnt from gene expression and functional genomics? *Pediatric Nephrology* **25**: 1005-1016.

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Combes, A.N. *et al.* (2009). Three-dimensional visualisation of testis cord morphogenesis, a novel tubulogenic mechanism in development. *Developmental Dynamics* **238**: 1033-1041.

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LAB MEMBERS

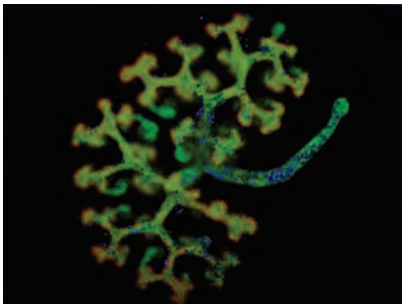
Research Officers: Dr Lorine Wilkinson, Dr Joan Li, Dr Minoru Takasato, Dr Fiona Rae, Dr David Pennisi

Research Assistants: Bree Rumballe, Kylie Georgas, Jess Ineson, Melissa Becroft, Han Chiu, Norseha Mohammed Suhaimi

PhD Students: Caroline Hopkins, Yu Leng Phua

Honours Student: Adler Ju

Undergraduate Student: Stephanie Aroney



GEORGE MUSCAT

NUCLEAR HORMONE RECEPTORS, AND METABOLIC DISEASE

NUCLEAR HORMONE RECEPTORS (NRs) function as ligand-dependent DNA-binding proteins that translate nutritional, 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. Moreover, we exploit these animal models and studies to gain insights into dyslipidemia, obesity, type II diabetes and cancer. The insights obtained from in vivo studies in animal models will be utilised to translate this research into understanding human health and disease.

Our group has investigated the functional role of the retinoic acid receptor - related orphan receptor (*Ror*) alpha - a member of the nuclear hormone receptor (NR) superfamily. We have previously demonstrated that homozygous *staggerer* mice (*sg/sg*), with decreased and dysfunctional retinoic acid receptor-related orphan receptor alpha (*Rora*) expression in all tissues, display a lean and dyslipidaemic phenotype. Furthermore, these mice are resistant to (high-fat) diet-induced obesity. This phenotype was mediated by the suppression of SREBP-1c (a master lipogenic transcription factor) and its downstream targets (involved in fatty acid biosynthesis). Recently, we have targeted muscle-specific expression of a truncated (dominant negative) ROR alpha 1ΔDE in transgenic mice to investigate ROR alpha 1 signalling in this tissue. Expression profiling, qPCR, pathway, western and metabolic profiling analysis indicated that ROR alpha influenced pathways irregulating: (i) lipid and carbohydrate metabolism, cardiovascular and metabolic disease; (ii) LXR nuclear receptor signalling and (iii) Akt and AMPK signalling. The identified genes and pathways were in concordance with the demonstration that aberrant RORa1 expression/function affected glucose tolerance, insulin-stimulated phosphorylation of Akt and glucose uptake in the transgenic animals. In conclusion, we propose that Rora plays an important role in the regulation of lipogenesis, adiposity, and the AKT2 signalling cascade controlling glucose uptake in skeletal muscle.

We have utilised the Ski transgenic mouse model to investigate the role of c-ski and NR crosstalk in regulating body composition, and the response to dietary (high fat) challenges. Currently, other studies have produced transgenic mouse lines with muscle-specific perturbation of the nuclear receptor NOR-1 (a member of the NR4A subgroup of NRs) to investigate the effects of selective and specific crosstalk between beta-adrenergic and NOR-1 signalling in skeletal muscle. These studies have indicated NOR-1 signalling controls glucose tolerance, and oxidative metabolism in muscle. Moreover, we have shown selective crosstalk between melanocortin 1 receptor (MC1R) and NR4A signalling in adipose in the context of metabolism.

Current and future directions involve translating this research into human health and disease. For example, the insights obtained from the studies in lean, obese and diabetic murine models are being utilised (in collaboration with Dr Gary Leong) 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. Furthermore, in the context of cancer, we are also involved in an NBCF-funded large collaborative research program to completely profile NR and NR cofactor expression in several human cohorts, including (pre- and post-menopausal) normal breast, estrogen receptor (ER)-positive and -negative breast cancers.

For more information, please see *www.imb.uq.edu.au/index.html?page=11687*

RESEARCH PROJECTS

- Examining the in vivo role of the ROR and NR4A subgroups in lipid and glucose homeostasis
- Elucidating the metabolic role of the NR4A subgroup (Nur77 and NOR-1) in adrenergic and melanocortin signalling
- Determining the role and function of the Ski gene in body composition and metabolism via modulation of NR-dependent metabolism in skeletal muscle, fat and liver
- Profiling NR and cofactor expression in normal, estrogen receptor (ER)-positive and ER-negative breast cancers

KEY PUBLICATIONS

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Pearen, M.A., and Muscat, G.E. (2010). Minireview: Nuclear hormone receptor 4A signaling: implications for metabolic disease. *Molecular Endocrinology* **24:** 1891-1903.

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LAB MEMBERS

Research Officers: Dr Patrick Lau, Dr Michael Pearen, Dr Mary Wang, Dr Gary Leong (50% each IMB & NHMRC Clinical CDA, Mater Children's Hospital)

Research Assistants: Rebecca Fitzsimmons, Nick Martel

PhD Students: Natalie Eriksson, Lisa Crowther

ANDREW PERKINS
BLOOD DEVELOPMENT

OUR GROUP IS INTERESTED IN the transcriptional regulation of blood formation. We are primarily concerned with transcriptional hierarchies and how transcription factors work within biochemical and genetic pathways, and also how deregulation of such programs leads to cancer. We have four primary focus areas:

1. Transcriptional hierarchies which are active during embryonic stem (ES) cell differentiation into mesoderm-derived tissues. The methodologies used include: directed differentiation of ES cells in various recombinant growth factors, gene targeting and BAC recombineering for generating reporter ES cell lines and mice in which stem cells can be followed by epifluorescence and FACS, expression profiling and chromatin immuno-precipitation.
2. Transcriptional regulation of erythropoiesis. Mutations in the globin genes 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. The long-term goal is to design new drugs that target key regulators of this process and thereby reactivate foetal haemoglobin in adults.
3. The role played by the Kruppel-like factor (KLF) family of zinc finger genes in normal differentiation and human skin, colon and blood cancers.
4. The genetics underpinning gastrulation and subsequent generation of haematopoietic stem cells in the mammalian embryo.

RESEARCH PROJECTS

- Investigating the transcriptional regulation of erythropoiesis
- Studying the roles of Kruppel-like factors in human diseases
- Using chemical mutagenesis to discover new genes that regulate HSC generation and behaviour
- Studying the role of long non-coding RNAs in gastrulation

KEY PUBLICATIONS

Papathanasiou, P., Tunningley, R., Pattabiraman, D.R., Ye, P., Gonda, T.J., Whittle, B., Hamilton, A.E., Cridland, S.O., Lourie, R., and Perkins, A.C. (2010). A recessive screen for genes regulating hematopoietic stem cells. *Blood* **116**: 5849-5858.

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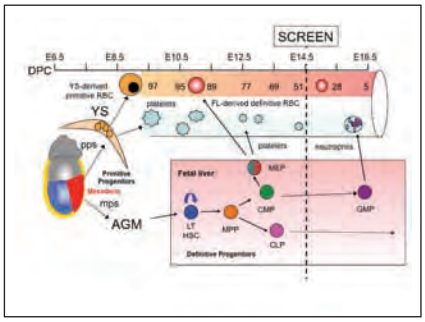


Absent B cells and relatively reduced T cells in boo/boo *spleen. (I-J) Increased frequency of CD71+/TER119+ mature erythroid cells and also CD71^{lo} immature cells in* boo/boo *spleen. (K-L) Increased Gr1^{hi} neutrophils, Gr1^{int} monocytes and TER119+ erythroid cells in* boo/boo *spleen. (M-N) Pie graphs show percentage contribution of B220+ B cells ('B'), CD3+ T cells ('T'), TER119+ erythroid ('E') cells, Gr1 bright granulocytes ('Gr'), Gr1 intermediate macrophages ('M'), and precursor cells ('Pr', which are mostly CD71 weak early erythroid lineage cells) to the spleen. Numbers represent the mean of FACS analyses from 6* boo/boo *mice and 6 wild-type (+/+) littermate controls.*

Bruce, S.J., Gardiner, B.B., Burke, L.J., Gongora, M.M., Grimmond, S.M., and Perkins, A.C. (2007). Dynamic transcription programs during ES cell differentiation towards mesoderm in serum versus serum-free (BMP4) culture. *BMC Genomics* **8**: 365.

Perkins, A.C., Sharp, A.H., and Orkin, S.H. (1995). Lethal β-thalassemia in mice lacking the erythroid CACCC-transcription factor EKLF. *Nature* **375**: 318-322.

LAB MEMBERS

Research Officer: Dr Michael Tallack

Research Assistant: Graham Magor

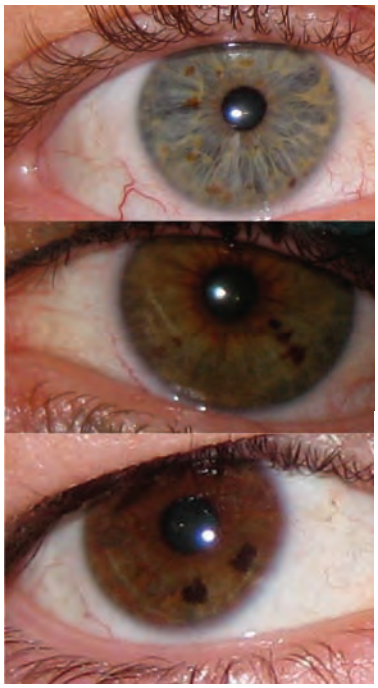
PhD Student: Paulo Amaral

Honours Student: Jessica Fittock

RICK STURM
MELANOGENIX RESEARCH GROUP

THE MELANOGENIX (MELANOCYTE biology and pigmentation genetics) laboratory is studying the molecular, genetic and cellular basis underlying normal human variation in the pigmentary traits of skin, hair and eye colour. Several genome-wide association studies (GWAS) for pigmentation have now been conducted and identified SNP markers in known (*TYR*, *TYRP1*, *OCA2*, *SLC45A2*, *SLC24A5*, *MC1R*, *ASIP*, *KITLG*) and previously unknown (*SLC24A4*, *IRF4*, *TPCN2*) candidate genes. We have investigated skin and hair colour genetic associations in Europeans, and discovered that responsible polymorphisms are found within a range of pigmentation genes, whereas blue-brown eye colour can be explained by a single SNP proposed to regulate *OCA2* expression. There is a strong genotype-by-age effect of *IRF4* on nevus count, and the responsible SNP is associated with increased melanoma risk. In addition, we have found that this SNP can modulate the transcriptional expression of the IRF4 gene in melanocytes.

Functional analysis of the human pigmentation gene set will ultimately provide a full appreciation of this biological system linking genotype with phenotype. Specifically the role of the MC1R gene variants in directing skin phototype and response to UV-induced ligand binding and receptor activation is a major area of investigation. In addition, the group is studying the process of development and differentiation of the melanocytic cell lineage using primary melanoblast and melanocyte cell culture, as well as coculture of these cells with keratinocytes. This will provide information to allow the genes and processes involved in melanoma tumour formation and metastasis to be examined. Each of these aims centres on the identification and molecular characterisation of genes involved in melanocyte cell function.



RESEARCH PROJECTS

- Understanding skin cancer risk phenotypes through studying the interaction of genes involved in skin, hair and eye colour
- Molecular, genetic and cellular analysis of melanin formation
- Analysis of MC1R genotyped human melanocytes in monoculture and in coculture with keratinocytes
- Melanoma spheres as a model for melanoma development and metastasis
- Role of NR4A nuclear hormone receptors in melanocytic cells

KEY PUBLICATIONS

Duffy, D.L. *et al.* (2010). IRF4 variants have age-specific effects on nevus count and predispose to melanoma. *American Journal of Human Genetics* **87**: 6-16.

Duffy, D.L., Zhao, Z.Z., Sturm, R.A., Hayward, N.K., Martin, N.G., and Montgomery, G.W. (2010). Multiple pigmentation gene polymorphisms account for a substantial proportion of risk of cutaneous malignant melanoma. *Journal of Investigative Dermatology* **130**: 520-528.

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Sturm, R.A., and Larsson, M. (2009). Genetics of human iris colour and patterns. *Pigment Cell and Melanoma Research* **22**: 544-562.

LAB MEMBERS

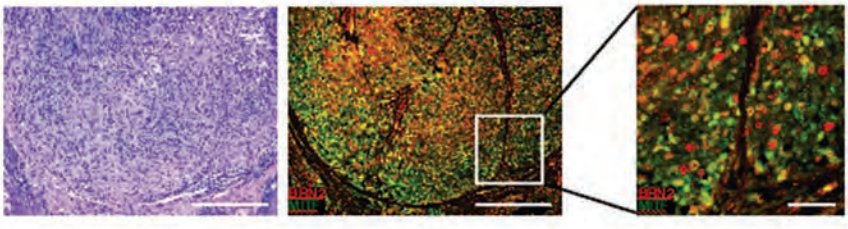
Research Officers: Dr Kimberley Beaumont, Dr Aaron Smith, Dr Shu Shyan Wong

Research Assistants: Garth Douglas, Matthew Harrison, Kasturee Jagirdar, Wen Lim, Darren Smit, Caroline Sturm

PhD Students: Stephen Ainger, Helene Johanson

Honours Student: Amanda Ong

Visiting Students: Puya Gharahkhani (PhD Vet Science), Elizabeth Webb (USA Fulbright Scholar)



Human melanoma tumour.

MATT SWEET

PATHOGEN SURVEILLANCE, INNATE IMMUNITY AND INFLAMMATION

ALL MULTICELLULAR ORGANISMS are equipped with an immune system, which provides protection against infectious diseases. In mammals, the innate immune system acts as the first line of defence. Once activated, innate immunity attempts to trigger direct microbial destruction, and to contain the invading pathogen by promoting inflammation. Innate immune cells such as macrophages use several families of pattern recognition receptors (PRRs) to detect specific structural components on pathogens. PRRs also respond to endogenous host ligands that are present in inflammatory disease settings. Thus, PRRs are essential for host defence against invading microbes, but also contribute to the pathology of many inflammatory diseases. The most widely studied PRRs are the Toll-like Receptors (TLRs). We study TLR-dependent and TLR-independent mechanisms by which macrophages sense and respond to invading microorganisms by focusing on recognition of Gram-negative bacterial pathogens (e.g. *Salmonella* Typhimurium, uropathogenic *E. coli*), as well as individual microbial components (e.g. lipopolysaccharide, double-stranded DNA).

Our interests cover the actual PRR systems themselves (e.g. TLRs), the downstream signalling pathways that are activated by TLR ligands (including cross-talk with other signalling pathways e.g. CSF-1 signalling), and the functions of TLR target genes, which ultimately promote inflammation and anti-microbial responses. Research highlights for 2010 include: (1) the identification of a specific histone deacetylase (HDAC7) that promotes TLR-activated inflammatory pathways; (2) the identification of widespread differences between humans and mice in TLR target genes; (3) the identification of macrophages as an intracellular reservoir for the urinary tract pathogen, uropathogenic *E. coli*; and (4) the mapping of molecular mechanisms involved in immune cell death triggered by foreign DNA detected in the cytoplasm. Our immediate research objectives are to develop small molecule inhibitors against HDAC7 for testing as anti-inflammatory agents, to validate the importance of species differences in TLR-activated anti-microbial pathways, and to determine the mechanisms used by uropathogenic *E. coli* to subvert macrophage anti-microbial responses. Our ultimate goals are to generate new insights into the mechanisms used by the host innate immune system to destroy invading microbes, and to develop novel approaches to targeting inflammatory diseases.

RESEARCH PROJECTS

- Characterising the role of specific histone deacetylases in Toll-like Receptor-mediated inflammatory responses
- Human macrophage anti-microbial responses to Gram-negative bacterial pathogens such as *Salmonella typhimurium*
- Role of macrophages in uropathogenic *E. coli* pathogenesis
- Characterisation of the cellular recognition system for detection of foreign DNA in the cytoplasm
- Involvement of novel TLR-regulated genes in inflammatory and anti-microbial responses

KEY PUBLICATIONS

Halili, M.A., Andrews, M.R., Labzin, L.I., Schroder, K., Matthias, G., Cao, C., Lovelace, E., Reid, R.C., Le, G.T., Hume, D.A., Irvine, K.M., Matthias, P., Fairlie, D.P., and Sweet M.J. (2010). Differential effects of selective HDAC inhibitors on macrophage inflammatory responses to the Toll-like Receptor 4 agonist LPS. *Journal of Leukocyte Biology* **87**: 1103-1114.

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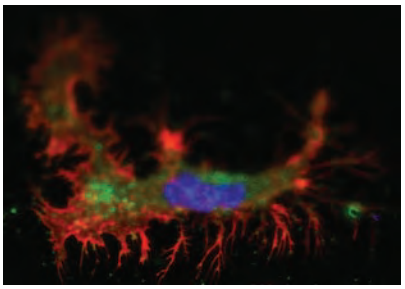

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LAB MEMBERS

Senior Research Officer: Dr Kate Stacey

Research Officers: Dr Steve Broomfield, Dr Vitalia Sagulenko

Research Assistants: Greg Kelly, Juliana Ariffin, Jasmyn Dunn

PhD Students: Melanie Andrews, Dr Nilesh Bokil, Divya Ramnath, Kylie Alexander

Honours Student: Nabilah Ahmad Kamal

BRANDON WAINWRIGHT

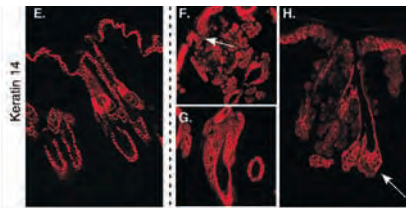
TISSUE REPAIR AND CANCER

USING GENOMIC APPROACHES, our group mapped and isolated the gene for the heritable cancer disorder, naevoid basal cell carcinoma syndrome (NBCCS). The patched gene, discovered from our studies on NBCCS, has defined a signalling pathway known as the "hedgehog pathway", which appears to be mutated or perturbed in a wide range of tumour types, including lung, gastro-intestinal, skin, pancreatic, prostate, brain and ovarian cancer. This has led us to focus on the role of hedgehog signalling, not only in cancer but also on the regulation of stem cell compartments. Increasingly it appears that in some tumour types there are cells known as "cancer stem cells" which reside within the tumour and are responsible for the overall phenotype. Currently such cells can be partially defined functionally but their molecular signature remains elusive. We believe that the patched/hedgehog pathway defines many of the characteristics of such stem cells and is a powerful starting point for understanding tumour biology and the development of new therapeutics.

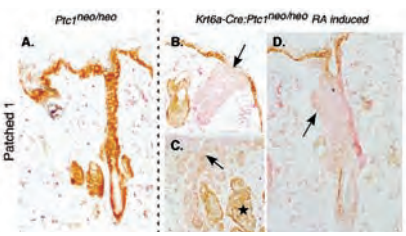
Given that cancer represents a state of unregulated cell growth, it is likely that the pathways that lead to cancer are also involved in the normal process of tissue growth and repair. Several of our studies are particularly directed at the role of the hedgehog (and other pathways) in repair and regeneration. The two most common cancer types in NBCCS patients are basal cell carcinoma of the skin and medulloblastoma, a common brain tumour occurring predominantly in children. In the example of both tumour types we are examining how activation of the hedgehog pathway causes the tumour, and defining the cell of origin of the tumour using a combination of molecular genetics and cell biology. We are also defining the interaction of the hedgehog pathway with other genetic pathways, such as Notch signalling, in order to understand the normal development of the skin and the cerebellum, but also what therapeutic strategies might be useful to treat the tumours. In addition to studying known pathways, we are seeking new interactions through genomic approaches to discovering new genes and pathways in model systems such as mice and zebrafish. The IMB has a well-developed drug discovery platform and we are using our knowledge of the biology of these tumours to look for potential new therapeutics.

As part of our experimental approach our laboratory makes extensive use of transgenic and knockout mice. However at all points we refer back to the human diseases under study and have major activities based around mutation analysis, transcriptomics and proteomics of human material, integrating the data from all systems.

As a result of these studies we have a particular interest in the interface between developmental cell biology and human genetics, and in therapeutic interventions such as gene or cell therapies.



Above and below: Loss of patched leads directly to skin tumours.



RESEARCH PROJECTS

- Controlling neuronal stem cells and CNS by the patched/hedgehog pathway
- Investigating the molecular basis of primary brain tumours
- Controlling the stem cell niche in mammalian epidermis and skin cancer
- Discovery of new genes capable of suppressing tumour growth
- The role of microRNAs in brain tumour development

KEY PUBLICATIONS

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Adolphe, C., Hetherington, R., Ellis, T., and Wainwright, B. (2006). Patched1 functions as a gatekeeper by promoting cell cycle progression. *Cancer Research* **66**: 2081-2088.

LAB MEMBERS

Research Officers: Dr Richa Dave, Dr Rehan Villani, Dr Christelle Adolphe, Dr Jonathan Robson, Dr Elaine Julian

Research Assistant: Melissa Bourboulas

PhD Students: Uda Ho, Lena Constantin, Rhonda Kan, Peter Yee

Undergraduate Students: Eriza Secondes, Paul Joosa, Stephanie Kamp, Chun Tatt Lim

Visitors: Luis Milla

CAROL WICKING

DEVELOPMENTAL GENES AND HUMAN DISEASE

DEFECTS ARISING FROM ABNORMAL embryonic development are a major cause of infant mortality and childhood disability. Many such disorders are characterised by anomalies of the limbs and craniofacial region, making an understanding of the molecules involved in patterning these structures vital. The hedgehog pathway is one of the most pivotal signalling cascades governing embryogenesis and its inappropriate activation in the adult leads to a myriad of tumours. My lab is focused on understanding the role of hedgehog signalling in development of the limb and face, and more broadly in organogenesis.

We primarily use the mouse as a model system and have a number of engineered mouse mutants as well as those arising from forward genetic screens. These mutants have allowed us to uncover novel patterning and skeletal defects arising from misregulation of hedgehog signalling in the limb and face. In addition, in collaboration with Emma Whitelaw at QIMR, we have identified a mouse with an N-ethyl-N-nitrosourea (ENU) induced point mutation in a gene involved in maintaining the primary cilium. The primary cilium is a solitary non-motile organelle that protrudes from the surface of virtually every vertebrate cell. Over the past several years the primary cilium has emerged as a novel cellular compartment required for hedgehog signalling, and aberrant function leads to an array of human disorders known as ciliopathies. Characterisation of mouse mutants along with detailed cellular trafficking studies is allowing us to unravel the function of this important organelle.

In parallel studies Dr Kelly Smith has introduced the zebrafish model into the lab, having arrived from post-doctoral studies at the Hubrecht Institute in the Netherlands to continue her characterisation of early heart development. This is based on mutants identified in a forward genetic screen and has implications for human congenital heart disease.

RESEARCH PROJECTS

- Using an ENU-derived mouse mutant to investigate the role of the primary cilium in hedgehog signalling and disease
- Trafficking within the primary cilium
- Investigating the role of patched in development of the face through mouse knockout studies
- A novel role for hedgehog signalling in the very early stages of chondrogenesis in the limb
- Analysis of early heart development in the zebrafish

KEY PUBLICATIONS

Bruce, S.J., Butterfield, N.C., Metzis, V., Town, L., McGlinn, E., and Wicking, C. (2010). Inactivation of *patched1* in the mouse limb has novel inhibitory effects on the chondrogenic programme. *Journal of Biological Chemistry* **285**: 27967-27981.

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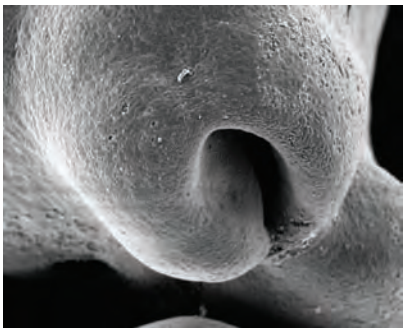

A scanning electron micrograph showing the surface of the embryonic mouse face looking into the nasal pit (image by Ashley Cooper).

Skeletal structure of the wild-type mouse skull at 16.5dpc (image by Vicki Metzis).

Buchtova, M., Handrigan, G.R., Tucker, A.S., Lozanoff, S., Town, L., Fu, K., Diewert, V.M., Wicking, C., and Richman, J.M. (2008). Initiation and patterning of the snake dental lamina are dependent on Sonic Hedgehog signalling. *Developmental Biology* **319**: 132-145.

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LAB MEMBERS

Research Officers: Dr Steve Bruce, Dr Fredrik Olsson, Dr Liam Town, Dr Kelly Smith

Research Assistant: Andrew Courtney

PhD Student: Vicki Metzis

Honours Student: Ashley Cooper

DAGMAR WILHELM

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

OUR GROUP FOCUSES ON THE elucidation of regulatory mechanisms that control gene expression during embryonic development. One of the most amazing biological processes is the development of a fertilised egg into a complex organism. It involves the orchestration of cellular processes such as cell proliferation, migration, differentiation and apoptosis, which is 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 cancer, and often lethality. Therefore, each of these processes must involve a large number of regulatory mechanisms.

Until recently our work centred around the conventional dogma, which states that gene activity is controlled by transcription factor binding to proximal promoters and/or enhancers adjacent to genes. We are now extending these studies to include the fact that gene activity is also regulated post-transcriptionally by non-coding RNAs (ncRNAs), such as microRNAs. In addition to investigating the role of microRNAs during development, we have discovered a new class of ncRNAs, uaRNAs (3'UTR-associated non-coding RNAs), that displays a highly regulated stage- and sex-specific expression pattern during embryogenesis.

Furthermore, we want to use the knowledge of small RNA processing and function, also called RNA interference (RNAi), as a tool to control pest species in Australia. The common carp represents an increasing menace to Australian freshwater ecosystems. Further unchecked growth and spread of the carp population poses a threat to many native fish species. In this project we are investigating the biology of RNAi in carp and zebrafish, to investigate the potential of a "daughterless" approach by making use of the endogenous RNAi processing machinery to knock down aromatase and thereby control carp numbers.

Our research uses mouse and zebrafish as model systems and integrates molecular and developmental biology to study mechanisms of gene regulation by transcription factors as well as ncRNAs during embryonic development, concentrating on sex determination and gonad development but extending to other developmental systems such as chondrogenesis.

The aims of our research are to address the intersections of the following questions:

1 What are the regulatory mechanisms underlying the development of the ovary?

2 What are the roles of ncRNAs, including long and small RNAs, during the development of testes and ovaries?

3 What are the mechanisms of processing and function of small RNAs in fish?

RESEARCH PROJECTS

- Characterisation of the role of *miR-202* and *miR-140* during embryonic development
- Analysis of novel microRNAs involved in gonad development
- Functional characterisation of ncRNAs during embryonic development
- Studying the cellular and molecular regulation of foetal ovary development
- Characterisation of RNAi in fish

KEY PUBLICATIONS

Mercer, T.R.*, Wilhelm, D.*, Dinger, M.E.*, Solda, G.*, Korbie, D.J., Glazov, E.A., Truong, V., Schwenke, M., Matthaei, K.I., Saint, R., Koopman, P., and Mattick, J.S. (2010). Expression of distinct RNAs from 3' untranslated regions. *Nucleic Acids Research* Epub November 12.

McFarlane, L., and Wilhelm, D. (2009). Non-coding RNA in mammalian sexual development. *Sexual Development* **3**: 302-316.

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Wilhelm, D., Martinson, F., Bradford, S., Wilson, M.J., Combes, A., Beverdam, A., Bowles, J., Mizusaki, H., and Koopman, P. (2005). Sertoli cell differentiation is induced both cell-autonomously and through prostaglandin signalling to activate Sox9 during mammalian sex determination. *Developmental Biology* **287**: 111-124.

Wilhelm, D., and Englert, C. (2002). The Wilms tumour suppressor WT1 regulates gonadal development by activation of Sf1. *Genes and Development* **16**: 1839-1851.

LAB MEMBERS

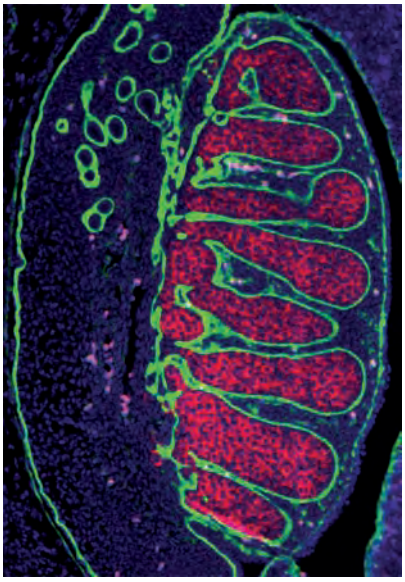
Research Officer: Dr James Palmer

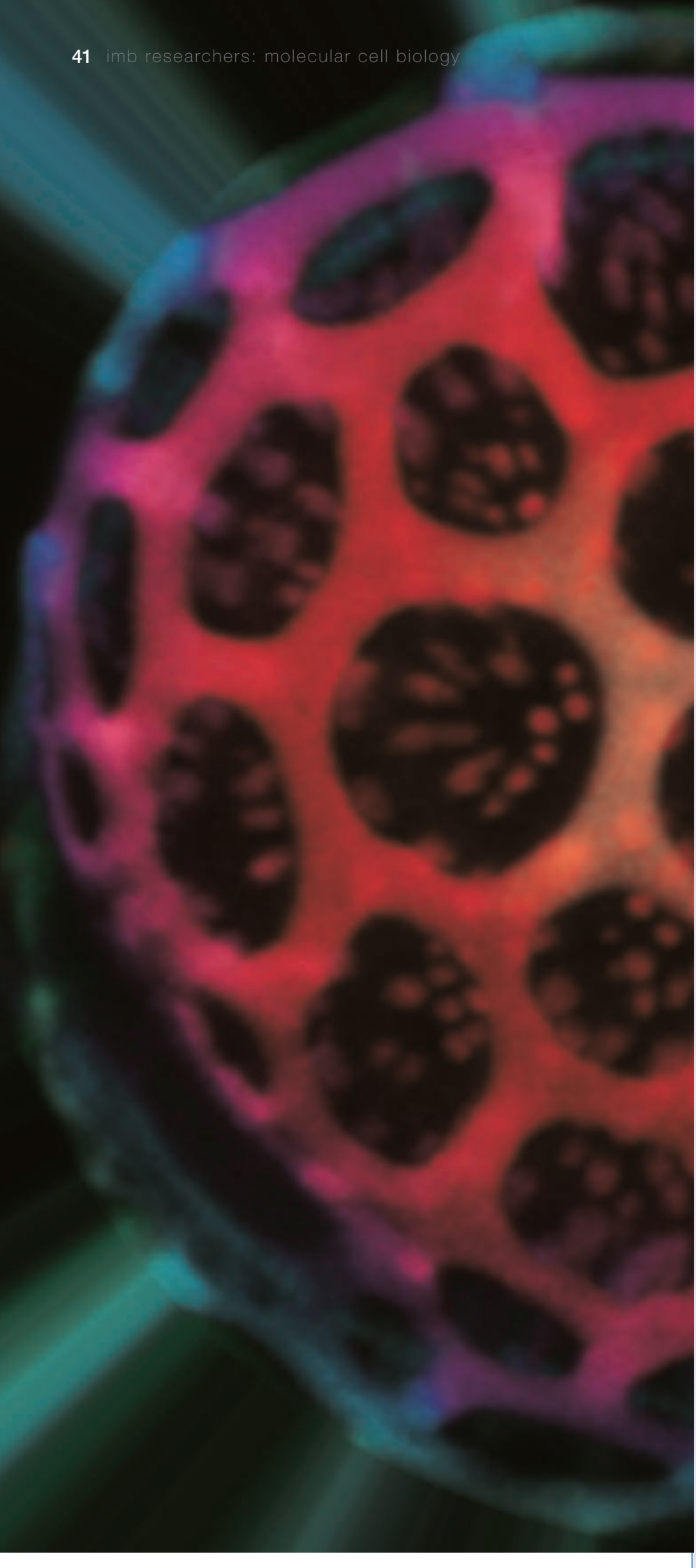
Research Assistants: Vy Truong, Huijun Chen, Emmanuelle Frampton

PhD Students: Lindsey McFarlane, Elanor Wainwright

Occupational Trainee: Nicolas Melin

Honours Student: Joanna Rakoczy





Division of
MOLECULAR CELL BIOLOGY

Cell Biology seeks to understand the molecular workings of the cell. This ambition encompasses efforts to elucidate how molecular and biochemical mechanisms are integrated to drive fundamental cellular events, such as metabolism, intracellular transport, growth, division and signalling. Ultimately such integration must extend to encompass the differentiation events and the interaction of cells with their environment that are the basis for tissue function. Such fundamental knowledge also forms the basis for a detailed understanding of cellular pathology in human diseases, such as inflammation and cancer.

THE RESEARCH GROUPS OF THE Division of Molecular Cell Biology are tackling individual problems that speak to various key problems in cell biology. These include the trafficking of cytokines in inflammation (Stow); the biochemical dynamics of GTPase signalling (Alexandrov); 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); high-throughput computational analysis of cellular imaging (Hamilton, joint appointment with GCB); and cell biology of growth hormone (Waters). These snapshots highlight, however, only part of each group's research program, the range of which can be well appreciated in their individual laboratory reports.

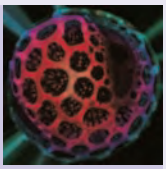
All the individual groups of the Division are supported by external research funding. These include project and program grants from the NHMRC, and project grants from the ARC, Cancer Council, and Human Frontiers Science Program (HFSP). Many group leaders in the Division are also supported by Fellowships from the NHMRC and ARC. The awarding of $2.5 million from the Australian Cancer Research Foundation allowed the establishment of the ACRF Cancer Biology Imaging Facility, which was officially opened in February 2010 by Queensland Governor Her Excellency Dr Penelope Wensley AO. Professor Rob Parton received an award from the NHMRC for having the highest-ranked project grant in the nation. Each grant is ranked according to its suitability for receiving funding, and of the 2984 project grants submitted to the Council, Professor Parton's was awarded the most points. New grants awarded in 2010 included a $5m grant from the National Breast Cancer Foundation to a team of eight chief investigators, including Professor Alpha Yap. The team aims to develop treatments to tackle the recurrence of breast cancer, and is led by Professor Erik Thompson from St Vincent's Institute and the University of Melbourne. The division received $1.1 million from the NHMRC from two grants awarded to Professors Yap and Mike Waters, to investigate cell adhesion and permanently activated growth hormone respectively. Professor Jenny Stow received a Discovery grant from the ARC worth $315k to examine the secretory pathways that play a role in immune defence and are dysfunctional in disease. She was also awarded an NHMRC Research Fellowship to study protein trafficking in diseases including inflammation. Dr Brett Collins received an ARC Future Fellowship to study the control of protein transport in cells.

Members of the Division maintained extensive engagement in the scientific community both nationally and internationally. Professor Stow is a member of the Medical Advisory Board of the Australian Cancer Research Foundation; Professor 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 Professor Alpha Yap served as the Convenor of the 2010 Hunter Cellular Biology Meeting.

The Division played host to several distinguished national and international scientists who spoke at the IMB's Friday Seminar Series. These included Professor Frances Brodsky (University of California San Francisco, USA), Professor Vojo Deretic (University of New Mexico, Albuquerque, USA), Dr Michael Way (Cancer Research UK London Research Institute, U.K.), Dr Brian Burke (Institute of Medical Biology, Singapore), and Professor Angel Lopez (Institute of Medical & Veterinary Science, Adelaide).

In addition to external visitors, a major part of the intramural academic life of the Division is the Cell Biology Forum (CBF). First established by Professor Parton, and currently coordinated by Brett Collins, this weekly meeting is dedicated to research presentations by the students, post-doctoral fellows, and affiliates of the Division. It serves both to provide essential training in research presentations, and also to promote scientific exchange at all levels within the Division.

Finally, Mr Darren Brown, a research assistant in the Stow group, was the winner of the 2010 Ångström Art™ Centenary Competition. His winning image is featured on the front cover of this report. One of Mr Brown's images was also chosen as one of two runner-up images. The Stow group researchers focus on protein trafficking, particularly in the context of disease and the immune system, and this is reflected in many of the images Mr Brown contributed to the competition. All of the images submitted to the competition, and more information about each, can be viewed at the Ångström Art™ website: www.angstrom-art.com



JOHN GRIFFIN: POINCIANA POLLEN

Curiosity is an important quality for scientists and artists alike. Knowing that pollen can exhibit beautiful and surprising forms, I succumbed to my curiosity when the Poinciana trees were in full bloom on our campus and collected some Poinciana stamens on my way to the IMB one morning. This image was acquired on a Zeiss LSM 510 confocal laser scanning microscope and the resulting confocal sections were depth-coded individually in Adobe Photoshop CS3 and processed in ImageJ.

KIRILL ALEXANDROV

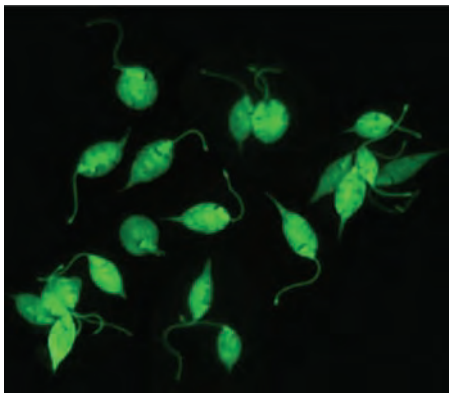
NEXT-GENERATION TECHNOLOGIES FOR PROTEIN RESEARCH

ADVANCES IN LIFE SCIENCES AND biotechnology are driven by our ability to replicate the building blocks of life in vitro, modify them, and use them in academic and industrial applications. Much biotechnological progress in the last 40 years 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 group is focusing on 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 protozoan *Leishmania tarentolae*. We demonstrate that, using this technology, large sets of genes can be converted into proteins within hours. We apply this technology to study cellular processes controlled by Rab GTPases and the role of protein prenylation in this process. Due to their importance in many signalling and trafficking pathways, a deregulation of the GTPases (expression defects, mutations, or defects in their prenylation status) is associated with numerous human pathologies.

RESEARCH PROJECTS

- Development of high-yield cell-free protein expression system based on *Leishmania tarentolae*
- Quantitative analysis of protein:protein protein:small molecule interactions using in vitro protein expression systems
- Proteome-wide analysis of protein prenylation and its variation in human diseases
- Understanding of mechanisms regulating protein prenylation machinery
- Identification of small molecules modulating prenylation and localisation of RabGTPases



Suspension culture of Leishmania tarentolae *cells expressing GFP protein.*

KEY PUBLICATIONS

Kovtun, O., Mureev, S., Johnston W., and Alexandrov, K. (2010). Towards the construction of expressed proteomes using a *Leishmania tarentolae* based cell-free expression system. *PLOS One* **5**: e14388.

Mureev, S., Kovtun, O., Nguyen, U.T.T., and Alexandrov, K. (2009). Species-independent translational leaders enable the rapid development of novel cell-free expression systems. *Nature Biotechnology* **27**: 747-752.

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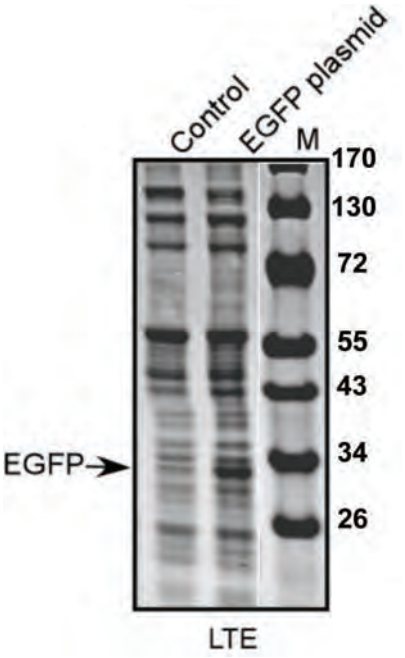


Expression of EGFP in L. tarentolae *cell-free system.*

LAB MEMBERS

Research Officers: Dr Sergey Mureev, Dr Viktor Stein, Dr Wayne Johnston, Dr Zhong Guo

Research Assistants: Virajitha Rajagopalan, Veronika Schreiber, Regina Hartmann, Nichole Giles, Florian Gebhardt, WooRam Jung

PhD Students: Oleksiy Kovtun, Zakir Tnimov, Marta Kubala, Monika Koenke

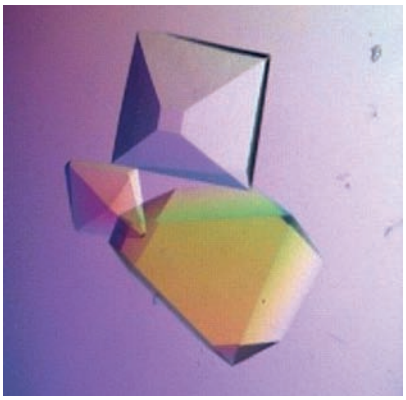
BRETT COLLINS

CELLULAR TRAFFICKING AT ATOMIC RESOLUTION

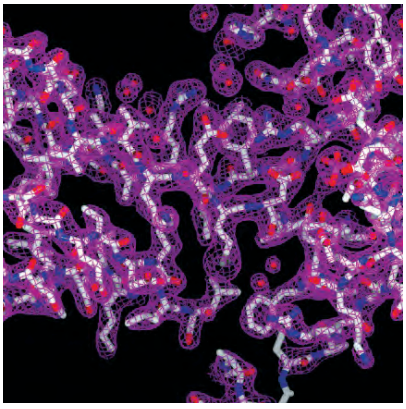
OUR LAB IS FOCUSED ON understanding the processes of intracellular membrane trafficking within the secretory and endocytic systems of the human cell. We do this using a multidisciplinary approach that integrates the high-resolution structural characterisation of essential membrane trafficking machinery by X-ray crystallography with biochemical and cell biological experiments guided by these mechanistic details.

We concentrate primarily on the process of protein sorting within the dynamic organelles known as endosomes, which are key sorting stations for regulated exo- and endocytosis of cell surface receptors, signalling molecules and many other cellular components. The regulated trafficking of proteins and their ligands between membrane-bound endosomal compartments, the plasma membrane and other internal organelles is a fundamental process in human cells, and indeed in all eukaryotes. Defects in the endosomal membrane transport system are linked to many different human diseases, including a number of cancers, Alzheimer's, lysosomal storage disease and hypercholesterolemia, and it is also exploited by bacterial toxins and viral pathogens such as HIV to gain entry into the cell.

Membrane sorting between secretory and endocytic organelles is predominantly controlled by small carrier vesicles and tubules that are layered on their cytoplasmic faces by specific protein machineries. The roles of these protein coats are threefold: (i) to select transmembrane and lipid cargo to be packaged into vesicles forming at the donor membrane, (ii) to control vesicle budding and scission and (iii) to specify the final destination of the transport intermediates. Using a multidisciplinary structural biology/biochemistry/cell biology approach, our goal is to reveal how these machineries assemble, how they are recruited to membranes and how they control receptor trafficking at the molecular level. Current work focuses on the multi-subunit retromer protein complex with a central role in directed transport of endosomal cargo proteins, the PX-domain family of proteins involved in sorting of diverse proteins such as ion transporters and amyloid precursor protein, and a novel family of arrestin-related trafficking proteins.



Crystals of the retromer subunit VPS26B.



Electron density for the VPS26B subunit of retromer.

RESEARCH PROJECTS

- Structure and function of the retromer protein complex and its interaction with cargo proteins and regulatory molecules
- Molecular characterisation of endosomal sorting by PX-domain proteins and their associations with effector molecules
- Structure and function of arrestin-related proteins
- Munc/SNARE interactions during neurosecretion

KEY PUBLICATIONS

Norwood, S.J., Shaw, D.J., Cowieson, N.P., Owen, D.J., Teasdale, R.D., and Collins, B.M. (2010). Assembly and solution structure of the core retromer protein complex. *Traffic* Epub 23/9/2010

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LAB MEMBERS

Research Officers: Dr Suzanne Norwood, Dr Ramya Mandyam

Research Assistant: Jasmine Davis

PhD Students: Daniel Shaw, Rajesh Ghai

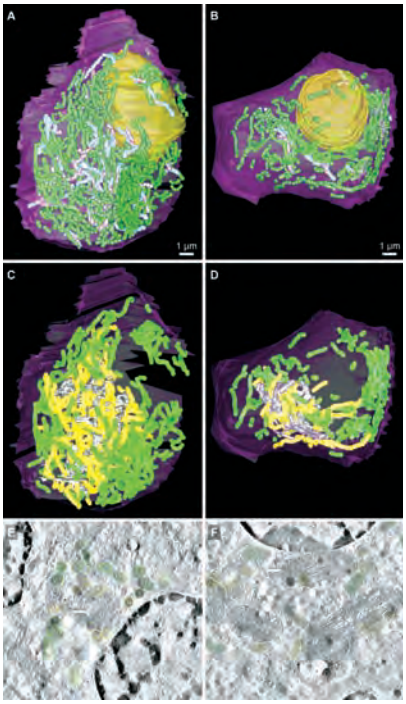
BRAD MARSH

STRUCTURE-FUNCTION STUDIES OF THE PANCREATIC BETA CELL – MAPPING INSULIN BIOSYNTHESIS AND TRAFFICKING IN SITU IN 3D AT THE NANOSCALE

OUR RESEARCH FOCUSES ON THE detailed characterisation of fundamental structure-function relationships underpinning the biosynthesis, trafficking and secretion of the hormone insulin in mammalian cells - specifically, the pancreatic beta cell. To achieve this goal, we quantitatively map cellular organisation in beta cells in 3D at the nanoscale under a range of physiological/disease conditions using cellular electron tomography (ET). Electron tomography uses mathematical methods to computationally reconstruct a 3D volume from a set of 2D images. This is very similar to how diagnostic imaging techniques like computed tomography (CT), magnetic resonance imaging (MRI) and positron electron tomography (PET) are able to computationally reconstruct 3D image maps for different parts (or even all) of the body. In our case, however, we generate 3D image maps for different parts (or even all) of the cell at nanometre resolution. This allows us to unambiguously visualise and characterise machinery in the 'insulin factory' at high spatial resolution to gain fundamental new insights into how insulin is manufactured and released, and to identify how and where defects in these basic processes contribute to beta cell failure and/or death, which leads to the set of diseases broadly referred to as diabetes. Type 1 diabetes is now one of Australia's fastest-growing chronic childhood diseases; currently, type 1 diabetes cannot be prevented, and a cure remains to be found.

RESEARCH PROJECTS

- 3D reconstruction and quantitative/ computational analysis of mammalian (insulin-secreting) cells in situ in tissue at intermediate (~10nm) and high (~4nm) resolutions
- Rotavirus-infection of pancreatic islets/ beta cells
- Correlative light and electron microscopy of Golgi organisation and membrane traffic in mammalian cells
- High-content screening of small bioactive molecules as potential therapeutic agents for promoting healthy pancreatic beta cell growth and function
- Development/characterisation of optimised liposomes as regulated nanodevices for targeted peptide delivery



KEY PUBLICATIONS

Noske, A.B., and Marsh, B.J. (2011). Mapping the Beta Cell in 3D at the Nanoscale Using Novel Cellular Electron Tomography and Computational Approaches, in: *BetaSys - Systems Biology of Regulated Exocytosis in Pancreatic βCells* (B Booß-Bavnbek, B Klösgen, J Larsen, F Pociot, E Renström, Eds.). Series: Systems Biology. Springer (In Press)

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Emr, S., Glick, B.S., Linstedt, A.D., Lippincott-Schwartz, J., Luini, A., Malhotra, V., Marsh, B.J., Nakano, A., Pfeffer, S.R., Rabouille, C., Rothman, J.E., Warren, G., and Wieland, F.T. (2009). Journeys through the Golgi - taking stock in a new era. *Journal of Cell Biology* **187**: 449-453.

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Richter, T., Floetenmeyer, M., Ferguson, C., Galea, J., Goh, J., Lindsay, M.R., Morgan, G.P., Marsh, B.J., and Parton, R.G. (2008). High-resolution 3D quantitative analysis of caveolar ultrastructure and caveola-cytoskeleton interactions. *Traffic* **9**: 893-909.

LAB MEMBERS

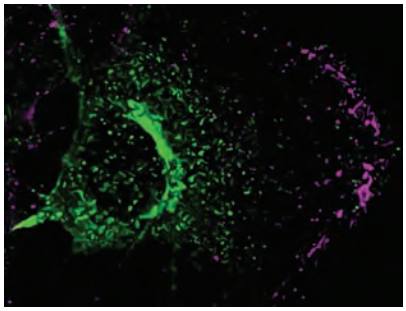
Research Officers: Dr Isabel Morrow, Dr Neelima Sidharthan, Dr Massimo Micaroni

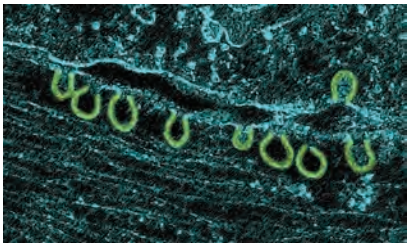
Research Assistant: Garry Morgan

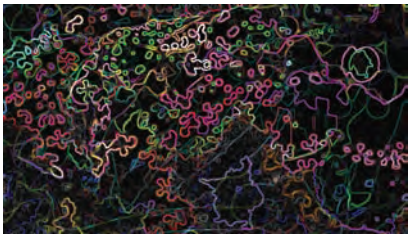
PhD Students: Adam Costin, Alex Foo, Andrew Noske, Peter van der Heide, Timothy Pan, Nur Intan Ruhaiyem

ROB PARTON
THE CELL SURFACE IN HEALTH AND DISEASE

OUR GROUP IS INTERESTED IN THE organisation, dynamics, and functions of the plasma membrane. The properties of the plasma membrane rely on the specialisation of the plasma membrane into microdomains of specific function. We are studying two types of surface microdomains: caveolae, a specialised domain of the cell surface with a distinct structure, and clathrin-independent endocytic carriers (CLICs), that form the major endocytic pathway in mammalian cells. Caveolae have been implicated in regulation of cell growth and in maintaining the balance of lipids in the cell. In addition, caveolins, the major membrane proteins of caveolae, and cavins, a newly-discovered family of caveolar coat proteins, have been implicated in a number of disease states including tumour formation, lipodystrophies, and muscular dystrophy. To study caveolae function we are using caveola-null mice, cells lacking caveolins and/or cavins, and zebrafish embryos. These systems are also being used to study the role of caveolae in muscle and the molecular changes associated with muscular dystrophy. An additional aim of our work is to understand the link between caveolae and lipid-filled organelles termed lipid droplets, which are major storage organelles involved in obesity. We are also using our knowledge of caveolin-induced vesicle formation to develop novel drug encapsulation systems with potential therapeutic applications.







RESEARCH PROJECTS

- Analysis of the role of caveolae in lipid regulation and mechanosensing
- Caveolae and obesity: dissecting the role of caveolins and Rab proteins in lipid droplet formation and function in adipose tissue and during liver regeneration
- Caveolae, caveolin-3, and cavins in muscle: analysing the role of caveolae in muscle development and in muscular dystrophy
- Caveolins and caveolin-interacting proteins in zebrafish: using zebrafish as a model system to understand the role of caveolae during development and the effect of muscular dystrophy mutants of caveolin-3 on muscle structure and function
- Clathrin-independent endocytosis: characterising the structure and function of a novel endocytic pathway in mammalian cells and the zebrafish
- Caveola formation and structure: studying caveola biogenesis and caveolae structure in health and disease using electron tomography and novel cell systems
- Caveola formation in bacteria: characterisation of novel nanovesicles and their use as drug delivery vehicles

KEY PUBLICATIONS

Howes, M.T., Kirkham, M., Riches, J., Cortese, K., Walser, P.J., Simpson, F., Hill, M.M., Jones, A., Lundmark, R., Lindsay, M.R., Hernandez-Deviez, D.J., Hadzic, G., McCluskey, A., Bashir, R., Liu, L., Pilch, P., McMahon, H., Robinson, P.J., Hancock, J.F., Mayor, S., and Parton, R.G. (2010). Clathrin-independent carriers form a high capacity endocytic sorting system at the leading edge of migrating cells. *Journal of Cell Biology* **190**: 675-691.

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Hill, M.M., Bastiani, M., Luetterforst, R., Nixon, S., Kirkham, M., Kirkham, A., Nixon, S.J., Walser, P., Abankwa, D., Ooschot, V.M.J., Martin, S., Hancock, J.F., and Parton, R.G. (2008). PTRF-cavin, a conserved cytoplasmic protein required for caveola formation and function. *Cell* **132**: 113-124.

LAB MEMBERS

Senior Research Officer: Dr Susan Nixon

Research Officers: Dr Manuel Fernandez-Rojo, Dr Harriet Lo, Dr Kerrie-Ann McMahon#, Dr Mark Howes#, Dr Michele Bastiani#, Dr Ramya Mandyam#*

Research Assistants: Robert Luetterforst*, Leanne Cooper, Rachel Hancock*, Charles Ferguson, James Rae, Nicole Schieber*

PhD Students: Samantha Murphy, Carol Kistler, Nick Ariotti, Natalya Leneva, Satomi Okano#, Natasha Chaudhary

Visitors: Dr. Ian Prior#, Lindsey Murphy#

part of year
* part-time

JENNY STOW

PROTEIN TRAFFICKING IN HUMAN DISEASE

Our research group studies protein trafficking in human and animal cells. The intracellular trafficking of membranes and proteins is a fundamental cell process that also impacts on all human diseases. Our studies in cells of the immune system relate to infectious and inflammatory diseases and our work in epithelial cells aims to investigate their transition to cancer cells. In macrophages and other cells of the immune system, we are studying the process of phagocytosis and other pathways through which bacterial pathogens enter cells, escape our immune defenses and set up infections. Our goal in this work is to identify new targets for anti-bacterial treatments or disease prevention. Immune cells also secrete a plethora of cytokines as part of their immune response. Our studies are revealing the genes, molecules and cell compartments involved in secretory pathways for inflammatory cytokines in macrophages, natural killer cells and other cell types. This work aims to develop new therapeutic strategies for controlling cytokines in chronic inflammatory diseases. Trafficking regulators, including Rabs, SNAREs and PI3K proteins, are investigated as part of our research, and key functional members of these protein families have been identified. In epithelial cells we are interested in many of these same proteins and their roles in cell polarity and cancer prevention. Gene expression arrays, gene knockouts or mutations, and biochemical analyses are used in our research. Since trafficking is a highly dynamic process in cells, a major scientific approach we employ is live cell fluorescence imaging to track fluorescently tagged proteins and fluorescent probes. Imaging cells and molecules in three and four dimensions is a core technology for the research in our group and a rapidly advancing technology of the future.

RESEARCH PROJECTS

- Secretory pathways for cytokines and anti-microbial peptides in immune cells
- New targets for regulating cytokine secretion in arthritis and inflammatory bowel disease
- Structure and function of recycling endosomes in secretory and endocytic pathways
- Phagocytosis and trafficking of bacterial pathogens, including *Salmonella*
- Epithelial cell polarity and tumour prevention
- Imaging live cells to create 3D and 4D maps of trafficking pathways: fluorescence imaging, computer modelling and animation

KEY PUBLICATIONS

Low, P.C., Misaki, R., Schroder, K., Stanley, A.C., Sweet, M.J., Teasdale, R.D., Vanhaesebroeck, B., Meunier, F.A., Taguchi, T., and Stow, J.L. (2010). Phosphoinositide 3-kinase regulates membrane fission of Golgi carriers for selective cytokine secretion. *Journal of Cell Biology* **190**: 1053-1065.

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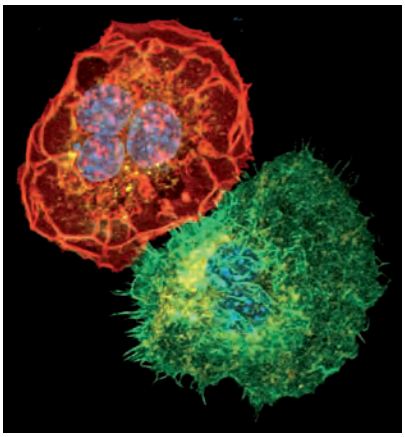
Wood, S.M., Meeths, M., Chiang, S.C., Bechensteen, A.G., Boelens, J.J., Heilmann, C., Horiuchi, H., Rosthøj, S., Rutynowska, O., Winiarski, J., Stow, J.L., Nordenskjöld, M., Henter, J.I., Ljunggren, H.G., and Bryceson, Y.T. (2009). Different NK cell-activating receptors preferentially recruit Rab27a or Munc13-4 to perforin-containing granules for cytotoxicity. *Blood* **114**: 4117-4127.

Lieu, Z.Z., Lock, J.G., Hammond, L.A., La Gruta, N.L., Stow, J.L., and Gleeson, P.A. (2008). A trans-Golgi network golgin is required for the regulated secretion of TNF in activated macrophages in vivo.



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Bryant, D.M., Kerr, M.C., Hammond, L.A., Joseph, S.R., Mostov, K.E., Teasdale, R.D., and Stow, J.L. (2007). EGF induces macropinocytosis and SNX1-modulated recycling of E-cadherin. *Journal of Cell Science* **120**: 1818-1828.

Manderson, A.P., Kay, J.G., Hammond, L.A., Brown, D.L., and Stow, J.L. (2007). Subcompartments of the macrophage recycling endosome direct the differential secretion of IL-6 and TNFalpha. *Journal of Cell Biology* **178**: 57-69.

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Murray, R.Z., Kay, J.G., Sangermani, D.G., and Stow, J.L. (2005). A role for the phagosome in cytokine secretion. *Science* **310**: 1492-1495.

LAB MEMBERS:

Senior Research Officers: Dr Tom Taguchi, Dr Amanda Stanley

Research Officers: Dr Ryo Misaki, Dr Adam Wall

Research Assistants: Darren Brown, Tatiana Khromykh, Juliana Venturato, Teresa Munchow, John Griffin

Research Coordinator: Dr Fiona Wylie

PhD Students: Carolin Offenhauser, Regine Low, Marga Gual Soler

MIKE WATERS

ROLE OF GROWTH HORMONE AND RELATED CYTOKINES IN GROWTH, CANCER, DIABETES AND OBESITY

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 regulating body composition, opposing the actions of insulin. In old age, growth hormone status determines lifespan, at least in animal models. We study the means used by growth hormone to achieve these changes, using a variety of approaches directed to the growth hormone receptor, from high-resolution protein structures to genetically-engineered animals.

The growth hormone receptor determines the degree of the cell response to growth hormone, which we originally cloned collaboratively with Genentech. Through FRET, BRET, crystallography and targeted mutagenesis we have developed a new model of how the GH receptor is activated by GH, involving realignment of receptor subunits within a constitutive dimer. An extension of this model describes how a rearrangement of an extracellular b-loop of the GH receptor selectively controls ERK activation without influencing Stat5 activation through the use of an alternate: Src kinase.

By creating targeted knock-in mutations to signalling domains within the GH receptor cytoplasmic domain, we have shown that enhancement of postnatal somatic growth by GH is dependent on its ability to activate the transcription factor Stat5. Because these mice become strikingly obese after 6 months of age, we are currently investigating the role of Stat5a/b in control of lipid and carbohydrate metabolism using tissue-targeted gene deletion of Stat5a/b. We have found that insulin secretion and action are altered in these mice, and their livers are grossly steatotic. We are identifying the molecular targets of GH that regulate these changes, using in vivo Cre deletion of key transcription factors.

The surprising finding that the growth hormone receptor is located in the cell nucleus of dividing cells has led us to discover that nuclear localised receptor induces the expression of a key stem cell marker. Because we have shown that GH promotes neural stem cell proliferation, we are studying the mechanism of this direct gene induction by the GH receptor.

The absolute requirement for GH in liver regeneration has led us to use our panel of GH receptor signalling mutants to find the identity of the regeneration signal.

RESEARCH PROJECTS

- Investigating the mechanism of activation of growth hormone and related cytokine receptors, including the mechanism of activation of the Src kinase constitutively bound to the receptor
- Elucidating the role of the growth hormone receptor in the cell nucleus in relation to proliferation, oncogenesis and stem cell proliferation
- Determining the role of GH-dependent Stats 5/3/1 in lipid and carbohydrate metabolism, including insulin action
- Establishing the molecular basis for GH-dependent liver regeneration
- Establishing the molecular mechanism underlying the long-term activation of neural stem cells by GH

KEY PUBLICATIONS

Blackmore, D.G., Golmohammadi, M.G., Large, B., Waters, M.J., and Rietze, R.L. (2009). Exercise increases neural stem cell number in a growth hormone-dependent manner, augmenting the regenerative response in aged mice. *Stem Cells* **27**: 2044-2052.

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Lichanska, A.M., and Waters, M.J. (2008). How growth hormone controls growth, obesity and sexual dimorphism. *Trends in Genetics* **24**: 41-47.

Rowlinson, S.W., Yoshizato, H., Barclay, J.L., Brooks, A.J., Behncken, S.N., Kerr, L.M., Millard, K., Palethorpe, K., Nielsen, K., Clyde-Smith, J., Hancock, J.F., and Waters, M.J. (2008). An agonist-induced conformational change in the growth hormone receptor determines the choice of signalling pathway. *Nature Cell Biology* **10**: 740-747.

Schirra, H.J., Anderson, C.G., Wilson, W.J., Kerr, L., Craik, D.J., Waters, M.J., and Lichanska, A.M. (2008). Altered metabolism of growth hormone receptor mutant mice: a combined NMR metabonomics and microarray study. *PLoS ONE* **3**: e2764.

LAB MEMBERS

Research Officers: Dr Andrew Brooks, Dr Tim McPhee

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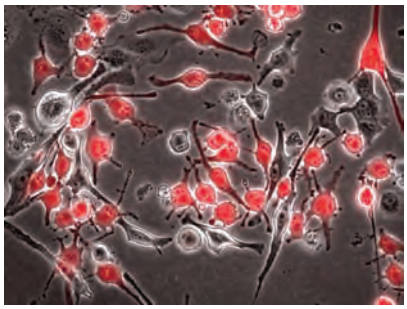
Masters Student: Qiushi Chen

Occupational Trainee: Morgane Roussel



Human melanoma line infected with mKATE2 expressing chicken virus, demonstrating ability to deliver STAT5 dominant negative to halt metastasis.

ALPHA YAP

CADHERIN ADHESION AND TISSUE ORGANISATION IN HEALTH AND DISEASE

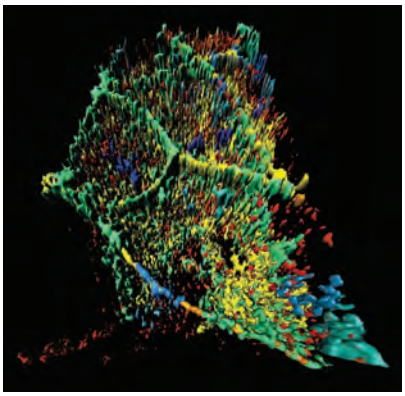
CELLS ARE THE BUILDING BLOCKS of our bodies. Interactions between different cells are important to shape our developing bodies and maintain the organisation of our tissues in health. A range of diseases occur when those interactions are disturbed, including cancer and inflammation. My laboratory studies 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 thus hope to provide vital insights into the basis of developmental patterning and common human diseases.

Currently we focus on understanding how cadherins cooperate with the actin cytoskeleton, long believed to be central to cadherin function. Our experience makes it increasingly clear that this cooperation involves a complex interplay between adhesion receptors and diverse distinct states of the cytoskeleton, coordinated by a variety of signalling pathways at the cell membrane. In particular, our work demonstrates that cadherins function as adhesion-activated cell signalling receptors that stimulate pathways to regulate the actin cytoskeleton, thereby influencing cell shape, adhesion, and cell-cell cohesion. Relevant signals include the Rho family GTPases and Src family kinases. These affect a range of cytoskeletal regulators, including actin nucleators, cross-linking proteins, scaffolds and the myosins II and VI. We aim to understand the dynamic spatial and temporal regulation of the cytoskeleton by cadherin signalling, with a view to understanding how these key elements are used during development and tissue maintenance, and how they are disrupted in human disease.

An important challenge we are beginning to confront is how to understand the complexity of cytoskeletal regulation at cell-cell junctions. Our research experience, accrued over the past several years, indicates that multiple cytoskeletal regulators are coordinated at cadherin adhesion to control junctional dynamics, homeostasis and integrity. How then do we develop a coherent model to encompass this complex system? A significant breakthrough is our recent discovery, published in *Nature Cell Biology* (Smutny *et al.*, 2010), that these cell signals and effectors function in modules, where key effectors are subject to specific signal regulation and have distinct cellular functions, that synergise to support junction integrity. This work was the subject of an editorial review in *Nature Cell Biology* and highlighted on Faculty of 1000. We are now working with Dr Nick Hamilton to develop mathematical tools to measure and model these complex systems.

RESEARCH PROJECTS

- Regulation of the actin cytoskeleton by E-cadherin
- Cooperation between cadherins and myosin motors at cell-cell contacts
- Cooperativity between cadherins and microtubules
- Cadherin signalling to Src family kinases: defining the pathway(s)
- The morphogenetic consequences of cadherin-activated cell signalling and cooperativity with the actin cytoskeleton



KEY PUBLICATIONS

Smutny, M., Cox, H.L., Leerberg, J., Kovacs, E.M., Conti, M.A., Ferguson, C., Hamilton, N.A., Parton, R.G., Adelstein, R.S., and Yap, A.S. (2010). Myosin II isoforms identify distinct functional modules that support integrity of the epithelial zonula adherens. *Nature Cell Biology* **12**: 696-702.

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Ren, G*., Helwani*, F.M., Verma*, S., McLachlan, R.W., Weed, S.A., and Yap, A.S. (2009). Cortactin is a functional target of E-cadherin-activated Src family kinases in MCF-7 epithelial monolayers. *Journal of Biological Chemistry* **284**: 18913-18922. (*Equal contributions)

Akhmanova, A. and Yap, A.S. (2008). Organizing junctions at the cell-cell interface. *Cell* **135**: 791-793.

LAB MEMBERS

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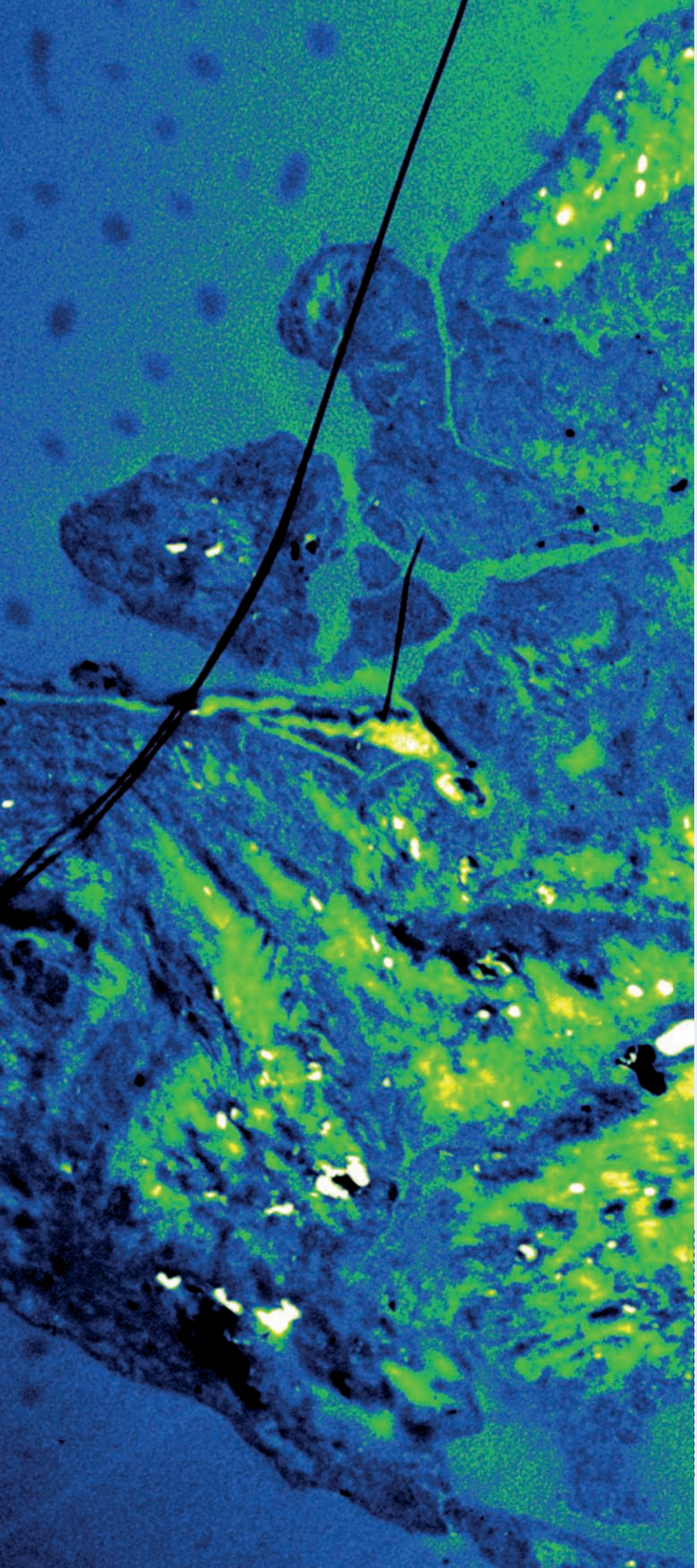
Research Officers: Dr Guillermo Gomez, Dr Michael Smutny, Dr Aparna Ratheesh, Dr Robert McLachlan, Dr Karen Chambers, Dr Siew Ping Han

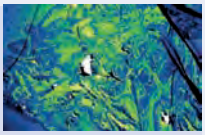
Research Assistants: Suzie Verma, Kris Blucher

PhD Students: Sabine Mangold, Joanne Leerberg, Vincent Leong, Selwin Wu



Division of CHEMISTRY AND STRUCTURAL BIOLOGY

In 2010, the Division of Chemistry and Structural Biology consisted of 10 groups led by Professors David Fairlie, Jenny Martin, Paul Alewood, David Craik, Richard Lewis, Rob Capon, Glenn King, Matt Cooper, and Associate Professors Mark Smythe and Ben Hankamer, with five Affiliates: Professors Alan Mark, Bostjan Kobe, Istvan Toth, Paul Young, and Kirill Alexandrov. The group collectively published 135 papers in the chemical and biological sciences; held ARC Federation, Laureate, Professorial and Future Fellowships as well as NHMRC Australia, PRF and SRF Fellowships; operated 2 NHMRC program grants; and participated in over 20 international and national conferences.



EMILY KNAUTH: PREPARATION

The preparation of any experiment is of utmost importance. Here is an example of algae cell Chlamydomonas reinhardtii *that have been badly damaged by ice crystal formation. The ice crystal form when the cells are not frozen fast enough to form vitreous ice. But just because preparations can leave a lot to be desired, it doesn't mean you can't get a pretty picture out of it.*

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

FELLOWSHIPS & AWARDS

Professor David Craik won the prestigious Ralph F. Hirschmann Award in Peptide Chemistry bestowed by the American Chemical Society, the world's largest scientific society. Professor Craik was recognised for his studies on circular peptides, particularly those related to plant peptides called cyclotides and venom-derived conotoxins. Dr Richard Clark, a postdoc in the Craik group, was named Senior Researcher of the Year at the Queensland Health and Medical Research Awards for engineering a compound that was effective in a rodent model of chronic pain. Dr Richard Allen, who is currently at the Australian National University, won an NHMRC Postdoctoral Training Fellowship to join the King group and study the physiological processes the malaria parasite employs to survive in the red blood cells of its host. Dr Tim Hill in the Fairlie group won a University of Queensland Early Career Researcher grant to work on diabetes. Professor Martin and Evan Stephens, a PhD student in the Hankamer group, were awarded Queensland International Fellowships from the State Government, which allowed them to spend time working with collaborators overseas. Professor Martin travelled to Cambridge to learn new technologies in membrane protein structural biology with Professor So Iwata, particularly focussing on bacterial infection and diabetes. Mr Stephens visited collaborators in Germany, with whom he and Associate Professor Hankamer are developing a bioreactor to produce biofuels from algae. Ernest Tee, an honours student in the Cooper group, was named Valedictorian among 492 students in the UQ Bachelor of Science achieving a perfect 7.0 grade point average. Dr Conan Wang from the Craik group and Dr Markus Mutthenthaler from the Alewood group were both named on the Dean's List for Outstanding Research Higher Degree Theses. Dr Wang's thesis focused on cyclotides, a family of circular proteins, while Dr Mutthenthaler studied molecules isolated from the venom of marine cone snails. Dr Joshua Mylne from the Craik group was named the first IMB Fellow. This position offers support to senior postdoctoral scientists to transition towards independent research. Dr Mylne studies the protein processing machinery of sunflowers, which could be used as a quicker and cheaper method of producing drugs.

The IMB recognises its top-performing honours student each year with the Amgen Award. The Award is presented to the student who achieved the highest honours mark in the previous year, so in 2010, the award was presented based on 2009 results. Two students tied for the award, and both were from the Chemistry and Structural Biology division. Sheila Barbero from the Fairlie group and Anne Sawyer from the Hankamer group were presented with their awards in a ceremony in late March. Ms Barbero investigated inhibitors of secretory phospholipase A2 enzymes that are important in inflammatory diseases, while Ms Sawyer studied the protein NAB-1 from a species of green algae that the Hankamer group is genetically modifying to produce commercial quantities of biofuels.

Finally, a divisional researcher was a runner-up in the Ångström Art™ Centenary Competition. Dr Michael Landsberg from the Hankamer group entered the image 'Insect Assassin', which depicts an insecticidal molecule. It is featured on page 81 of this report.

RESEARCH GRANTS

The Division's Group Leaders were lead investigators in attracting 7 new NHMRC project grants (>$3M, 47% success) and 2 new ARC Discovery grants (~$1M) for commencement in 2011. This compares favourably with the IMB (NHMRC $6M, 36% success; ARC $3.5M). In addition, significant grants were received by Professors Lewis and Alewood (NHMRC Program grant, ~$6.4M) and Associate Professor Hankamer (Queensland State Government National and International Research Alliances Program, $1.5M). Professors Cooper and King both received ARC Linkage grants to partner with Alere Australia and Barmac respectively; Professor Fairlie received a Development grant from the NHMRC; while teams of group leaders from the Division led by Professors Alewood and Lewis received separate ARC LEIF equipment grants. For more details on these grants, please see the News section of the IMB website.

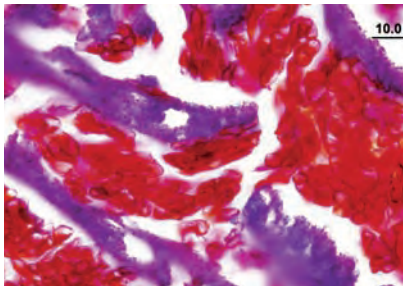
DIVISION PROMOTION

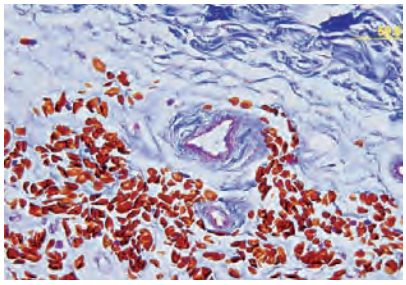
In 2010 the Division instituted a promotional and marketing campaign, including targeted symposia, a promotional booklet and a new website. The inaugural Chemistry and Structural Biology Divisional Symposium was held on the 18th of November 2010, with an Industry Affiliate Program on 17th November. Group leaders, researchers, students and industry affiliates attended to hear about our discoveries in structural biology, chemistry, biochemistry, pharmacology and drug discovery and to discuss collaborative opportunities. It was a great success, with nearly 300 attendees and numerous sponsors, and has resulted in new research and development collaborations in 2011. A similar event will be held on 9th and 10th November 2011. The website showcasing the division is: *http://casb.imb.uq.edu.au/*.

PAUL ALEWOOD

DESIGN AND DISCOVERY OF BIOACTIVE PEPTIDES AND PROTEINS

THE OVERALL FOCUS IN THE group *www.uq.edu.au/alewood/* is the identification of bioactive 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 peptides (toxins) from Australia's venomous creatures; the chemical synthesis of proteins and bioactive peptides; the development of new synthetic and analytical chemistry; and 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 characterisation of toxins from snakes, spiders, cone snails, platypus, ticks and scorpions; mimetics of calcium-binding inflammatory proteins from the S100 class; the chemical engineering of disulfide-rich peptides and proteases; elucidating the structure and function of milk proteins and their role in human health; and uncovering new pain pathways in chronic pain.





RESEARCH PROJECTS

- Identification and characterisation of novel peptides from Australian animals that target ion channels, transporters and GPCR receptors
- Dissecting chronic neuropathic pain pathways with receptor-selective toxins
- Protein mimetics
- Development of new enabling synthetic chemistry to access disulfide-rich peptides and small bioactive proteins and enzymes (up to 200 residues)
- Design and synthesis of novel small molecules that mimic peptide structure and function (peptidomimetics)

KEY PUBLICATIONS

Morales, R.A.V., Daly, N.L., Vetter, I., Mobli, M., Napier, I.A., Craik, D.J., Lewis, R.J., Christie, M.J., King, G.F., Alewood, P.F., and Durek, T. (2010). Total chemical Synthesis and Structure of the Prokineticin Bv8. *Chembiochem* **11**: 1882-1888.

Muttenthaler, M., Nevin, S.T., Grishin, A.A., Ngo, S.T., Choy, P.T., Daly, N.L., Hu, S.-H., Armishaw, C.J., Wang, C.I.A., Lewis, R.J., Martin, J.L., Noakes, P.G., Craik, D.J., Adams, D.J., and Alewood, P.F. (2010). Solving the a-conotoxin folding problem: selenium-directed on-resin generation of more potent and stable nicotinic acetylcholine receptor antagonists. *Journal of the American Chemical Society* **132**: 3514-3522.

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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: Rod Morales, Jen Smith, Kalyani Akondi, Simone Vink, Vincent Lavergne

Visiting Students: Soren Langer (University of Copenhagen), Louise Anker (University of Copenhagen), Claudia Hjørringgård (Aarhus University, Denmark)

ROB CAPON

BIODISCOVERY: PATHWAYS TO NEW BIOACTIVE CHEMICAL DIVERSITY

MY RESEARCH GROUP EXPLORES the chemical diversity of Australian plants, animals and microbes as a source of novel products to (i) advance our knowledge of the natural world, (ii) provide insights into chemical ecology to assist in the control of invasive pests, and (iii) inspire the development of new pharmaceuticals, agrochemicals and bioprobes. These investigations require the use and continued refinement of sophisticated chromatographic (HPLC-DAD-ELSD), spectroscopic (NMR, MS) and chemical (synthesis, degradation, derivatisation, biotransformation) technologies, supported by a wide array of innovative bioassays aimed at multiple targets across such indications as infectious and neurodegenerative disease, pain, cancer and diabetes. Metabolites encountered during our studies span all biosynthetic pathways, feature unprecedented carbon skeletons, heterocycles and functional groups, and can possess potent and selective biological properties with high value across basic and applied science. Recent examples include:

Franklinolides: the first reported natural example of a polyketide-phosphodiester, with an exceptional enhancement in cytotoxicity (target - cancer).

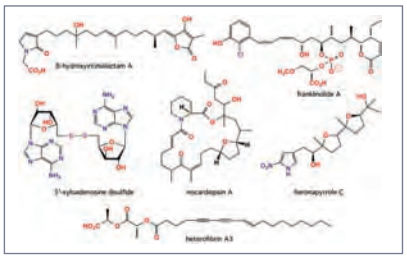
Heterofibrins: the first reported natural examples of lactyl-lipid esters and a new class of lipid droplet inhibitor (target - obesity, atherosclerosis and diabetes).

Nocardiopsins*:* the first reported natural examples of the rapamycin class to be described in over a decade (target - immunosuppressive agents).

5'-Xyloadenosine Disulfide: the first reported natural example of a nucleoside disulfide and only the second known natural nucleoside to incorporate a xylose sugar residue.

Heronapyrroles: the first reported natural examples of nitropyrroles, and a new class of Gram +ve selective antibacterials (target – antibiotics).

Ircinialactams: new examples of a rare class of terpenyl glycinyl-lactams, and the first reported isoform selective potentiators of GlyR (target – chronic inflammatory pain).



KEY PUBLICATIONS

Zhang, H., Conte, M.M., and Capon, R.J. (2010). Franklinolides A-C from an Australian marine sponge complex: Phosphodiesters dramatically enhance polyketide cytotoxicity. *Angewandte Chemie International Edition* **122**: 1-4.

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Raju, R., Piggott, A.M., Barrientos Diaz, L.X., Khalil, Z., and Capon, R.J. (2010). Heronapyrroles A-C: Farnesylated 2-nitropyrroles from an Australian marine-derived *Streptomyces* sp. *Organic Letters* **12**: 5158-5161.

Balansa, W., Islam, R., Fontaine, F., Piggott, A.M., Zhang, H., Webb, T.I., Gilbert, D.F., Lynch, J.W., and Capon, R.J. (2010). Ircinialactams: Subunit-selective glycine receptor modulators from Australian sponges of the family Irciniidae. *Bioorganic & Medicinal Chemistry* **18**: 2912-2919.

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LAB MEMBERS

Personal Assistant: Naomi Epstein

Research Officers: Dr Angela Salim, Dr Andrew Piggott, Dr Hua Zhang, Dr Sean Xiao

PhD Students: Walter Balansa, Raju Ritesh, Soumini Vijayasarathy, Fabien Plisson, Zeinab Khalil, Victor Huang, Venkat Kamalakkannan

Undergraduate Students: Siti Zulkifli, Angel Koo, Ahmad Bin Rosli, Kylie James

International Occupational Trainee: Olusegun Ajala (Nigeria)

International Visiting Scientists: Fuhang Song (China), Leticia Barrentos Diaz (Chile)

MATT COOPER

CHEMICAL AND BIOPHYSICAL TOOLS FOR HEALTH MANAGEMENT: DIAGNOSIS AND THERAPY

OUR RESEARCH INVOLVES THE discovery and exploitation of novel biophysical methods for characterising molecular pathways involved in disease, and for rapid in vitro and ex vivo diagnosis of disease, with an emphasis on viral and bacterial infection.

We have a major effort on rational design and development of novel antibiotics and anti-virals active against drug-resistant pathogens, in particular those responsible for hospital-acquired infections such as MRSA.

We have a strong translational research focus in all of our project areas and work on those indications in which there is a clear commercial case and market need for innovative and disruptive solutions. 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 and companies locally in Australia and internationally in the US, UK, and Europe.

RESEARCH PROJECTS

- Antibiotic derivatives active against drug-resistant bacteria
- Interfacial chemistries for facilitated capture of biological molecules
- Novel approaches for mapping protein signalling pathways with GPCRs
- Bacterial and viral bioinformatics for target validation and development of tests for rapid early-onset diagnosis of infection
- Integrated diagnostics and discovery for theranostic intervention against flaviviruses such as dengue
- Drug screening against novel and validated biological targets

KEY PUBLICATIONS

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Uluda, Y., Hammond, R., and Cooper, M.A. (2010). A signal amplification for HSV type 1 viral DNA detection using nanoparticles and direct acoustic profiling. *Journal of Nanobiotechnology* **8**: 3.

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Ellson, C. *et al.* (2001). Phosphatidylinositol 3-phosphate regulates the neutrophil oxidase complex by binding to the PX domain of p40phox. *Nature Cell Biology* **3**: 679-682.

LAB MEMBERS

Senior Professional Officers: Dr Mark Blaskovich, Dr Mark Butler

Senior Research Officers: Dr Bernd Becker, Dr Frank Fontaine, Dr Tomislav Karoli, Dr Craig Muldoon, Dr Rajaratnam Premraj, Dr Johannes Zuegg

Research Officers: Dr Yujing Gong, Dr Reena Halai, Dr Xiao (Johnny) Huang

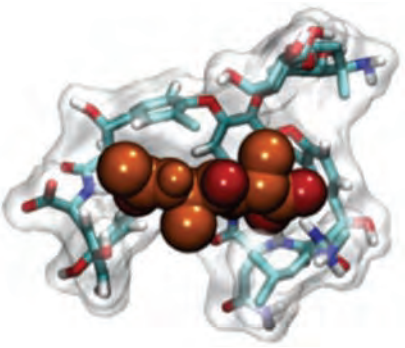
Research Assistants: Yuen Chi (Ann) Lam, Ruby Pelingon, Soumya Ramu

PhD Students: Mu Cheng, Daniel Croker, David Thomson

Honours Students: Noor Huda Daud, Nor Hana Hamzah, June Lee, Ernest Tee

Summer Students: Joanna Adie, Matthew Heidecker, Andrew Laloo, Nurzatil Matjalaluddin, Mahitha Ramakrishna, Karen Wong, Benjamin Yakimoff

Office Coordinator/Team Support: Jan Pinder



Vancomycin binding to Ac-D-Ala-D-Ala subunit of Lipid II.

DAVID CRAIK

NMR AND PROTEIN STRUCTURE IN DRUG DESIGN

OUR GROUP USES PEPTIDE chemistry and NMR spectroscopy to determine the structures of proteins that are important in drug design and in agriculture. By elucidating the structures of biologically active proteins we are able to identify regions crucial for activity and use this information to design new drugs or crop protection agents. The proteins we study come from a range of animal and plant sources. Examples include conotoxins (venom components from marine snails) and cyclotides (ultra-stable circular proteins from plants).

We have a particular interest in the discovery and structural characterisation of novel protein topologies. We aim to determine the mechanisms of biosynthesis and evolutionary origin of circular proteins and to apply protein-engineering principles to explore applications of circular proteins in drug design and agriculture. Circular proteins are particularly stable and thus have advantages over conventional proteins.

We undertake protein-engineering studies in which we modify protein frameworks by "grafting" new biologically active epitopes onto them, or by stabilising them by cyclisation. We currently 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 that 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. We also study the protein-folding problem, i.e., how do proteins fold into the complex shapes that determine their functions?

Highlights of 2010 included the development of an orally active peptide for the treatment of pain. This molecule, IMB007, is an engineered form of a native conotoxin that we had earlier structurally characterised. Our structural studies were used to design a cyclic analogue that proved to be more potent and more stable than the natural conotoxin, and is orally active in an animal model of neuropathic pain. We also developed cyclotides with improved potency against parasites of sheep and cattle and have advanced our understanding of structure-activity relationships in this class of cyclic proteins.

RESEARCH PROJECTS

- Discovery, biosynthesis and applications of circular proteins
- Defining the structure-activity relationships of toxins
- Development of new drugs for pain, cancer and cardiovascular disease
- Investigating plants as production factories to make peptide-based drugs

KEY PUBLICATIONS

Clark, R.J., Jensen, J., Nevin, S.T., Callaghan, B.P., Adams, D.J., and Craik, D.J. (2010). The engineering of an orally active conotoxin for the treatment of neuropathic pain. *Angewandte Chemie* **49**: 6545-6548.

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Craik, D.J. (2006). Seamless proteins tie up their loose ends. *Science* **311**: 1563-1564.

Viola hederaceae *in flower with the structure of a cyclotide overlaid.*

LAB MEMBERS

Research Officers: Dr Norelle Daly, Dr Richard Clark, Dr Masa Cemazar, Dr Joshua Mylne, Dr Quentin Kaas, Dr Jan Westermann, Dr Sonia Henriques, Dr Karl Johan Rosengren

Research Assistants: Dr David Wilson, Chia-Chia Tan, Ashley Cooper, Aurelia Chanson, Amy Argyros, Uru Malik, Phillip Walsh, Philip Sunderland, Olivier Cheneval, Dr Peta Harvey

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

Masters Students: Bodil Carstens, Tilman Plass, Zhinous Nowrouzi, Zai Yang Phua

Occupational Trainees/Visiting Students: Elizabetha de Souza, Philipp Cromm, Marcus Gerlach, Iselin Elvheim

Undergraduate Student: Reynold Phillip

Sabbatical Visitors: Dr Octavio Franco, Dr Chongxu Fan

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.

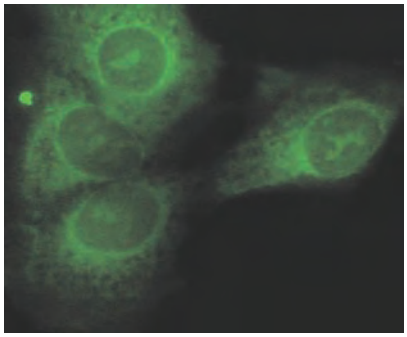
Chemistry researchers develop expertise in: organic, medicinal or biological chemistry; computer-aided drug design; organic synthesis; structure determination using 2D NMR; and interactions between small molecules, proteins, RNA and DNA. Outcomes are new compounds/structures, chemical reactions/mechanisms, enzyme inhibitors, protein agonists/antagonists, and structural mimics of protein surfaces.

Biology researchers use our novel compounds to interrogate human protein, cellular and animal function and to elucidate mechanisms of protein activation, biological/physiological processes, disease development, and drug action. Researchers gain insights to processes pivotal to human physiology or aberrant in disease, and develop skills in pharmacology, enzymology, biochemistry, immunology, virology, oncology or neurobiology.

RESEARCH PROJECTS

(http://fairlie.imb.uq.edu.au/)

- Drug discovery (for inflammatory disorders, cancers, viral infections, neurodegeneration, obesity and metabolic dysfunction)
- Organic and medicinal chemistry
- Pharmacology: molecular (cellular) and experimental (animal models)
- Structures by 2D NMR spectroscopy
- Enzymes, GPCRs & protein-protein interactions
- Mimicry of protein surfaces



KEY PUBLICATIONS

Barry, G.D., Suen, J.Y., Le, G.T., Cotterell, A., Reid, R.C., and Fairlie, D.P. (2010). Novel Agonists and Antagonists for Human Protease Activated Receptor 2. *Journal of Medicinal Chemistry* **53**: 7428-7440.

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Harrison, R.S., Ruiz-Gómez, G., Hill, T.A., Chow, S.Y., Shepherd, N.E., Lohman, R.J., Abbenante, G., Hoang, H.N., and Fairlie, D.P. (2010). Novel Helix-Constrained Nociceptin Derivatives Are Potent Agonists and Antagonists of ERK Phosphorylation and Thermal Analgesia in Mice. *Journal of Medicinal Chemistry* Epub ahead of print November 10.

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Stoermer, M.J., Chappell, K.J., Liebscher, S., Jensen, C.M., Gan, C.H., Gupta, P.K., Xu, W.J., Young, P.R., and Fairlie, D.P. (2008). Potent cationic inhibitors of West Nile virus NS2B-NS3 protease with serum stability, cell permeability and antiviral activity. *Journal of Medicinal Chemistry* **51**: 5714-5721.

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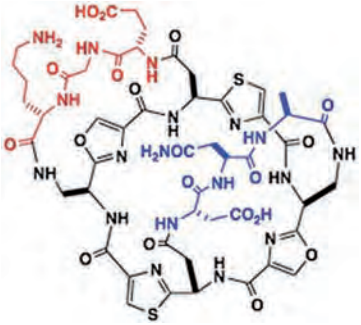

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LAB MEMBERS

Senior Research Officers: Dr Ligong Liu, Dr Robert Reid, Dr Martin Stoermer

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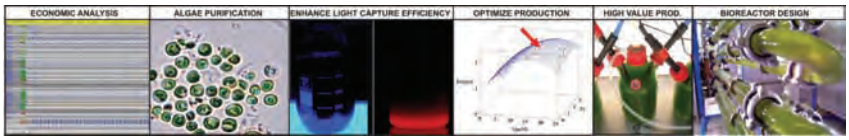
Undergraduate Students: Sok Lin Foo, Lisa Redlingshoefer, Annette Spierings, Benjamin Wong

Occupational Trainee: Daniel Nielsen

Office Manager: Barbara Feenstra/ Lyn Fairlie

BEN HANKAMER

STRUCTURAL BIOLOGY OF MEMBRANE PROTEINS, MACROMOLECULAR ASSEMBLIES AND VIRUSES



THE SOLAR BIO-FUELS CONSORTIUM (***www.solarbiofuels.org***), co-directed by Ben Hankamer, has brought together eight international teams and approximately 100 researchers to develop high-efficiency microalgal bio-fuels and bio-product production systems. This represents a rapidly expanding area of biotechnology of global significance. The consortiums work covers all aspects of the process from economic modelling, purification of microalgae, optimisation of production conditions and the scale up of photobioreactor systems.

Structural Biology: The first step of all biofuel production processes is light capture. Using single particle analysis, crystallography and electron tomography as part of the IMB *Visible Cell*® project we are developing a pseudo-atomic resolution 3D atlas of the model alga *Chlamydomonas reinhardtii*. Such 3D molecular atlases guide the enhancement of light capture and conversion efficiency of the photosynthetic machinery.

Membrane proteins, macromolecular assemblies and viruses: To increase the speed of structure determination we have established a powerful *single particle analysis pipeline*, as well as new biotechnologies for *template assisted 2D crystal production*. The single particle process involves the semi-automated merging of large numbers of 2D projection images of randomly-oriented molecules to calculate 3D reconstructions. Our current benchmark resolution is ~10 Å at which individual a-helices begin to be resolved, and we are actively developing processes to improve this further. In parallel we have developed detergent-resistant 2D templates that chelate Ni at the surface, to facilitate the systematic production of 2D crystals of tethered His-tagged membrane proteins. Using these twin approaches we are studying a wide range of important membrane proteins (e.g. photosynthetic membrane protein complexes, ATPases, mechanosensitive channels), macromolecular assemblies (AAA ATPases and related proteins, ferritin, NS1 & toxin complexes) as well as icosahedral viruses. These structures provide fundamental new insights into many fascinating molecular machines and feed into the Visible Cell® project.

RESEARCH PROJECTS

- High-Resolution Single Particle Analysis: biology and process development
- The Visible Cell® Project: resolving the 3D structure of the macromolecular assemblies and biophysical modelling
- Template mediated 2D crystallisation: towards streamlined membrane protein crystallisation
- Micro-algal biofuel and bioproduct systems: development of bio-fuels systems for bio-H_2, bio-diesel and BTL-diesel production that are coupled to CO_2 sequestration

KEY PUBLICATIONS

Stephens, E., Ross, I.L., King, Z., Mussgnug, J.H., Kruse, O., Posten, C., Borowitzka, M.A., and Hankamer, B. (2010). 2nd generation microalgal biofuels: Economic and technical evaluation of the hope, hype and reality. *Nature Biotechnology* **28:** 126-128.

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Mussgnug, J., Thomas-Hall, S., Rupprecht, J., Foo, A., Klassen, V., McDowall, A., Schenk, P., Kruse, O., and Hankamer, B. (2007). Engineering photosynthetic light capture: Impacts on improved solar energy to biomass conversion. *Plant Biotechnology Journal* **5**: 802-814.

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LAB MEMBERS

Research Officers: Dr Ian Ross, Dr Michael Landsberg, Dr Melanie Oey

Research Assistant: Rosalba Rothnagel

PhD Students: Evan Stephens, Erin Ahern, Drew Ringsmuth, Emily Knauth, Winnie Waudo, Khairul Radzun, Maurizio Chioccioli, Eugene Zhang, Alex Foo

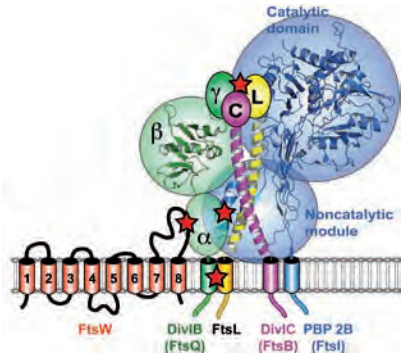
MSc Students: Gisela Jakob, Johannes Kügler

Honours Students: Hong Wai Tham, Anne Sawyer

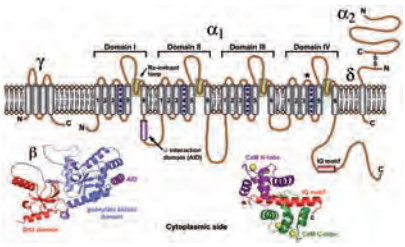
GLENN KING

BUGS AND DRUGS: RATIONAL DEVELOPMENT OF NOVEL ANTIBIOTICS, ANALGESICS, AND ENVIRONMENTALLY-FRIENDLY INSECTICIDES

RESEARCH IN MY LABORATORY is aimed at the development of novel pharmaceutical agents and environmentally-friendly insecticides. Approximately half of the group is studying bacterial cytokinesis or signalling by bacterial histidine kinases in order to provide a molecular understanding of these key biological processes and to establish a platform for the development of novel antimicrobial agents. The remainder of the group is focused on developing novel antinociceptive agents and environmentally-friendly insecticides by harnessing the remarkable chemical diversity encoded in the venoms of spiders and scorpions. 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 three ARC and five NHMRC research grants.



Model of the interactions between various components of the Escherichia coli *divisome.*



Schematic of a voltage-gated calcium channel.

Mexican red-kneed tarantula (Brachypelma smithii).

RESEARCH PROJECTS

- Developing novel antibiotics targeted against Gram-positive pathogens
- Investigating the architecture of the bacterial cell division machinery
- Using venom peptides to characterise ion channels involved in sensing pain
- Developing environmentally-friendly insecticides based on spider-venom peptides

KEY PUBLICATIONS

Mobli, M., Dantas de Araújo, A., Lambert, L., Pierens, G.K., Alewood, P.F., and King, G.F. (2009). Direct visualization of disulfide bonds via diselenide proxies using ^{77}Se NMR. *Angewandte Chemie International Edition* **48:** 9312-9314.

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Sollod, B.L., Wilson, D., Zhaxybayeva, O., Gogarten, J.P., Drinkwater, R., and King, G.F. (2005). Were arachnids the first to use combinatorial peptide libraries? *Peptides* **26**: 131–139.

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LAB MEMBERS

Senior Research Officers: Dr Susan L. Rowland, Dr Mehdi Mobli

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Research Assistant: Radha Seshadri

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Honours Students: Carus Lau, Tomas Miljenovic, Darshani Rapasinghe

Home page for the ArachnoServer database (www.arachnoserver.org).

RICHARD LEWIS

MOLECULAR PHARMACOLOGY OF MARINE PEPTIDES

A MAJOR FOCUS OF MY GROUP is the discovery and development of peptides as research tools and leads to new therapeutics, especially the conotoxins from predatory marine snails that have potential in pain management. This research involves the assay-guided isolation of venom peptides, peptide synthesis, tissue and receptor pharmacology, high-content cellular imaging of functional effects, radioligand binding to receptor mutagenesis, homology modelling, and finally co-crystal structures and docking of the peptide to its target to identify how it binds. Most of our research focuses on the discovery and characterisation of venom peptides, especially the conotoxins produced by the predatory cone snails found on the Great Barrier Reef. These highly structured peptides, or mini-proteins, act selectively at a wide range of ion channels, G-protein coupled receptors and transporters found in the membranes of cells. Interestingly, several conotoxins have been taken into the clinic, including Xen2174 for severe pain, developed from a lead originally discovered in my group. In addition, we are studying how ciguatoxins produce the debilitating disease known as ciguatera, and working towards improving methods to detect these toxins at sub ppb levels in fish flesh.

Highlights for 2010 include the renewal of our Program Grant for a further five years, award of a Linkage grant for a FLIPR platform that allows rapid functional screening of ion channels and GPCRs, and the announcement of the next Venoms to Drugs meeting scheduled for May 2011. Research highlights include the discovery and patenting of a new ω-conotoxin that can reverse pain responses without the side effects that currently limit the clinical potential of this class of analgesics. Our research into the mechanisms of α-conotoxin interaction with nicotinic acetylcholine receptors resulted in the discovery of a new allosteric site on the receptor and uncovered a pharmacologically important role for the fifth subunit in heteromeric forms of this petameric receptor.

RESEARCH PROJECTS

- Discover conopeptides that modify pain pathways (NHMRC Program Grant)
- Determine the sites of conotoxin binding to membrane proteins including the α_1-adrenoceptor, noradrenaline transporter and nicotinic acetylcholine receptor
- Discover conotoxins that modulate calcium and sodium channels
- Use high-content functional screens to discover and characterise new bioactives
- Develop mass spectrometric and transcriptomic approaches to unravel the peptide diversity of cone snail venoms (venomics)
- Determine the mode of action and improve the detection of ciguatoxins responsible for ciguatera

KEY PUBLICATIONS

Berecki, G. *et al.* (2010). Analgesic ω-conotoxins CVIE and CVIF selectively and voltage-dependently block recombinant and native N-type calcium channels. *Molecular Pharmacology* **77**:139-48.

Luo, S. *et al.* (2010). The atypical α-conotoxin LtIA from *Conus litteratus* targets a novel microsite of the α3β2 nicotinic receptor. *Journal of Biological Chemistry* **285**: 12355-12366.

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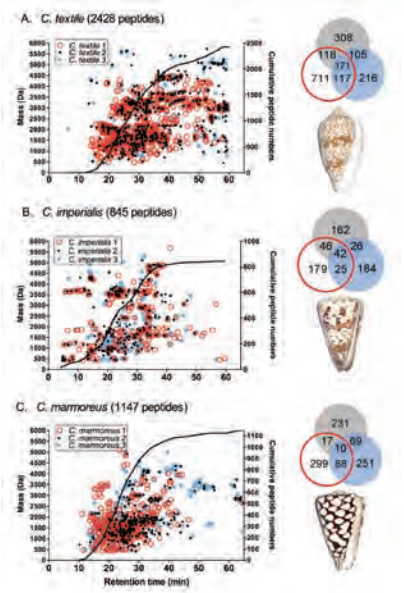
Lewis, R.J., Yang, A., and Jones, A. (2009). Rapid extraction combined with LC-tandem mass spectrometry (CREM-LC/MS/MS) for the determination of ciguatoxins in ciguateric fish flesh. *Toxicon* **54**: 62-66.



LC/MS reveals 1000s of different venom peptides in each species of cone snail (from Davis et al., Peptides *2009).*

Dutertre, S., Ulens, C., Büttner, R., Fish, A., van Elk, R., Kendel, Y., Hopping, G., Alewood, P.F., Schroeder, C., Nicke, A., Smit, A.B., Sixma, T.K., and Lewis, R.J. (2007). AChBP-targeted α-conotoxin correlates distinct binding orientations with nAChR subtype selectivity. *EMBO Journal* **26**: 3858-3867.

Lewis, R.J., and Garcia, M.L. (2003). Therapeutic potential of venom peptides. *Nature Reviews Drug Discovery* **2**: 790-802.

LAB MEMBERS

Research Officers: Dr Irina Vetter (CDA), Dr Anderson Wang, Dr Sebastien Dutertre (UQ Fellowship), Dr Lotten Ragnarsson-McGrath

Research Assistant: Asa Anderson

PhD Students: Marco Inserra, Vu Bach, Josh Wingerd, Silmara Rodrigues de Sousa

MSc Students: Dewi Fajarningsih, Prerna Jha, Mriga Dutt, Nikita Abraham, Prasanth Jutty Rajan

Honours Student: Zhenyao Luo

Program Grant Administration Officer: Thea Monks

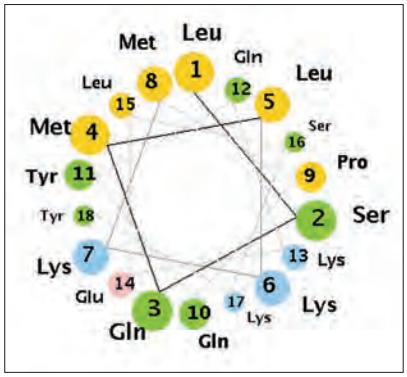
International Visiting Scientists: Dr Katharina Zimmermann (Germany), Dr Cheryl de Valliere (Switzerland)

JENNY MARTIN
PROTEIN STRUCTURE AND DRUG DESIGN

OUR GOAL IS TO BETTER UNDERSTAND the role of proteins in disease and to develop novel drugs targeting disease-causing proteins. We use a range of biochemical and biophysical techniques to investigate the structure, function and interactions of proteins, with a particular emphasis on high-throughput protein crystallography and structure-based approaches for inhibitor design.

A major outcome over the past few years has been the tremendous advance in our understanding of the regulation of SNARE proteins involved in insulin-stimulated trafficking of the GLUT4 glucose transporter. This process, which is critical to the regulation of blood glucose levels, is affected in Type II Diabetes. We had shown in collaboration with Professor David James (Garvan Institute), that the regulatory protein Munc18c may stimulate delivery of GLUT4 vesicles to the cell membrane, through binding to a short N-terminal peptide of the SNARE syntaxin4 protein (Latham *et al*. *Traffic* 2006; Hu *et al. Proc Natl Acad Sci USA* 2007). Very recently we identified that the Syntaxin N-peptide does not discriminate well between cognate and non-cognate Munc18 proteins and that its role may instead be to induce a conformational change in Munc18 proteins (Hu and Christie *et al. Proc Natl Acad Sci USA* 2010).

Our long-running interest in bacterial redox folding factors led to the determination of the crystal structure of a key virulence factor, DsbA from *Pseudomonas aeruginosa* (Shouldice *et al., AntiOx Redox Signal* 2009) using data measured at the Australian Synchrotron. We are now focusing our attention on developing inhibitors of several DsbA proteins as potential antibacterial agents (Heras *et al. Nature Rev Microbiol* 2009), using a range of techniques. Collaborations have been established with Associate Professor Martin Scanlon at Monash and Professors David Fairlie, Matt Cooper and Mark Schembri at UQ. This research led to the award of an ARC Australian Laureate Fellowship that was taken up in late 2009.



We have successfully applied a fragment-screening approach to PNMT, the adrenaline synthesising enzyme, using the automated UQ ROCX diffraction facility (Drinkwater *et al., Biochem J* 2010). More than 140 PNMT crystals were used to screen ~380 drug-like fragments: 12 hits were identified and confirmed by isothermal calorimetry. Six elaborated compounds were designed and synthesised (in collaboration with Gary Grunewald, Kansas U) and shown to inhibit enzyme activity (in collaboration with Michael McLeish, Indiana U).

RESEARCH PROJECTS

- Structure, function and interactions of proteins associated with insulin action
- Structure, function and inhibition of redox folding factors involved in disease
- Novel inflammation drug targets using high-throughput structure approaches
- Structure, function and inhibition of transferase enzymes involved in disease

KEY PUBLICATIONS

Drinkwater, N. *et al.* (Martin, J.L. listed as senior author) (2010). Fragment-screening by X-ray crystallography, mass spectrometry and isothermal titration calorimetry to identify PNMT inhibitors. *Biochemical Journal* **431**: 51-61.

Hu, S.-H. *et al.* (Martin, J.L. listed as senior author) (2010). Possible roles for Munc18-1 domain 3a and Syntaxin1 N-peptide and C-terminal anchor in SNARE complex formation.] *Proceedings of the National Academy of Sciences USA* Epub December 30.

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Heras, B. *et al.* (Martin, J.L. listed as senior author) (2009). Dsb proteins and bacterial pathogenicity. *Nature Reviews Microbiology* **7**: 215-225.

Hu, S.-H., Latham, C.F., Gee, C.L., James, D.E., and Martin, J.L. (2007). Structure of the Munc18c/Syntaxin4 N-peptide complex defines universal features of the N-peptide binding mode of SM proteins. *Proceedings of the National Academy of Sciences USA* **104**: 8773-8778.

Gruber, C., Cemazar, M., Heras, B., Martin, J.L., and Craik, D.J. (2006). Protein disulfide isomerase: The structure of oxidative folding. *Trends in Biochemical Sciences* **31**: 455-464.

LAB MEMBERS

Senior Research Officers: Dr Begoña Heras, Dr Shu-Hong Hu

Research Officers: Dr Andrew Whitten (NHMRC Fellow), Dr Stephen Shouldice (UQ Postdoctoral Fellow), Dr Gordon King, Dr Maria Halili, Dr Karl-Fredrik Lindahl, Dr Morten Groftehauge, Dr Mathieu Coincon

UQ ROCX Diffraction Facility Manager: Karl Byriel

Research Assistants: Russell Jarrott, Stephanie Tay, Fabian Kurth

PhD Students: Michelle Christie, Kevin Chen, Asma Rehman, Patricia Walden, Wilko Duprez

Undergraduate Student: Heather Nutt

Visiting Student: Pooja Sharma (Monash University)

MARK SMYTHE

COMBINATORIAL CHEMISTRY AND MOLECULAR DESIGN

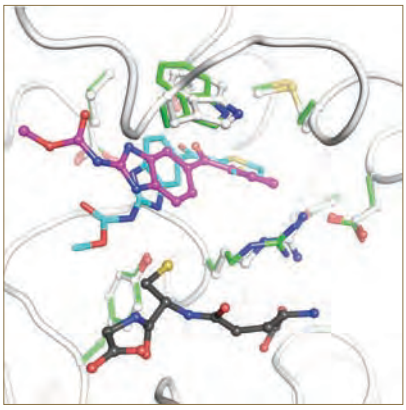
OUR RESEARCH FOCUSES ON advancing drug design and synthetic organic and peptide chemistry to discover novel biologically-active molecules. We apply these new drug design and discovery methodologies to discover drugs to treat unmet medical needs or provide better therapeutic solutions to existing marketed drugs.

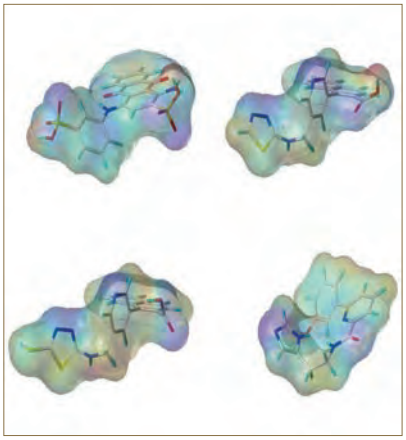
Using a combination of mathematics, software development, drug design, combinatorial chemistry and phage display, we are developing new approaches to identify biologically-active molecules. Thus, projects are multidisciplinary and focused on achieving medical outcomes.

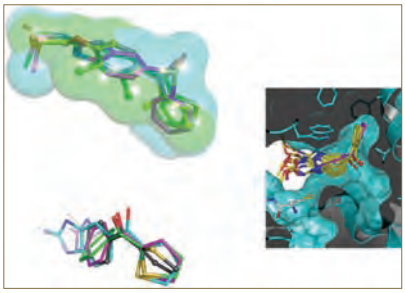
We have recently developed several small molecule anti-TNF compounds for treatment of inflammatory diseases and specific small molecule modulators of prostaglandin D_2 synthase for treatment of asthma. In addition we have designed and synthesised a new spin label to accurately determine distances in biological systems.

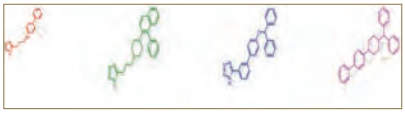
RESEARCH PROJECTS

- Modulating haematopoietic prostaglandin D_2 synthase for allergic disease
- Studying antagonists of Myb for treatment of leukaemia
- Designing SHP-1 inhibitors to boost haematopoiesis
- Developing antipathogenic compounds to treat microbial infections
- Developing structure-based phage display
- Developing new computational algorithms and strategies for sampling biologically-relevant chemistries
- Developing a synthetic process for the combinatorial synthesis of biologically-relevant compounds
- Developing in vitro and cell-based assays for screening arrays of compounds









KEY PUBLICATIONS

Horton, D.A., Horton, G.T., Coughlan, J., Kaiser, S.M., Jacobs, C.M., Jones, A., Ruhmann, A., Turner, J.Y., and Smythe, M.L. (2008). Cyclic tetrapeptides via the ring contraction strategy: chemical techniques useful for their identification. *Organic & Biomolecular Chemistry* **6**: 1386-1395.

Severinsen, R., Bourne, G.T., Tran, T.T., Ankersen, M., Begtrup, M., and Smythe, M.L. (2008). Library of Biphenyl Privleged Substructures using a Safety-Catch Linker Approach. *Journal of Combinatorial Chemistry* **10**: 557-566.

Horton, D.A., Severinsen, R., Kofod-Hansen, M., Bourne, G.T., and Smythe, M.L. (2005). A versatile synthetic approach to peptidyl privileged structures using a safety catch linker. *Journal of Combinatorial Chemistry* **7**: 421-435.

Horton, D.A., Bourne, G.T., and Smythe, M.L. (2003). The Combinatorial Synthesis of Bicyclic Privileged Structures or Privileged Substructures. *Chemical Reviews* **103**: 893-930.

Meutermans, W.D.F., Bourne, G.T., Golding, S.W., Horton, D.A., Campitelli, M.R., Craik, D., Scanlon, M., and Smythe, M.L. (2003). Difficult Macrocyclisations: New Strategies for Synthesising Highly Strained Cyclic Tetrapeptides. *Organic Letters* **5**: 2711-2714.

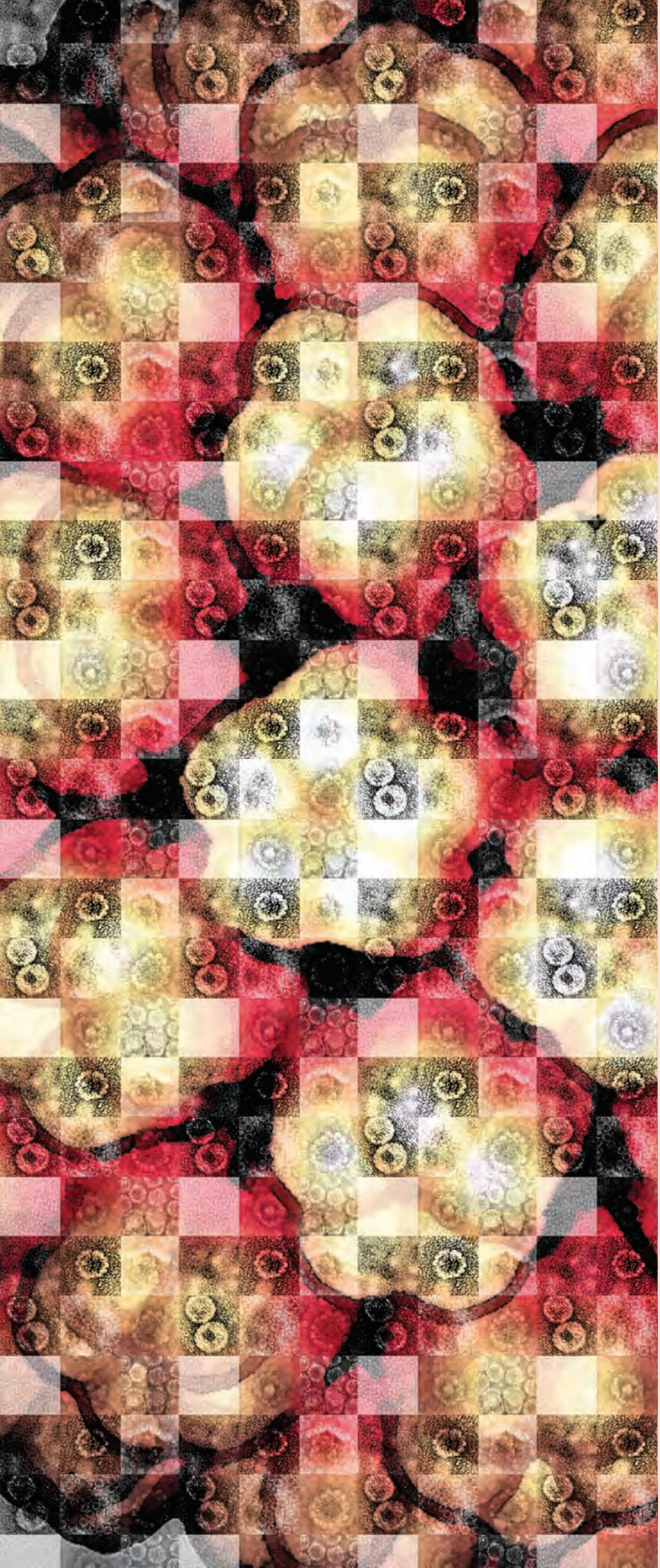
LAB MEMBERS

Senior Research Officers: Dr Craig Murphy, Dr Greg Bourne, Dr Nicole Lawrence

Research Officers: Dr Katie Glenn, Dr Jenny Zhang, Dr Rosemary Harrison

Research Assistants: Jill Turner, Jaimee Duncan, Angelika Christ, Aleisha Griffin, Phillip Walsh

PhD Student: Christina Kulis



JOINT APPOINTMENTS at the IMB

The purpose of joint appointments is to foster collaborations in teaching, research and related activities between the IMB and Schools of The University of Queensland.

Joint appointments involve a split in salary between the IMB and the relevant UQ School, and a joint appointee's commitment to the research and teaching activities at the IMB is greater than that of affiliate appointees.

Joint appointees participate in all Institute activities, including laboratory research, supervision of research higher degree students, and attendance at seminars, Divisional meetings and IMB Group Leader retreats.

Joint appointees in 2010 were Professor Alan Mark and Professor Geoffrey McLachlan.

LINDA LUA AND PANG CHUAN: BOUQUET

A virus is a piece of mosaic art perfected by Nature. The viral shell is made up of hundreds of copies of identical protein molecules arranged in a highly sophisticated pattern, giving a unique architecture for each type of virus. A close-up of the computer-generated three dimensional structure of a mouse polyomavirus particle is shown here. In the background, an assemblage of electron micrographs depicting viral shells constructed at UQ.

ALAN E. MARK

MOLECULAR DYNAMICS OF BIOMOLECULAR SYSTEMS

THE GROUP CONCENTRATES ON modelling the structural and dynamic properties of biopolymers such as proteins, nucleic acids and lipid aggregates. In particular, we use computer simulations to understand and predict the macroscopic (experimentally observable) behaviour of complex biomolecular systems based on the interactions between atoms. We develop the software, atomic force fields and theoretical models needed to address a range of fundamental questions.

First, how do proteins fold? Understanding how proteins fold is one of the grand challenges of modern biology and a critical test of our ability to accurately predict interactions in protein systems. The failure of proteins to fold correctly is also linked to a range of debilitative diseases including Alzheimer's Disease, BSE and some forms of Type II diabetes where misfolded proteins form destructive aggregates called amyloid fibrils. Dramatic progress is being made in the de novo folding of small peptides and the refinement of larger proteins. Research on folding is conducted at multiple levels. Small model systems are used to refine force fields and simulation techniques. On a larger scale we are simulating how multiple copies of certain peptides aggregate in order to understand how amyloid fibrils form.

Second, how do cell surface receptors transmit a signal through the cell membrane? Receptor proteins on the surface of cells play a vital role in cellular communication. However, little is known in regard to the mechanism by which the binding of a molecule to an extracellular receptor transfers a signal across the cell membrane or even how changes in the environment can activate certain cell surface receptors. In particular, we are investigating how the binding of human growth hormone to the extra-cellular growth hormone receptor is coupled to structural changes within the cell. We are also investigating the mechanism by which the E or envelope proteins of the Dengue and Ebola viruses facilitate the entry of these viruses into cells.

Third, how do membrane-protein complexes assemble? Cell membranes are the archetypal self-organised supramolecular structure. In addition to being of critical importance in structural biology, membrane-protein complexes are also prime therapeutic targets. Using simulations, we are investigating the assembly of functional structures such as the assembly of anti-microbial peptides into transmembrane pores. This is being used to understand the mechanism by which larger complexes form in heterogeneous environments as well as to understand in detail how smaller antibiotics such as vancomycin recognise membrane targets.

RESEARCH PROJECTS

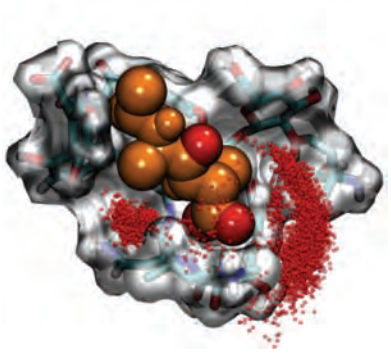
- Peptide folding and assembly
- Mechanism of action of antimicrobial peptides.
- The nucleation and growth of amyloid fibrils
- Mechanism of activation of type 1 cytokine receptors

KEY PUBLICATIONS

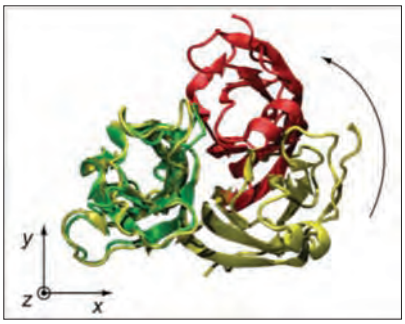
Malde, A., and Mark, A.E. (2010). Challenges in the determination of the binding modes of non-standard ligands in X-ray crystal complexes. *Journal of Computer-Aided Moecular Design* **25**: 1-12.

Poger, D., and Mark, A. E. (2010). Turning the growth hormone receptor on: Direct evidence that hormone binding induces subunit rotation. *Proteins: Structure, Function, and Bioinformatics.* **7**: 1163-1174.

Periole, X., Rampioni, A., Vendruscolo, M., and Mark, A.E. (2009). Factors that affect the degree of twist in b-sheet structures: A molecular dynamics simulation study of a cross-ß filament of the GNNQQNY peptide. *Journal of Physical Chemistry B* **113**: 1728-1737.



The interaction of the peptide D-ala-D-ala (solid representation) with the antibiotic vancomycin. The red spheres indicate the distribution of structural waters observed during the simulations.



Rotation of the extracellular domains of the growth hormone receptor associated with activation by growth hormone. A superposition of the hormone free form obtained from the simulations (green and red) on to the hormone bound (activated) conformation (yellow)

Yesylevskyy, S., Marrink, S.J., and Mark, A. E. (2009). Alternative mechanisms for the interaction of the cell-penetrating peptides Penetratin and the TAT peptide with lipid bilayers. *Biophysical Journal* **97**: 40-49.

van Gunsteren, W.F., Dolenc, J., and Mark, A.E. (2008). Molecular simulation as an aid to experimentalists. *Current Opinion in Structural Biology* **18**: 149-153.

LAB MEMBERS

Research Officers: Dr David Poger, Dr Alpesh Malde, Dr Megan O'Mara, Dr Mortiz Wigner

PhD Students: Daniela Mueller, Ying Xue, Rong Chen, Pramod Nair, Zhi Guang Jia

GEOFFREY McLACHLAN
APPLIED STATISTICS AND BIOINFORMATICS

MY RESEARCH IN APPLIED STATISTICS is in the related fields of classification, cluster and discriminant analyses, data mining, image analysis, intelligent systems, machine learning, neural networks, and pattern recognition, and in the field of statistical inference. The focus in the latter field has been on the theory and applications of finite mixture models and on estimation via the E(expectation)-M(maximisation) algorithm.

I am also actively involved in the field of bioinformatics with the focus on the development of methods and software for the analysis of data from high-throughput genomics projects, with particular emphasis on gene-expression profiles. The limitations of conventional methods of cancer classification and diagnosis based on the site and appearance of the tumour or organ are well known. With microarrays allowing genome-scale measures of gene expression, attention has turned to using differences in the activity of the gene expressions (gene profiling) to classify and diagnose tumours.

Concerning statistical methodology being developed for the aforementioned problems, I am working on very fast methods based on factor models for the analysis of observation vectors of extremely high dimension to produce observations on so-called meta-variables (metagenes) of small dimension. Consideration is given to the use of resources such as Gene Ontologies and pathway analysis to determine the biological significance of the metagenes. Specific applications include the supervised classification of tissue samples for use in diagnosis and prognosis of diseases and the unsupervised classification (clustering) of tissue samples in the search for new subclasses of diseases. I am also concerned with the development of methodology for the simultaneous testing of thousands of hypotheses at a time. This problem occurs in many applications in bioinformatics, such as with the detection of differentially expressed genes in two or more conditions (diseases). Methods that provide increased power in small-sample size situations are being developed.

Also, I have been working with computational and experimental biologists to develop a new approach to the analysis of the rich data generated by new and powerful flow cytometers. The team is led by Dr Jill Mesirov, a computational biologist at the Broad Institute of the Massachusetts Institute of Technology. In our initial work on this problem (Pyne *et al.*, 2009), we have produced a software tool called flow analysis with automated multivariate estimation (FLAME), for such flow cytometric data.

RESEARCH PROJECTS

- The development of automated, high-dimensional methods based on mixtures of skew normal and t-distributions for the rich data generated by new and powerful flow cytometers
- Development of very fast methods based on factor models for the analysis of data arrays, such as microarray data matrices, involving sets of extremely high dimensions, for use in supervised and unsupervised classification of tissue samples on patients
- Development of diagnostic methods for cancer, using multiple indices in conjunction with clinical factors
- Ongoing research into the modelling of gene profiles for use in the detection of differentially expressed genes and in time-course studies
- Modifications to existing statistical methodology and the development of new techniques for the next generation of high-throughput technology with fast sequencing platforms

KEY PUBLICATIONS

Baek, J., McLachlan, G.J., and Flack, L. (2010). Mixtures of factor analyzers with common factor loadings: applications to the clustering and visualisation of high-dimensional data. *IEEE Transactions on Pattern Analysis and Machine Intelligence* **32**: 1298-1309.

Le Cao, K.-A., Meugnier, E., and McLachlan, G.J. (2010). Integrative mixture of experts to combine clinical factors and gene markers. *Bioinformatics* **26**: 1192-1198.

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Pyne, S., Hu, X., Wang, K., Rossin, E., Lin, T.-I., Maier, L.M., Baecher-Allan, C., McLachlan, G.J., Tamayo, P., Hafler, D.A., De Jager, P.L., and Mesirov, J.P. (2009). Automated high-dimensional flow cytometric data analysis. *Proceedings of the National Academy of Sciences USA* **106**: 8519-8524.

McLachlan, G.J., Wang, K., and Ng, S.K. (2008). Large-scale simultaneous inference with applications to the detection of differential expression with microarray data (with discussion). *Statistica* **68**: 1-30.

McLachlan, G.J., Bean, R.W., and Ng, A. (2008). Clustering of microarray data via mixture models. In Statistical Advances in Biomedical Sciences: Clinical Trials, Epidemiology, Survival Analysis, and Bioinformatics, A. Biswas et al. (Eds.). Hoboken, New Jersey: Wiley, pp. 365-384.

McLachlan, G.J., and Krishnan, T. (2008). The EM Algorithm and Extensions. Second Edition. Hoboken, New Jersey: Wiley.

LAB MEMBERS:

Research Officer: Dr Suren Rathnayake

PhD Students: Leesa Wockner, Sharon Lee

AFFILIATE APPOINTMENTS

THE PURPOSE OF AFFILIATE appointments is to foster collaborations in teaching, research and related activities between the Institute for Molecular Bioscience (IMB) and Schools at The University of Queensland. Affiliate appointees to the IMB contribute through active involvement with relevant IMB Groups, facilities or research programs and through joint supervision of research higher degree students. Affiliate appointees contribute to the intellectual life of the Institute through attendance at IMB seminars, Divisional meetings and IMB Group Leader retreats. Salary for affiliate appointees is paid by the relevant University of Queensland School.

PROFESSOR MATT BROWN
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

ASSOCIATE PROFESSOR FRED MEUNIER
Queensland Brain Institute

DR ALLISON PETTIT
UQ Centre for Clinical Research

DR LIZA RAGGATT
UQ Centre for Clinical Research

ASSOCIATE PROFESSOR JOE ROTHNAGEL
School of Molecular and Microbial Sciences

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

PROFESSOR PAUL YOUNG
School of Chemistry and Molecular Biosciences


Prof.Matt Brown


Prof. Nicholas Fisk


Prof. Ian Frazer


Prof. Jane Hunter


Assoc. Prof. Stuart Kellie


Assoc. Prof. Bostjan Kobe


Prof Daniel Markovich


Assoc. Prof. Fred Meunier


Dr Allison Pettit


Dr Liza Raggatt


Assoc. Prof. Joe Rothnagel


Prof. Ranjeny Thomas


Assoc. Prof. Peter Thorn


Prof. Istvan Toth


Prof. Paul Young

IMB OCCUPATIONAL HEALTH AND SAFETY REPORT

THIS YEAR WAS AN EXTREMELY busy one. In addition to the normal schedule of audits by Biosafety, AQIS, ARPANSA and the local WHSO network, the IMB was visited and audited by representatives of Radiation Health and the Environmental Health Unit (Drugs and Poisons). The IMB was also visited by an external OH&S systems auditor working to assess risk for the University's application for renewal of its self-insurance policy.

Overall, the Institute's performance in all of these audits was strong. Where suggested, minor corrective actions have been taken. Thanks in part to the performance of the IMB, the University passed the audit and our self-insurance policy has been renewed. Passing the AQIS audits in 2010 allows us to move closer to earning the privilege of annual, rather than six-monthly, audits in 2011.

The hard work and dedication from the IMB Floor Managers and Support staff was pivotal to this success, and their commitment to maintaining safety and compliance systems in the building was clear to all auditors visiting us in 2010.

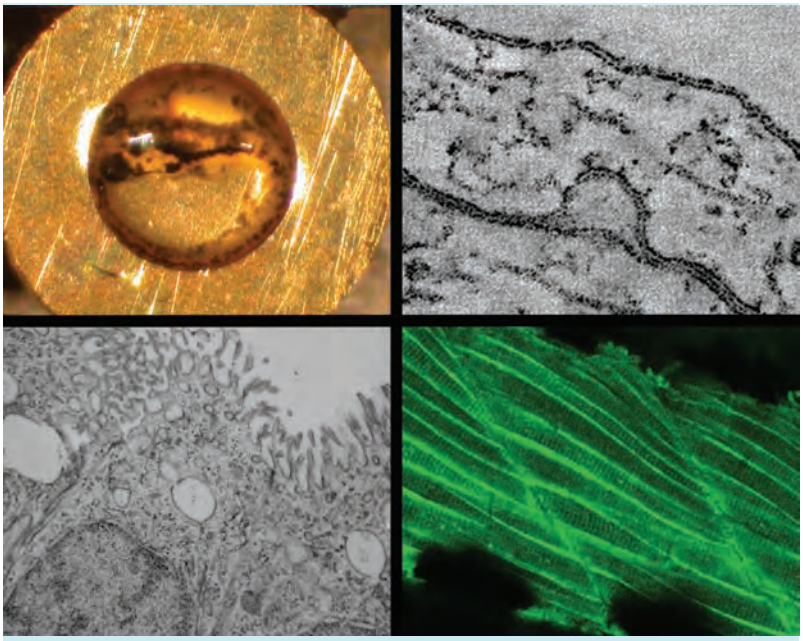
During the year, the OH&S infrastructure at the IMB continued to evolve, with the following main areas being developed for, or adapted to, a changing research environment:

- revised induction process to comply with UQ OH&S goals for 2010 and to simplify the process for users and trainers,
- risk assessment database review and modification to reflect new Australian Standards requirements,
- implementation of a scheduled Drugs and Poisons purchase alert system,
- continuation of periodic online safety audits,
- maintenance of a tasks database to systematically monitor compliance with various regulatory bodies and legislation,
- design and implementation of Safety-Based KPI for supervisors at the IMB.

Challenges for the IMB's safety infrastructure in 2011 include:

- implementing policies and procedures to ensure compliance with new Australian Standards such as AS2243.3 (2010),
- maintaining IMB's good safety record for hosting of summer students, volunteers and work experience personnel,
- monitoring infrastructural and staffing changes to ensure safe equipment and appropriate training needs analysis and provision,
- reducing the incidence of needlestick injuries - four incidents were reported in 2010 compared to one in 2009,
- maintaining compliance with UQ OH&S Goals for 2011.

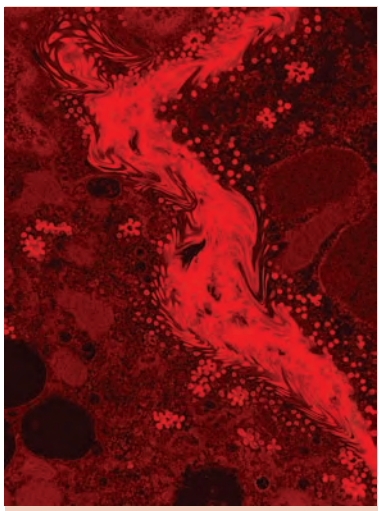
The overall performance of the IMB in terms of safety and compliance in 2010 has been high. Discussions at the quarterly floor safety committee meetings and in more informal venues reflect an active safety culture at the IMB, and provide a lively venue for the exchange of safety-related information and policies. Crucially, there is also significant 'buy in' to safety issues from upper management at the IMB - this factor particularly is of enormous value to maintaining a safety culture within any organisation.



SUSAN NIXON: iFISH
Zebrafish embryos have been used for fast freezing, electron microscopy and tomography, and immunofluorescence.

IMBcom

IMBCOM PTY LTD is The University of Queensland's company for commercialisation of valuable discovery research of the IMB. It is responsible for the protection and development of the University's IMB intellectual property portfolio. Established in 2000, the company has a skilled, independent Board of Directors, operating as a separate commercial entity, but with a charter of service to the University's commercialisation objectives. The company has ten employees who provide the specialist skills to commercialise the results of IMB researchers' discoveries.



ROB PARTON: FIRE

Electron micrograph from a mammalian cell that has been colourized and blurred.

IMBcom uses a model of cooperative integration with the discovery activities of the research labs. The company's staff are involved from the earliest disclosure stages with the planning and delivery of ways to add value to emergent innovations. The company manages the IMB's Intellectual Property as custodians, developers and drivers, resulting in licences, contracts and the formation of start-up companies to take discovery to products and services into markets.

IMBcom has had a historical strategic focus on developing new companies and has established 12 new biotechnology startup companies, two in conjunction with UniQuest. These companies have raised more than $80 million through private sector investment, $18 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. IMBcom has sold its interest in one of the companies developed in partnership with UniQuest, Xenome, and the funds generated for the IMB and IMBcom are being used to provide "proof-of-concept" funds for future IP and product development.

In 2010, IMBcom negotiated several significant biotechnology deals, including contracts for collaborative research, partnering and licences. The company helped secure more than $4 million in industry research grants for the IMB, with another $10 million in applications submitted.

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. IMBcom delivers 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.

IMBcom provides assistance to Queensland and Commonwealth government departments and agencies with respect to biotechnology industry development, and is well regarded as an effective advocate for Queensland's consistent promotion of the Smart Queensland agenda. IMBcom showcases not only the IMB and the University to industry and investment, but also Queensland as an industry destination.

Dr Peter Isdale, CEO of IMBcom, with Dr Jane Wilson, Chair of IMBcom Board

POSTGRADUATE RESEARCH

We had 31 students join the IMB program throughout the year, 21 of whom were international students from countries as diverse as China, India, Denmark, Norway, France and Singapore. This continues the recent trend of increased international enrolments, with overseas students now comprising slightly over 50 percent of our cohort. Our total number of active RHD students has stabilised at around 130 students, with 27 students completing their degree in 2010 (for a full list see page 73). While some of our graduates have remained within IMB to complete research projects, many have taken up positions both locally and overseas (for details see page 73).

AS IN PAST YEARS, a number of our students received accolades throughout 2010. Vicki Metzis from the Wicking group had a wonderful year, winning the David Walsh Prize for the best cell and development biology student presentation at Ozbio2010, from the Australian and New Zealand Society of Cell and Developmental Biology (ANZSCDB). She was also awarded a student travel award from ANZSCDB to attend the OzBio conference and was a winner of the ANZSCDB image competition to form part of the ANZSCDB logo (one of five selected). In addition, she was chosen to speak at the Gordon-Kenan Research Conference on Craniofacial Morphogenesis and Tissue Regeneration in Italy in April 2010 and, as a speaker, received a small travel award from the Society for Developmental Biology for attending and presenting. She also excelled in a number of "Three-Minute Thesis" (3MT) oral presentation competitions.

Ms Metzis won the IMB 3MT competition and thus went on to represent the Institute at the inter-Institute Semi-Final. At this event, she won the People's Choice Award and was also chosen by the judges as the overall winner, meaning Ms Metzis proceeded to represent all the Institutes at the UQ-wide competition as one of eight finalists. She also competed in the 3MT section of the UQ Centennial Postgraduate Biomedical Conference, coming second.

IMB did extremely well in this event with Elizabeth Skippington (Ragan group), who was runner-up in the IMB competition, receiving first place and Natalie Saez (King group) receiving the People's Choice Award. Ms Saez also won a poster award at the 2010 XXIVth International Conference on Magnetic Resonance in Biological Systems (ICMRBS). Maggie Hardy (also from the King group) continued as a high achiever in 2010, receiving the J. H. Comstock Graduate Student Award to promote interest in the science of entomology from the Entomological Society of America International Branch, and the First Place Poster Prize for the IMB Division of Chemistry & Structural Biology Symposium held in November 2010.

Stephen Ainger from the Sturm group won a poster prize of $250 at the Society for Melanoma Research Congress in Sydney and Oleksiy Kovtun of the Alexandrov group won 1st prize in the poster competition of the UQ Centennial Postgraduate Biomedical Conference. He also presented an oral talk at the XII ICOPA International Congress in Melbourne.

Sabine Mangold of the Yap group obtained an OzBio2010 conference registration fee waiver (from the ANZSCDB) and a poster award at the Brisbane Cell and Developmental Biology Meeting, while Caroline Hopkins of the Little group won the best PhD talk at the same meeting. Ms Hopkins also won an International Society for Stem Cell Research Travel Award to present in San Francisco and as part of this award presented her data to leaders of the field at both Harvard Medical School (Boston) and Mt Sinai School of Medicine (NYC). She subsequently received postdoctoral offers from both groups and will be taking up a position in NYC in mid-2011. In August she also received a travel award to present at the International Workshop in Developmental Nephrology in New York.

Muharrem Akcan from the Craik group received a Gordon Research Conference Travel Award to attend the meeting covering the Chemistry and Biology of Peptides and studied at the Fred Hutchinson Cancer Research Center, Seattle, USA, as a visiting scholar from January 16-April 16 2010, as part of a UQ Trans-Pacific Fellowship (see 2009 report). We also had five students appearing on the UQ Dean's List for 2009: congratulations to Ming Kang Chang (Sweet group), Tim Mercer (Mattick group), Markus Mutthenthaler (Alewood group), Ryan Taft (Mattick group) and Conan Wang (Craik group) for joining this elite group.

OUR HONOURS COHORT was small but continued to excel. We had 17 students commencing in Feb 2010, two students who carried over from July 2009 and four others who commenced in July 2010. As in previous years, 80 percent of those students completing their year in 2010 obtained a grade of First Class Honours. Amgen Australia has been presenting our honours students with the Amgen Award for the most outstanding honours student at the IMB for over a decade and we are thrilled by their continued support of our young researchers.

The Amgen Award for 2009 was jointly awarded to Anne Sawyer (Hankamer group) and Sheila Barbero (Fairlie group). Ms Sawyer's honours project investigated the Purification and characterization of NAB-1, an RNA binding protein from *Chlamydomonas reinhardtii,* while Ms Barbero's honours project was titled "Studies of Secretory Phospholipase A2 Inhibitors". We were naturally delighted when both Ms Sawyer and Ms Barbero indicated they wished to further pursue their studies at the PhD level, each subsequently being awarded an APA scholarship to undertake PhD studies at the IMB in the labs in which they had completed their honours years.

IN SEPTEMBER 2010, UQ conducted the Inaugural Undergraduate Research Conference, bringing students at the Bachelors and honours level from all Faculties and Institutes together for this cross-disciplinary event. Once again our students did us proud with Rebecca Johnston (an honours student from the Mattick group) winning a $600 "Best Poster Award" and Hilary Martin (an honours student from the Grimmond group) obtaining an honourable mention and a special prize ($500) in the oral presentation category.

The IMB also continued the Undergraduate Research Scholarship Scheme (URSS) in 2010, placing 20 second- and third-year students within laboratories in one of our four divisions for eight hours per week during semester. Additionally, a number of third-

Postgraduate research

year students completed mini-research projects as part of the "Introduction to Research" module of their degrees, and several Advanced Studies students completed research projects as part of their program. We also placed 19 students in summer projects of six to ten weeks duration as part of the UQ Summer Research program, which this year included students from New Zealand, Singapore, Western Australia and even a high-calibre candidate from the University of Belgrade.

Once again, the IMB hosted many international students, who joined IMB for up to one year as occupational trainees, undertaking overseas research placements as part of their degree requirements within their home institution. We also welcomed a number of Year 10, 11 and 12 students from schools throughout Queensland to undertake a brief period of work experience within research laboratories. This included the placement of 12 students from Gregory Terrace who completed a three-week Science Immersion program as part of their Year 10 curriculum, and three Year 12 students from Brisbane Boy's College who spent an afternoon a week for six months in a designated laboratory to complete an extended research project as part of their Year 12 assessment.

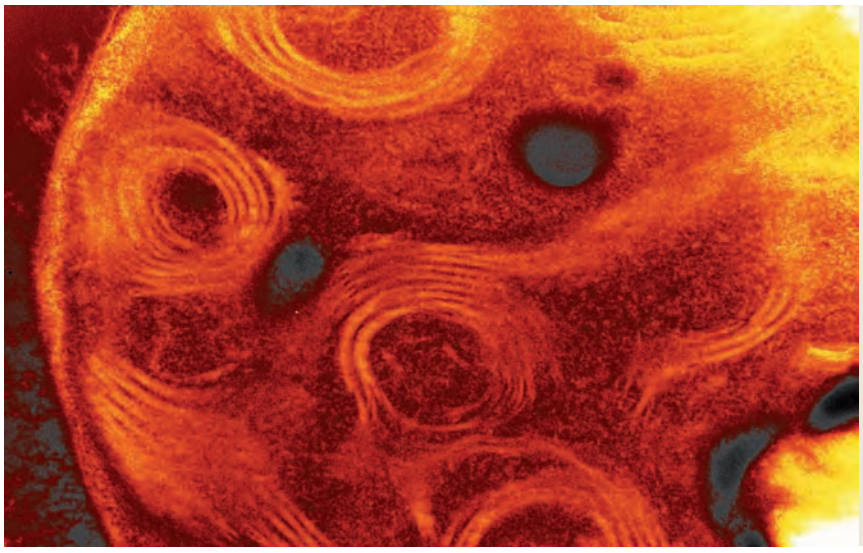
OUR IMB STUDENT ASSOCIATION, SIMBA, organised a range of social events throughout the year, which promoted engagement within our student body, with students from other research institutes on campus, and with members of the community.

The events conducted throughout 2010 included several themed movie nights, the annual IMB/AIBN Trivia night (which we won this year!), an opportunity to band together to join the "Brisbane Zombie Walk" in October as part of a charity event for the Brain Foundation of Australia, and a Movember moustache-growing competition to raise money for men's health issues.

There were also several IMB-based BBQs to meet and greet new students, and the AGM, held in August to usher in the new SIMBA Executive for 10/11. We welcomed Wilko Duprez (President), Drew Ringsmuth (Vice President), Silmara Rodrigues de Sousa (Secretary), Kalyani Akondi (Treasurer), Martin Smith (SIMBAlize editor-in-chief) and Baptiste Coxam (Event Co-ordinator).

Each year the SIMBA Executive brings an energy to the role which ensures our students have a collective identity within the institute. We continue to be delighted by their enthusiasm and commitment.

THE IMB EARLY CAREER Researcher (ECR) Committee also had a very productive year. In addition to again running the annual mentoring afternoon tea, the committee hosted Guntram Bauer for a session on the Human Frontier Science program of funding opportunities, initiated a Brisbane-wide meeting of ECR representatives from local institutes to allow ECRs from different organisations to meet and exchange ideas, contributed to the MMRI-run Hugh Kearns session "The Balanced Researcher" and continued to arrange for IMB ECRs (and occasional undergraduates) to meet and lunch with speakers after the Friday Seminar Series. They also launched the inaugural Brisbane Inter-Institute Poster Symposium held on 8th October at the IMB, which proved a huge success. This event brought together researchers from IMB, AIBN, DI, MMRI, QBI and UQCCR at UQ as well as scientists from the institutes at Griffith University, several from QIMR and some from IHBI at QUT, with slightly over 60 abstracts. The atmosphere was wonderful as young researchers from all over Brisbane exchanged ideas in this industry-sponsored event. The committee must be congratulated on organising what is definitely set to become an annual event.



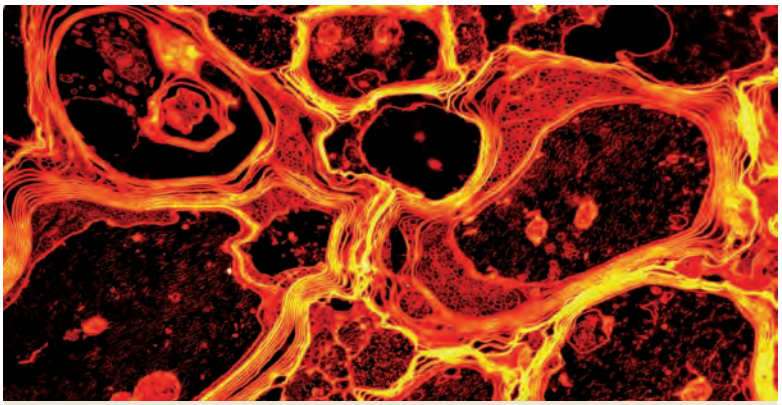
EMILY KNAUTH: SUNSPOT

Every organism on Earth is reliant on the sun for survival. Plants and algae use specialised structures to capture light and convert it into chemical energy which is used as a food and fuel source. The thylakoid membranes inside the chloroplast, pictured here, adapt their structure in response to light and other conditions and are a key factor in overall light capture. The algae cell pictured here has been purposely stylised to resemble the sun, an essential part of photosynthesis and life. Photosynthesis is Nature's solar cell.

In addition, the ECR committee continued to support an ECR website, produce a newsletter, and maintain an active and very positive presence throughout the IMB. During 2010, the members of the ECR committee were Dr James Palmer (President), Peter van der Heide (Vice-President), Natalie Eriksson (Treasurer), Amanda Stanley (Secretary), Dr Cassy Spiller (Friday Lunch Mediator), Dr Eva Kovacs (Website Coordinator), Dr Andrew Brooks, Dr Andrea Bugarcic, Dr Michael Hanzal-Bayer, Dr Elaine Julian, Dr Karin Kassahn, Vicki Metzis, Evan Stephens and Dr Rehan Villani.

THE WORKSHOPS RUN BY THE ECR committee were complemented by a set organised by the Postgraduate Program, designed to assist students in overall career development. These included IMBcom's three-day BioBusiness Retreat for the third-year PhD students. Once again, feedback from the retreat was extremely positive, with participants really enjoying the information and interactive sessions. Congratulation must go to Maggie Hardy (King group) who won best individual pitch at the retreat, the combination of Angeline Chan, Marco Inserra, Lindsey McFarlane, Tim Pan and Tom Whitington, who won the overall best Biopitch and Daniel Shaw who won the 180^0 award for demonstrating the biggest change in attitude during the event.

We also offered our students an introductory statistics course run by Carl Sherwood from the School of Economics at UQ, which provided 18 hours of tuition at IMB over eight weeks. Students from QBI, AIBN and DI also attended the course and overall we had over 50 registrants. In addition, Dr Joan Leach from the School of English, Media Studies, and Art History at UQ, who is also the Convener of the Science Communication Program on campus, delivered two sessions on scientific writing in October, which proved to be very popular. This was run in conjunction with the SCMB Honours coordinator, Dr Horst Schirra, and it is hoped this program will expand in 2011.



SAM MURPHY: LAVA FIELD

An electron microscopy image of mylinated nerves in the retina of a bamboo shark. Myolin sheaths form rivers of larva surrounding nerve cells which make gaping holes and hot rocks in a volcanic landscape.

Bronwyn Adams, our Marketing and Communications Officer, organised several training sessions for students chosen to be IMB Science Ambassadors (see page 81) and we again conducted the IMB Three-Minute Thesis challenge in which our 2^{nd} year PhD students gave presentations as part of their Candidature Milestone.

THE IMB, ONCE AGAIN, HAS been extremely fortunate to have Professor Rob Capon continue in his role as the IMB Postgraduate Coordinator and IMB representative on the UQ RHD Committee of the Academic Board. Part of this role involves informing the rest of the IMB about changes to the administration of RHD recruitment and candidature. For example, in 2010 the UQ Graduate School re-introduced scholarship rounds for international and domestic students.

This year, Professor Capon also served as an Elected Member of the UQ Academic Board and the Institutes' Elected Member of the Academic Board's Standing Committee. Although all these responsibilities are voluntary, he continues to take on these many additional tasks with enthusiasm and dedication in order to help shape a vibrant future for research science on campus.

His commitment to the IMB Postgraduate Program (and in fact all student matters) is amazing, and was highlighted in 2010 by the launch of his brainchild, PEBBLES, the web portal to the IMB postgraduate database. PEBBLES, created in conjunction with OzData Solutions, provides a secure and easily accessible link for IMB academics to keep pace with their student commitments, creates a repository for reports and notes and allows for the real-time generation of milestone reports online during student interviews. These can be freely shared and endorsed by IMB members of the candidature committee, triggering the automated generation of completed administrative forms for submission to the Graduate School to complete each Milestone process, both ensuring best practice in providing feedback to students and also markedly lessening the administrative burden.

Needless to say, the original IMB database and its new incarnation as PEBBLES is continuing to be adopted by other schools on campus, with several new schools purchasing the package in 2010. This innovative and constructive approach is yet another example of how Professor Capon ensures the IMB Postgraduate Program continues to remain fresh and proactive for its student body.

PhD conferrals for 2010

LAST NAME	FIRST NAME	GROUP	THESIS TITLE	WHERE ARE THEY NOW?
Abramyan	Oganes (John)	Koopman	Biology of Sex Determination and Sexual Development in the cane toad (*Bufo marinus*)	University of California at Riverside, USA
Alexander	Kylie	Sweet	Osteal macrophages (osteomacs) are pivotal for intramembranous bone formation in vivo: Osteomacs facilitate osteoblast maintenance in vivo and enhance osteoblast-mediated bone deposition in a murine model of bone healing	Queensland Institute of Medical Research, Brisbane
Arieshanti	Isye	Bailey	Integrating sequence and structure for annotating proeins in the twilight zone: A machine learning approach	Sepuluh Nopember Institute of Technology, Surabaya, Indonesia
Bastiani	Michele	Parton	The cavin proteins as regulators of caveolae formation and function	Parton group, IMB
Bauer	Denis	Bailey	Thermodynamic models for the analysis of quantitative transcriptional regulation	Queensland Brain Institute, UQ
Christie	Michelle	Martin	Characterization of interactions formed by the SNARE Syntaxin4 protein and the Sec/Munc protein Munc18c	Martin group, IMB
Cridland	Simon	Perkins	Stromal support of erythropiesis during development	Koopman group, IMB
Drinkwater	Nyssa	Martin	Substrate, inhibitor, and mutational studies of the human adrenaline synthesising enzyme Phenylethanolamine N-Methyltransferase	Kings College London, England, UK
Driver	Russell	Fairlie	Structural studies of Cyclic Peptides	Fairlie group, IMB
Goh	Felicia	Sweet	Antigen presenting cell involvement in Th2 response	Prince Charles Hospital, Brisbane
Halai	Reena	Craik	The story of a-conotoxins, Vc1.1 and RgIA, on their journey to becoming therapeutics	Cooper group, IMB
Halili	Maria	Fairlie	Regulation of inflammatory proteins	Martin group, IMB
Harrison	Rosemary	Fairlie	Alpha Helices Mimetics	Bain & Company, Sydney, New South Wales
Ho	Uda	Wainwright	Hedgehog signalling in lung development and airway regeneration	Queensland Institute of Medical Research, Brisbane
Howes	Mark	Parton	Clathrin Independent Carriers: Molecular characterisation of a novel clathrin-independent endocytic pathway	Parton group, IMB
Huang	Yen-Hua	Craik	The mode of action of cyclotides [electronic resource] : functional studies of the prototypic cyclotide kalata B1	Craik group, IMB
Julian	Elaine	Wainwright	The molecular basis of medulloblastoma: interaction of hedgehog and Notch signalling in brain development and cancer	Wainwright group, IMB
Jung	CholHee	Mattick	Classifying non-protein-coding RNA sequences	University of Melbourne, Victoria
McLachlan	Robert	Yap	The role of c-Src in E-cadherin activity	Yap group, IMB
Nahkuri	Satu	Mattick	Analysis of conservation and chromatin structure at metazoan splice sites	Swiss Federal Institute of Technology, Zürich
Noske	Andrew	Marsh	Multi-scale, spatio-temporal analysis of mammalian cell tomograms	University of California San Diego, USA
Pearen	Michael	Muscat	Beta-adrenergic regulation of the nuclear hormone receptor 4A subgroup in skeletal muscle: insights into the control of metabolism	Muscat group, IMB
Prakash	Surya	Muscat	Eludicating the metabolic function of RoR alpha and gamma in skeletal muscle	Lilly Pharmaceuticals, Singapore
Ramakrishnan	Sathiya	Muscat	Rev-erb beta regulates the expression of genes involved in metabolism	Harvard Medical School, Boston, Massachusetts, USA
Sprenger	Josefine	Teasdale	Computational methods to define the endosomal proteome	SmartNet Presence, and Information Professionals, Brisbane
Stephens	Amber	Munn/ Manners (CSIRO)	Molecular analysis of fungal pathogenicity in crown rot disease of wheat caused by *Fusarium graminearum*	Max Planck Institute for Plant Breeding Research, Cologne, Germany
Wang	Tsang-Hsing (Jack)	Teasdale	Investigating macropinocytosis: the role of sorting nexins in macropinosome biogenesis	School of Chemistry and Molecular Bioscience, UQ

VISITING SPEAKERS

Dr Ruben Abagyan
School of Pharmacy and Pharmaceutical Sciences
University of California San Diego, USA
Computational structural chemogenomics and drug discovery

Maud Achard
School of Chemistry and Molecular Biosciences, UQ
Copper trafficking in murine macrophages in response to Salmonella *infection*

Dr Daniel Aguirre
CSIRO, St Lucia, Brisbane
High-throughput technologies in the study of the gut microbiome; usefulness of numerical ecology methods and other considerations

Dr Florent Angly
Advanced Wastewater Management Centre, UQ
Computational methods for studying uncultured viral communities

Dr Ruth Arkell
Australian National University, Canberra, Australian Capital Territory
Building the mammalian forebrain: the role of the /Zic/ gene family of transcription factors

Professor Shankar Balasubramanian
Cambridge University, United Kingdom
Quadruplex nucleic acids as functional elements and therapeutic targets

Professor Philippe Bastiaens
Department of Systemic Cell Biology
Max Planck Institute for Molecular Physiology, Dortmund, Germany
Spatial organisation in growth factor signalling

Dr Denis Bauer
Queensland Brain Institute, UQ
Combined association and deep resequencing study of DISC1 in a population from Tamil Nadu, India

Adjunct Professor Peter Beattie
Former Premier & Queensland Trade Commissioner for the Americas
Our biotech future: not a destination but a continuing journey

Dr Jennifer Becker
US Army Research Office, Adelphi, Maryland, USA
Basic research needs in hazardous materials management

Dr Nouri Ben Zakour
School of Chemistry and Molecular Biosciences, UQ
Understanding the genome evolution of staphylococci of animal origin

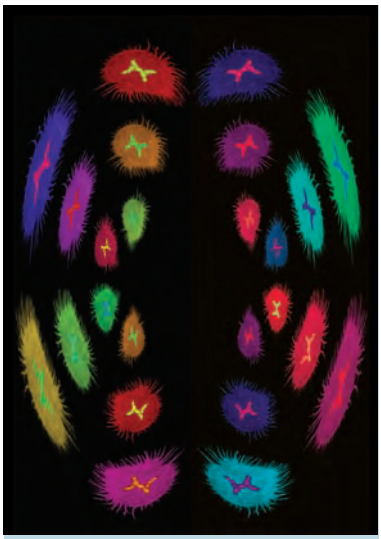
Paul Berkman
Australian Centre for Plant Functional Genomics, UQ
Towards sequencing the haploid wheat genome

Carlo Bertozzi
Department of Biochemistry
University of Zürich, Switzerland
Structural basis for ion permeation and block in a prokaryotic pentameric ligand-gated ion channel

Dr Helle Bielefeldt-Ohmann
School of Veterinary Science, UQ
Macaque rhadinoviruses: models for HHV-8 associated diseases?

Dr Antje Blumenthal
Diamantina Institute, UQ
Interactions between Mycobacterium tuberculosis *and the host*

Professor Alexandre Bonvin
Biojvoet Center for Biomolecular Research
Utrecht University, the Netherlands
Information-driven modelling of biomolecular complexes: challenges and perspectives



DARREN BROWN: NEWCLEUS
A fluroescent microscope image montage of a macrophage labelled with a probe to identify the nucleus. The image has been multicoloured and arranged in a really nice pattern.

Dr Toula Bouras
Walter & Eliza Hall Institute, Melbourne, Victoria
Notch signalling regulates mammary stem cell function and luminal cell-fate commitment

Associate Professor Neil Box
Department of Dermatology
University of Colorado at Denver, USA
Rpl27a mutation in the Sooty Foot Ataxia mouse phenocopies high p53 mouse models and identifies a new negative regulator of p53

Professor Frances Brodsky
University of California San Francisco, USA
Diversity of clathrin structure and function

Dr Brian Burke
Institute of Medical Biology, Singapore
Nucleocytoplasmic coupling and LINCs to human disease

Visiting speakers

Dr Alistair Chalk
Eskitis Institute
Griffith University, Brisbane

Stem cell bioinformatics in general and approaches towards understanding alternate splicing in stem cells and *Stem cell bioinformatics*

Dr Paul Chambers
Research Manager
The Australian Wine Research Institute, Urrbrae, South Australia

Lessons in winemaking: an example of integrated 'Omics at work

Dr Stephen Cohen
Deputy Director
Institute of Molecular and Cell Biology, Singapore

MicroRNA functions

Dr Alex Cristino
Queensland Brain Institute, UQ

Unravelling brain networks associated with cognitive disorders

Dr Robert James Dancer
H. Lundbeck A/S, Denmark
Re-examination of published procedures for the resolution of Citalopram and Didesmethylcitalopram

Nick Davis-Poynter
Sir Albert Sakzewski Virus Research Centre, Herston, Brisbane

Constitutive endocytosis and signalling of cytomegalovirus 7 transmembrane receptor homologues: importance for biological function

Professor Vojo Deretic
University of New Mexico, Albuquerque, USA

Autophagy – biological paradigm for everyone and
Autophagy in infection and immunity

Professor Simon Foote
Director
Menzies Research Institute
University of Tasmania, Hobart

Host response to malaria: a genetic approach

Dr Yann Gambin
Department of Molecular Biology
The Scripps Research Institute, USA

Combining single-molecule FRET and microfluidics to explore protein folding pathways

Professor Rex Gaskins
Visiting CSIRO Scientist
University of Illinois, Urbana-Champaign, USA

On contributions of sulfate-reducing bacteria to chronic disorders of the human colon

Dr Arnaud Gaudin
School of Biomedical Sciences, UQ

Axonal guidance defects in the forebrain: tracking down and identifying the culprits

Dr Tanja Gesell
Center for Integrative Bioinformatics Vienna (CIBIV)
Max F. Perutz Laboratories (MFPL), Vienna, Austria

Another view on RNA structure and
A phylogenetic structure (PS) and its application to gene predictions

Clare Giacomantonio
Queensland Brain Institute, UQ

Creating the cortex: modelling the patterns of gene expression underlying cortical development

Dr James Godwin
Australian Regenerative Medicine Institute
Monash University, Melbourne, Victoria

Characterising the immunological response to wounding and regeneration in the Salamander

Professor Christopher Goodnow
Director, Australian Phenomics Facility
Australian National University, Canberra, Australian Capital Territory

Genes, failsafes and control systems to avoid immunological catastrophes

Dr Albert Guskov
Nanyang Technical University, Singapore

The crystal structure of Photosystem II at 2.9 Å resolution: role of lipids, quinones and chloride ions

Professor John Hardy
Reta Lila Weston Institute of Neurological Studies
University College London, UK

Genetic analysis of neurodegeneration

Dr Dirk Haussecker
RNAi Therapeutics Consulting Service, Malaysia

RNAi therapeutics - where are we and where are we going?

Dr Jermone Korzelius
Utrecht University, the Netherlands

Cell cycle entry in C. elegans *development*

Professor Kurt Krause
Director
Webster Centre for Infectious Diseases
University of Otago, Dunedin, New Zealand

Alanine Racemase as a template for antimicrobial drug design

Dr Jens Krömer
Queensland Node Manager
Metabolomics Australia

Metabolomics and fluxomics: getting closer to the metabolic phenotype

Professor Sharad Kumar
Institute of Medical & Veterinary Science, Adelaide, South Australia

Expected and unexpected functions of the canonical cell death machinery

Dr Lawrence Lee
Victor Chang Cardiac Research Institute

The structure of the torque ring of the bacterial flagellar motor and the molecular basis for rotational switching

Professor Malcolm Harris Levitt FRS
Professor in Physical Chemistry, School of Chemistry
Southampton University, UK
Singlet nuclear magnetic resonance

Dr Graham Lieshke
Walter and Eliza Hall Institute, Melbourne, Victoria
Zebrafish mutants lead into unexplored corners of haemopoiesis

Dr Sara Linden
Mucosal Immunobiology and Vaccine Center, Gothenburg, Sweden
Mucins in Helicobacter phylori *infection: a dynamic defence which differs between individuals*

Dr Jimmy Liu
Queensland Institute of Medical Research, Brisbane
A versatile gene-based test for genome-wide association studies

Professor Angel Lopez
Institute of Medical and Veterinary Science, Adelaide, South Australia
The mechanism of cytokine receptor activation

Dr Madhavi Maddugoda
Molecular Research Centre for Molecular Medicine, Nice, France
Membrane and cytoskeletal dynamics during transendothelial permeability of pathogens

Dr Igor Makunin
Queensland Institute of Medical Research, Brisbane
Paucity and preferential suppression of transgenes in late replication domains of the D. melanogaster *genome*

Dr Jessica Mar
Harvard School of Public Health, Boston, Massachusetts, USA
Modeling variance as a measure of network topology in Waddington's canals

Nick Matigian
Eskitis Institute for Cell and Molecular Therapies
Griffith University, Gold Coast
Disease-specific, neurosphere-derived cells as models for brain disorders

Roberto Munita
Pontifica Universidad Catolica de Chile, Santiago
MirrorRNA and non-consensus splicing: experimental artefact or sign of another biological surprise?

Dr Gene Myers
Janelia Farms Research Campus
Howard Hughes Medical Institute, Ashburn, Viriginia, USA
Decoding the genome with bioimaging informatics

Professor Robert Nabi
University of British Columbia, Vancouver, Canada
Lattice, rafts and scaffolds: plasma membrane domain organisation in cancer

Professor Jim Naismith
Biomedical Sciences Research Complex
The University of St Andrews, Fife, Scotland, UK
Membrane protein conformation states

Dr Greg Neely
Marie Curie Fellow
Institute of Molecular Biotechnology Austria (IMBA), Vienna
Genome-wide screening in Drosophila *to identify new mammalian disease genes*

Dr Mathias Nilsson
School of Chemistry
University of Manchester, UK
Advances in DOSY and pure shift, techniques and applications

Dr Páraic Ó Cuív
CSIRO, St Lucia, Brisbane
Exploring the role of the colonic microbiota in human health and disease

Dr Megan O'Mara
School of Chemistry and Molecular Biosciences, UQ
Determining the physiological state of a membrane protein: a molecular dynamics odyssey

Professor Scott O'Neill
Head
School of Biological Sciences, UQ
Bacterial symbionts of insects and the possible control of dengue fever

Professor Arthur R Pardi
Department of Chemistry and Biochemistry
University of Colorado, Boulder, USA
NMR and single molecule studies of RNA folding and RNA-protein recognition

Dr Matt Perugini
Bio21 Institute
University of Melbourne, Victoria
Multiple personalities of an essential bacterial enzyme

Professor Robert Phillips
California Institute of Technology, Pasadena, USA
Order of magnitude biology

Dr Simon Phipps
School of Biomedical Sciences, UQ
Respiratory virus infections and innate inflammatory pathways that underlie the onset of asthma

Dr Pamela Pollock
Institute of Health and Biomedical Innovation
Queensland University of Technology, Brisbane
FGFR2 mutations in endometrial cancer: prognostic and therapeutic implications

Erin Poth
Department of Neuroscience
Johns Hopkins University School of Medicine, Baltimore, Maryland, USA
Teaching an old dogma new tricks: the role of the long ncRNA Six3OS in retinal development

Visiting speakers

Associate Professor Thomas Preiss
Victor Chang Cardiac Research Institute, Sydney, New South Wales
Mechanisms and patterns of post-transcriptional gene control

Dr Oliver Rackham
Western Australian Institute for Medical Research
University of Western Australia, Perth
Re-engineering cellular protein synthesis

Michael Reich
Director of Cancer Informatics Development
Broad Institute of MIT and Harvard, Boston, Massachusetts, USA
Broad Institute tools for integrative genomics

Professor Robert Richards
University of Adelaide, South Australia
FHIT happens when you get your WWOX off - or the contribution of chromosomal fragile site genes to cancer biology

Dr Kathy Ruggiero
School of Biological Sciences
University of Auckland, New Zealand
Designing experiments utilising multi-plexing biotechnologies

Adam Salmon
Eskitis Institute for Cell and Molecular Therapies
Griffith University, Gold Coast
Protein X-ray crystallography studies of metallocene-based sulfonamide/hCA II complexes

Dr Bernadette Saunders
Centenary Institute, Sydney, New South Wales
TNF, microparticles and regulation of macrophage activation and inflammation during tuberculosis infection

Dr Fiona Simpson
Diamantina Institute, UQ
EGF trafficking in squamous cell carcinoma

Hugh Simpson
Queensland Brain Institute, UQ
Computational modelling of visual topographic map development

Professor John A. Stamatoyannopoulos
Department of Genome Sciences, School of Medicine
University of Washington, Seattle, USA
The human cis-regulatory map

Professor Francis Stewart
Technische Universitaet and BioInnovationZentrum, Dresden, Germany
The epigenetics and development biology of histone 3 lysine 4 methylation

Dr Tuomas Tammela
Biomedicum Helsinki, Finland
Therapeutic targeting of the lymphatic system

Dr Tim Thomas
Walter & Eliza Hall Institute, Melbourne, Victoria
MYST histone acetyltransferases, chromatin structure and development

Dr Makrina Totsika
School of Chemistry and Molecular Biosciences, UQ
Understanding the role of macrophages in uropathogenic Escherichia coli *infections*

Thomas Ve
School of Chemistry and Molecular Biosciences, UQ
Molecular basis of plant disease resistance

Professor Mark Walker
University of Wollongong, New South Wales
Evolution and emergence of invasive serotype M1T1 group A streptococci

Dr Michael Way
Cancer Research UK London Research Institute
Using Vaccinia virus to understand signalling network dynamics and regulation of actin polymerisation

Dr Christine Wells
Eskitis Institute for Cell and Molecular Therapies
Griffith University, Gold Coast
Alternate splicing as a mechanism to diversify innate immune responses and *Australian stem cell database*

Dr Ian Wilkie
School of Veterinary Science, UQ
Acute cytokine responses by circulating macrophages, in chickens exposed to highly virulent & non-virulent strains of Pasteurella multocida

Dr Rohan Williams
John Curtin School of Medical Research
Australian National University, Canberra, ACT
A gene set approach to understanding inter-individual variation in mRNA levels

Thorsten Wohland
Chemistry Department
National University of Singapore
Quantitative measurements of molecular interaction in living organisms by Single Wave length Fluorescence Cross-correlation Spectroscopy (SW-FCCS)

Xing Yu
Glycomics Institute
Griffith University, Gold Coast
Rotavirus and sialic acid recognition

COLLABORATIVE RESEARCH PARTNERSHIPS

Further underlining the Institute's commitment to research excellence, IMB Group Leaders collaborate extensively with partners both within Australia and internationally. The IMB is a core partner and participant in many research centres around the country, including three Major National Research Facilities (MNRFs) and two Cooperative Research Centres (CRCs).

These programs are integral to building Australia's national and international research capabilities. They aim to create the scale and focus necessary to maintain and develop Australia's world-class standing in priority areas through highly innovative research that addresses challenging and significant problems. CRCs and COEs make vital contributions to Australia's research landscape and produce outcomes with economic, social and cultural benefits to the country. Involvement in these ventures reflects very highly on the participating researchers, indicating the value of their work in both scientific and commercial terms.

ARC CENTRE OF EXCELLENCE IN BIOINFORMATICS

The ARC Centre of Excellence in Bioinformatics, with headquarters at IMB, brings Australian and overseas researchers together into interdisciplinary programs designed to explore how information in the genome is transformed into structure and function in the mammalian cell. Perspectives and technologies of mathematics, statistics, high-performance computation, information technology, genomics and high-throughput experimental phenomic biology are focused on representing the mammalian cell as a complex system of molecular networks, and building a common modeling and visualisation environment to simulate its development and behaviour. Although directed in the first instance towards understanding human health and development, the Centre's technologies and output are generally applicable to biotechnology, while building critical mass in advanced bioinformatics is vital to Australia's international competitiveness in bio-based industries.

ARC CENTRE OF EXCELLENCE IN BIOTECHNOLOGY AND DEVELOPMENT

The ARC Centre of Excellence in Biotechnology and Development (CBD) was established in 2003 to focus on the biology of male germ cells – embryonic stem cells that eventually produce sperm cells in men. A review of the Centre in 2007 confirmed its status as a Centre of Excellence, and extended its funding

Collaborative research partnerships

for a further three years. Collaborating institutions include the IMB, the Universities of Queensland, Melbourne, and Newcastle, Monash University and the Australian National University, with Professor Peter Koopman from IMB one of the Centre's Chief Investigators. Unlike many other types of stem cells, germ cells represent a truly "blank slate" that can develop into any tissue in the body. Understanding their specification and programming is central to contemporary efforts to harness stem cell technologies. Since male fertility depends on generating sperm cells in vast numbers, and since genetic and environmental factors commonly disturb the quantity and quality of sperm produced, the research will further impact on understanding and possible treatment of infertility, a distressing condition that represents a massive healthcare burden in Australia and worldwide. Disorders of germ cells are often accompanied by testicular cancer, and so the potential medical significance of this research is twofold. It has become increasingly clear that manipulating the quantity and/or quality of germ cells, particularly male germ cells, presents powerful opportunities in the pest management arena, and in other biotechnological pursuits such as the management of endangered wildlife species.

AUSTRALASIAN INVASIVE ANIMALS CRC

Australasian Invasive Animals CRC is a venture aiming to counteract the impact of invasive animals through the development and application of new technologies and integrating approaches across agencies and jurisdictions. It is the first time that research, industry, environmental, commercial and government agencies have combined to create and apply solutions for invasive animal threats, which cost Australasia at least $720 million per annum. This unique partnership will deliver the means to deal with existing high-profile invasive animal pests as well as those that have the potential to cause catastrophic impacts in the future. Professor Peter Koopman from the IMB is part of the Daughterless Carp Program of the AIACRC. This program, based at CSIRO fisheries in Hobart, uses innovative technologies with a view to skewing the sex ratios of wild populations of the common carp, one of the most widespread threats to indigenous fish species in our larger waterways. Lindsay McFarlane, a PhD student from the Wilhelm group, is also a member of the AIACRC. His project focuses on gene silencing in fish as part of the Daughterless Carp Program.

AUSTRALIAN GENOME RESEARCH FACILITY

The Australian Genome Research Facility (AGRF) is an MNRF of the Commonwealth Government and was established in 1996 through an MNRF application led by Professor John Mattick, who served as the inaugural director until 2002, and Board Member until 2004. Professor Brandon Wainwright currently serves on the AGRF Board. The AGRF is a state-of-the-art facility for the collection of molecular genetic information covering large-scale DNA sequencing, genotyping, microarraying, agricultural genomic services and other resources for the genetic and physical mapping of chromosomes, mutation detection and associated bioinformatic analysis. It serves several hundred research groups across all states and territories of Australia from nodes at The University of Queensland, the Walter and Eliza Hall Institute of Medical Research in Melbourne, the Waite Campus of the University of Adelaide, the Western Australian Institute of Medical Research in Perth, and Sydney's Westmead Millennium Institute.

AUSTRALIAN MICROSCOPY & MICROANALYSIS RESEARCH FACILITY

The Advanced Cryo-Electron Microscopy Laboratory – the Queensland node of the Australian Microscopy & Microanalysis Research Facility – is housed in a purpose-built facility at IMB. This facility, funded under the National Collaborative Research Infrastructure Strategy, is a collaboration between the Universities of Queensland, Western Australia, Melbourne, New South Wales and Sydney. Its 300kV Technai microscope is one of the flagship instruments of the AMMRF. The facility is currently the only one in Australia or New Zealand capable of collecting and processing atomic-resolution images at low temperature, as well as undertaking a 3D electron microscope (EM) tomography of organelles, cells and tissues at both ambient and low temperature. Only a handful of international (and no other Australian) laboratories can offer researchers equivalent state-of-the-art research tools for high-resolution 3D structure studies of cells and molecules. The AMMRF is a successor to the Nanostructural Analysis Network Organisation (NANO).

AUSTRALIAN PHENOMICS FACILITY

The Australian Phenomics Facility (APF) is based at the John Curtin School for Medical Research at the Australian National University (ANU) and is a Major National Research Facility (MNRF) formed by support from the IMB, ANU and the Garvan Institute for Medical Research. The APF is based around the use of mouse genetics to discover novel genes that influence traits of medical relevance. Large populations of mice are exposed to a mutagen, traits are identified and selected then genetic mapping is used to locate the general regions where the genes reside. The mutagen used to create the mutants leaves a particular genetic fingerprint that can be discerned by sequencing candidate genes, thus identifying the gene responsible for the trait under

consideration. This is a very powerful approach to biology which enables gene function to be elucidated based upon the high-throughput analysis of phenotypes ("phenomics").

AUSTRALIAN STEM CELL CENTRE

The Australian Stem Cell Centre (ASCC) is a national research and funding facility set up by the ARC, the Victorian Department of Industry, Innovation and Regional Development, and the Federal Department of Education, Science and Training. The ASCC is primarily based at Monash University, but through the guidance of the Scientific Management Advisory Committee (SMAC) and a process of due diligence, the ASCC funds research which falls within its core expertise platform areas or its therapeutic focus areas. The IMB has very close links with the ASCC. Professor Brandon Wainwright served on the Board from April 2009 until October 2010. Professor Melissa Little spent a period as Chief Scientific Officer, responsible for developing strategy, scientific review and management, and developed a Queensland division of the ASCC based at UQ. She is a member of the Centre's Senior Scientific Faculty, a group of eminent and internationally regarded Australian researchers who monitor scientific progress, provide advice to the ASCC and act as the key public scientific spokespeople. The Centre distributes its funds to collaborative groups of researchers in four key areas, known as streams, of stem cell research. Professor Little is Deputy Leader of Collaborative Stream 4: Adult Stem Cell Program. She is also leader of a module within this stream that aims to further characterise the origin and properties of endogenous renal MSCs and investigate their role in responding to renal damage. Professor Little is leader of another module, "Regenerative Therapies for Renal Repair". This module is in Stream 3: Pluripotent Stem Cell Differentiation. Professor Little is screening for novel chemical compounds that can direct stem cells to form a kidney. One of Professor Little's PhD students, Caroline Hopkins, won an International Travel Award from the ASCC, designed to allow junior researchers to attend international stem cell meetings. Professor Sean Grimmond is also funded by the ASCC. He is leader of a module in Stream 2. This stream focuses on understanding reprogramming of cells and the introduction of pluripotency. Professor Grimmond's module is defining the underlying genetics of these processes. He is also a Chief Investigator on a project supported by the ASCC's Strategic Development Fund. He, along with Dr Christine Wells from Griffith University and Professor Doug Hilton from the Walter and Eliza Hall Institute, is developing a database containing multiple datasets of genetic information across stem cell lines to help Australian scientists to better compare the chracteristics of different types of stem cells.

NETWORK FOR PANCREATIC ORGAN DONORS WITH DIABETES (NPOD)

nPOD is an initiative of the Juvenile Diabetes Research Foundation International (JDRF) and brings together organ procurement organisations, academic institutions and leading diabetes researchers from Europe and America. IMB's Dr Brad Marsh is an investigator in the Pathology category. Dr Marsh studies the 3D characterisation of islet cell function and dysfunction. nPod aims to improve the procurement of pancreatic tissue specifically from patients and donors at high risk of developing type 1 diabetes. It is the first trial of its kind anywhere in the world and it is hoped that it will improve our understanding of the onset and progress of type 1 diabetes. Together with Professors Thomas Kay at St Vincent's Institute and Peter Colman at the Royal Melbourne Hospital, one goal of the nPOD program is to establish a similar initiative among groups leading type 1 diabetes research within Australia.

QUEENSLAND FACILITY FOR ADVANCED BIOINFORMATICS (QFAB)

QFAB is based at the IMB and was established in 2006 with a $1.9 million Queensland State Government grant that has been leveraged to provide $9 million worth of resources available for client projects. It supports the bioinformatics requirements of the biotechnology, pharmaceutical, clinical and research communities by providing broad expertise and access to large databases, high-performance computing and storage, and to specialist software and services. Since beginning operations, it has completed over 50 projects with another 15 underway. IMB projects on which QFAB has worked include helping to find the basis for childhood obesity (KOALA), building a database for spider venom research and analysis of a transposon-based forward genetic screen. QFAB has helped researchers attract $52.7 million in grant funding to Queensland.

RIKEN/FANTOM

RIKEN is the Institute for Physical and Chemical Sciences of the Japanese Science and Technology Agency, and a major site of genomics research in Japan. The RIKEN Genome Sciences Centre is based at Yokohama, Japan's second-largest city, and Wako, both in the Tokyo area. In the late 1990s, RIKEN established a program aimed at elucidating the complete transcriptional output of the mouse. More recently, the program has shifted focus towards the elucidation of transcriptional control networks. Both activities have involved the establishment of large international consortia, firstly the FANTOM consortium (Functional Annotation of Mouse), and more recently the Genome Network consortium. The consortium has previously published a comprehensive analysis of the human and mouse transcriptome and a series of papers on gene control in mammals. IMB researchers were involved as authors and senior authors on these papers.

COMMUNITY ENGAGEMENT

MUCH OF THE COMMUNITY engagement that took place in 2010 was based around UQ's Centenary year. IMB decided to mark the occasion by resurrecting the Ångström Art™ competition. Originally held in 2001, Ångström Art™ was the result of an Australia-wide imaging competition run by the IMB. Several collections of images were produced before the competition went on hiatus.

In 2010, we decided to restrict the competition to IMB researchers only, transforming Ångström Art™ into a visual showcase of the Institute's research. Researchers from all divisions of the IMB were inspired by the competition, with 62 images entered in total. A judging panel consisting of Professor Stephen Walker, Dean of UQ's Faculty of Science; Mrs Beverley Trivett, Director of the John Trivett Foundation, which supported earlier Angstrom Art competitions; and Mr Nick Mitzkevich, Director of the UQ Art Gallery; selected one winner and two runners-up.

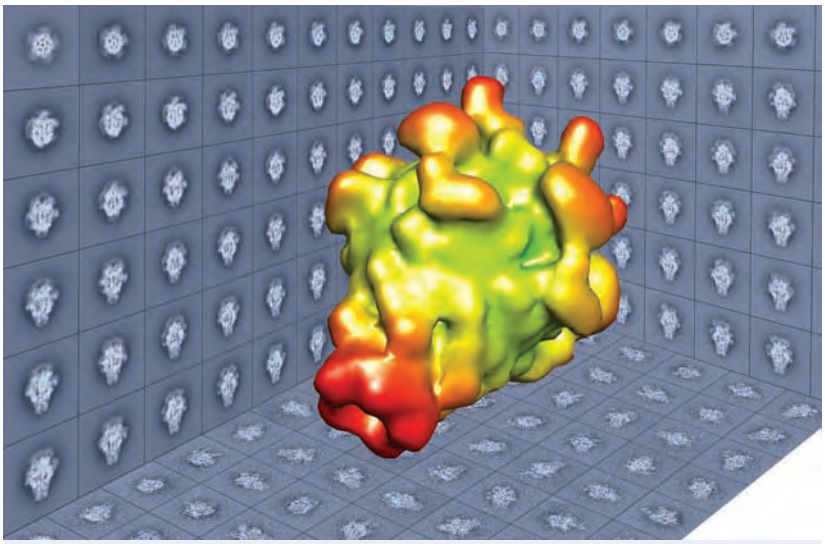
Mr Darren Brown from the Stow group contributed the winning image, MacBeads (seen on the front of this report) and runner-up image RealMacAlien. Dr Michael Landsberg from the Hankamer group was the other runner-up for his image, Insect Assassin. All 62 images can be viewed on the Angstrom Art website at *www.angstrom-art.com*. These images were displayed at an internal IMB exhibition, and at external exhibitions at UQ's Celebration of Centenary on Sunday April 18, and at UQ's Open Day on August 1.

IMB's Marketing team also produced iPhone skins and postcards with the Angstrom Art images, which have proven immensely popular at both community and scientific events. If you would like some postcards or an iPhone skin, please contact imb@imb.uq.edu.au

THE IMB WEBSITE (www.imb.uq.edu.au) continues to be the main portal of information about the institute, including its newsletter Output (to subscribe, please click on the green 'Subscribe' button on the IMB homepage). The IMB News section of the website nearly tripled the number of hits it received in 2010 compared to 2009, with around 125,000 in 2009 and nearly 350,000 in 2010. The website remains in the number one position when 'molecular bioscience' is searched in Google.

THE IMB SCIENCE AMBASSADOR program continued to be a success. We had some turnover of ambassadors from our first cohort, ending up with 18 ambassadors in total, including a mid-year intake. In its pilot year, the ambassador program was run by a committee consisting of two staff members and an ambassador. In 2010, the committee decided to expand, and allow more ambassadors a chance to assist in guiding the program. The 2010 committee was: Phillippa Smith (Craik group) – Co-ordinator; Dr Richa Dave (Wainwright group) – Worksheet Manager; Dr Denis Bauer (Bailey group) – Vodcast Manager; Maggie Hardy (King group) – Committee Adviser; Dr Amanda Carozzi – Postgraduate Student Co-ordinator; and Bronwyn Adams – Marketing and Communications Officer. Each of these committee members did an excellent job in ensuring the success of the program beyond its pilot year.

RUNNER UP: ÅNGSTRÖM ART CENTENARY COLLECTION



MICHAEL LANDSBERG: INSECT ASSASSIN

A number of techniques exist for studying the structure of proteins – the "worker molecules" of the cell. This image draws inspiration from the technique of single particle analysis, highlighting how it is now possible with current technology to reconstruct in three-dimensions, images of individual macromolecular protein complexes.

The "walls" of the room illustrate various steps in the process of single particle analysis – the visualisation of individual protein complexes, computational image averaging and three-dimensional reconstruction – to obtain a final three-dimensional structure.

The structure shown floating in the centre of the room is around 30 nanometres in length (around one millionth of a centimetre) and was determined by combining over 10 000 images captured by electron microscopy. It is being investigated because of its insecticidal properties.

Darren Brown and Dr Michael Landsberg, winner and runner-up of the Ångström Art™ Centenary competition.

The remaining ambassadors were: Dr Nilesh Bokil (Sweet group), Dr Andrew Brooks (Waters group), Natasha Chaudhary (Parton group), Dr Nicole Cloonan (Grimmond group), Baptiste Coxam (Hogan group), Dr Marcel Dinger (Mattick group), Marga Gual Soler (Stow group), Dr Michael Hanzal-Bayer (Teasdale group), Dr Elaine Julian (Wainwright group), Dr Praveen Madala (Fairlie group), Anne Sawyer (Hankamer group), Evan Stephens (Hankamer group), Dr Michael Tallack (Perkins group), and Dr Brit Winnen (King group).

These ambassadors promoted science at events such as Brisbane's Royal Show (the "Ekka"), UQ's Experience Science, Open Day, Celebration of Centenary and Biofutures. They also assisted with visits from groups ranging from international scientific and political delegates to the Double Helix Club for primary school children, and hosted work experience students from schools around Brisbane. Dr Michael Tallack even appeared on Channel 10 science show Scope, in a segment on bacteria and exponential growth. IMB welcomes enquiries from media and tour groups – please contact *imb@imb.uq.edu* to arrange a tour.

IMB SCIENTISTS WERE PART OF CSIRO's Scientists in Schools program, which pairs a teacher and a scientist. The partnership is flexible, allowing scientists to engage with the class in the way in which they and the teacher feel is best for both the time available and the needs of the students.

Dr Brad Marsh and Dr Melissa Davis continued their partnerships with Graceville State School and Ironside State School respectively. Dr Bernd Becker donated his time to both Centenary State High School and the Mater Hospital Special School, while Peter van der Heide spent time with Brisbane State High School students.

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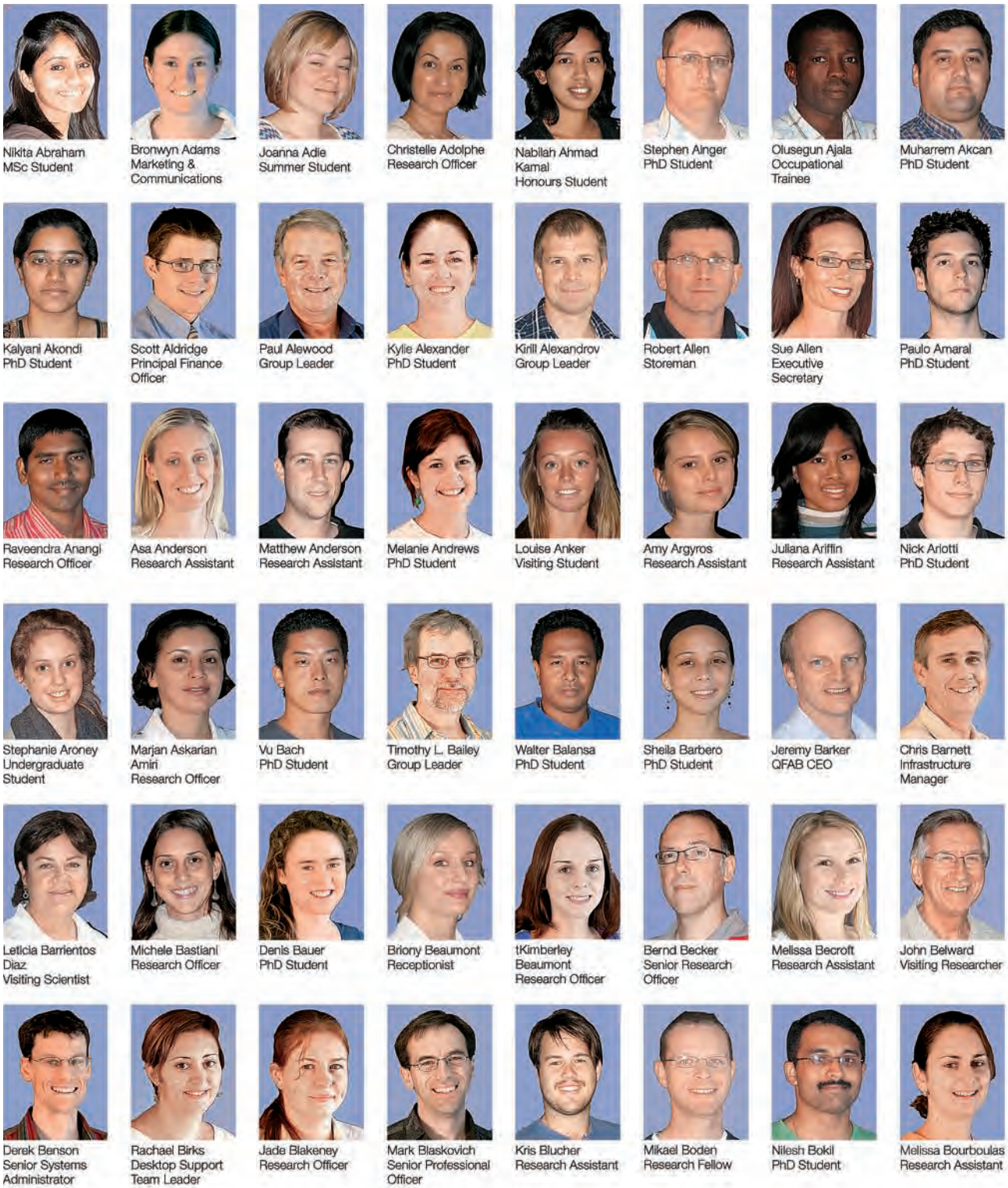

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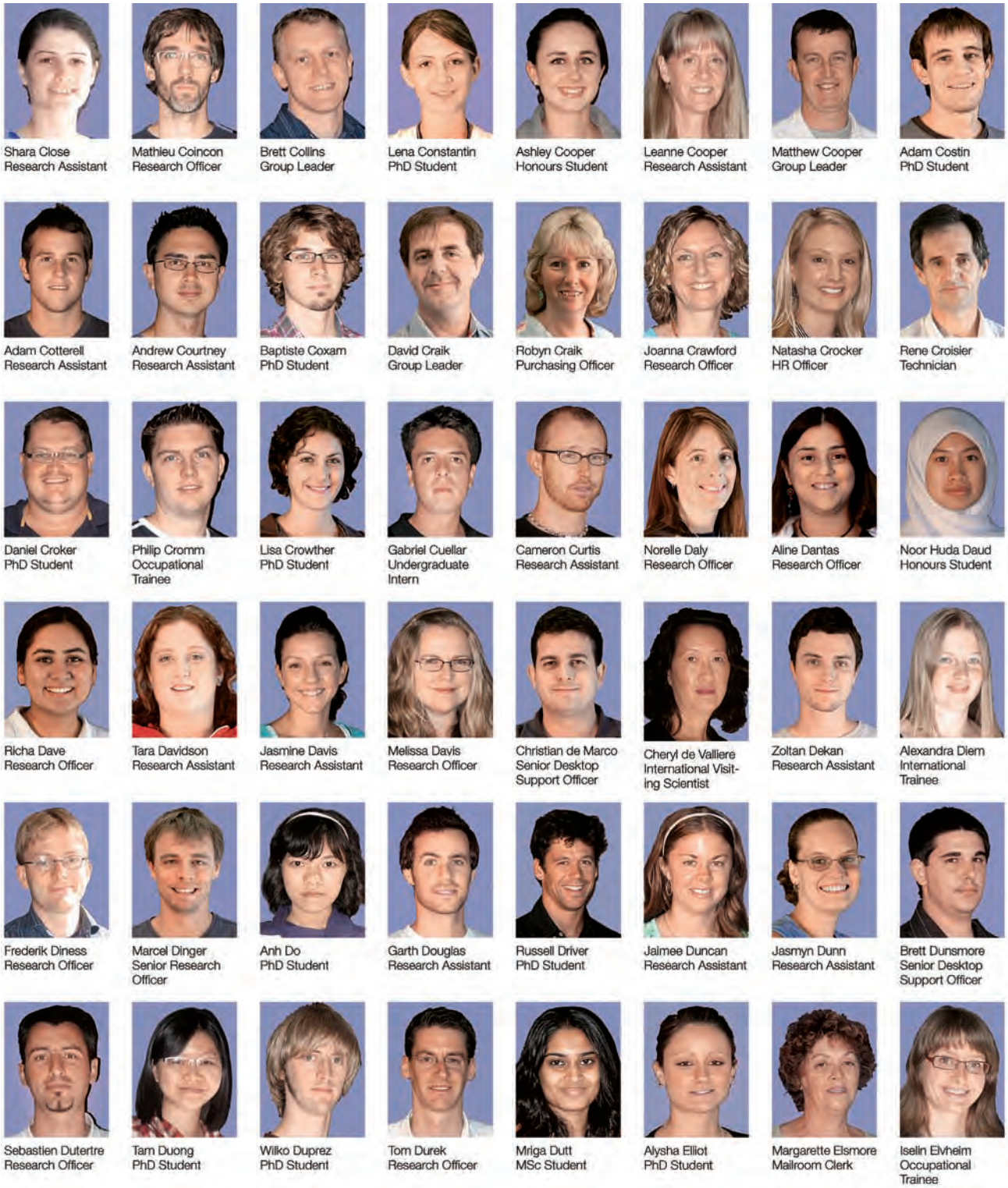

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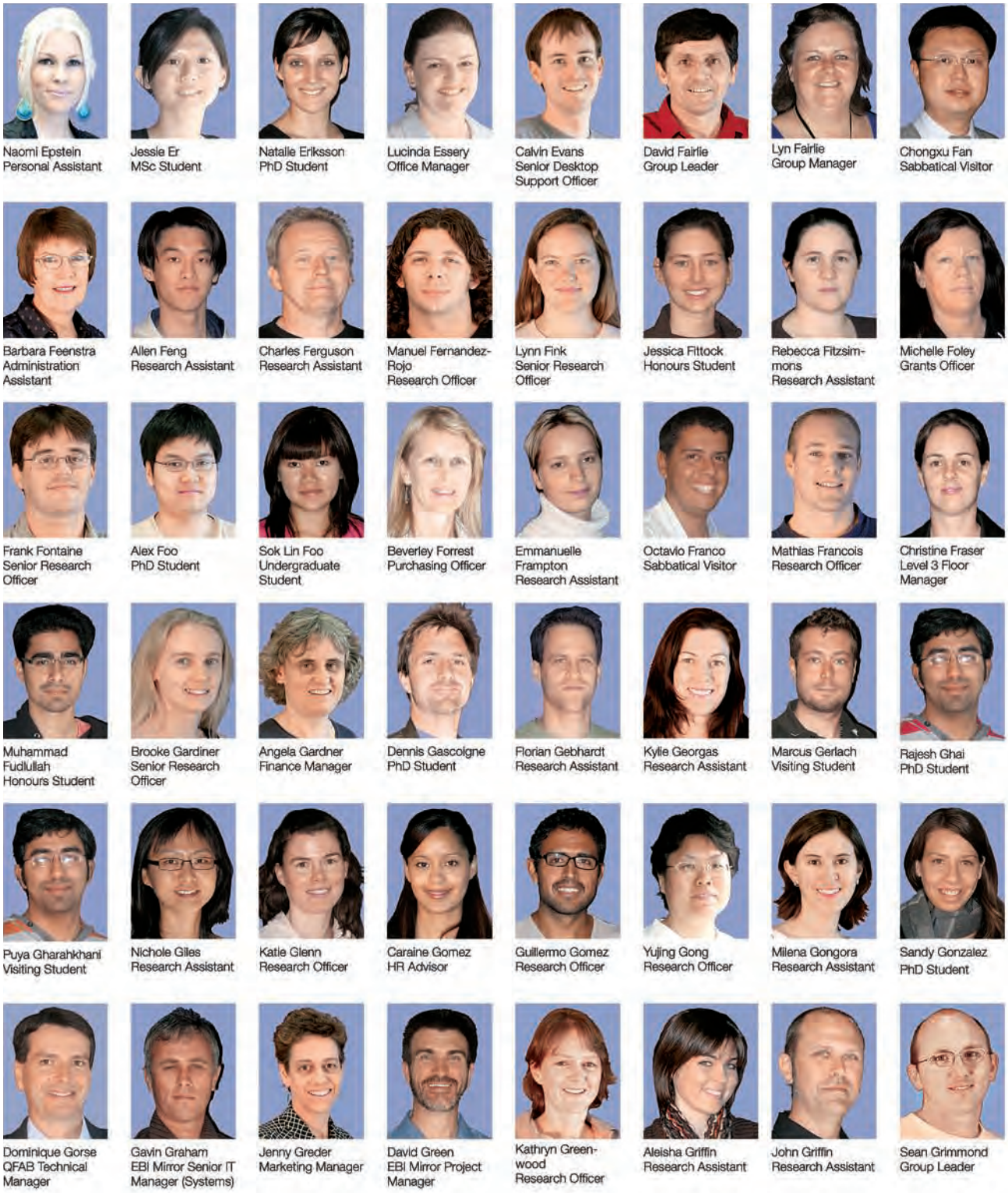

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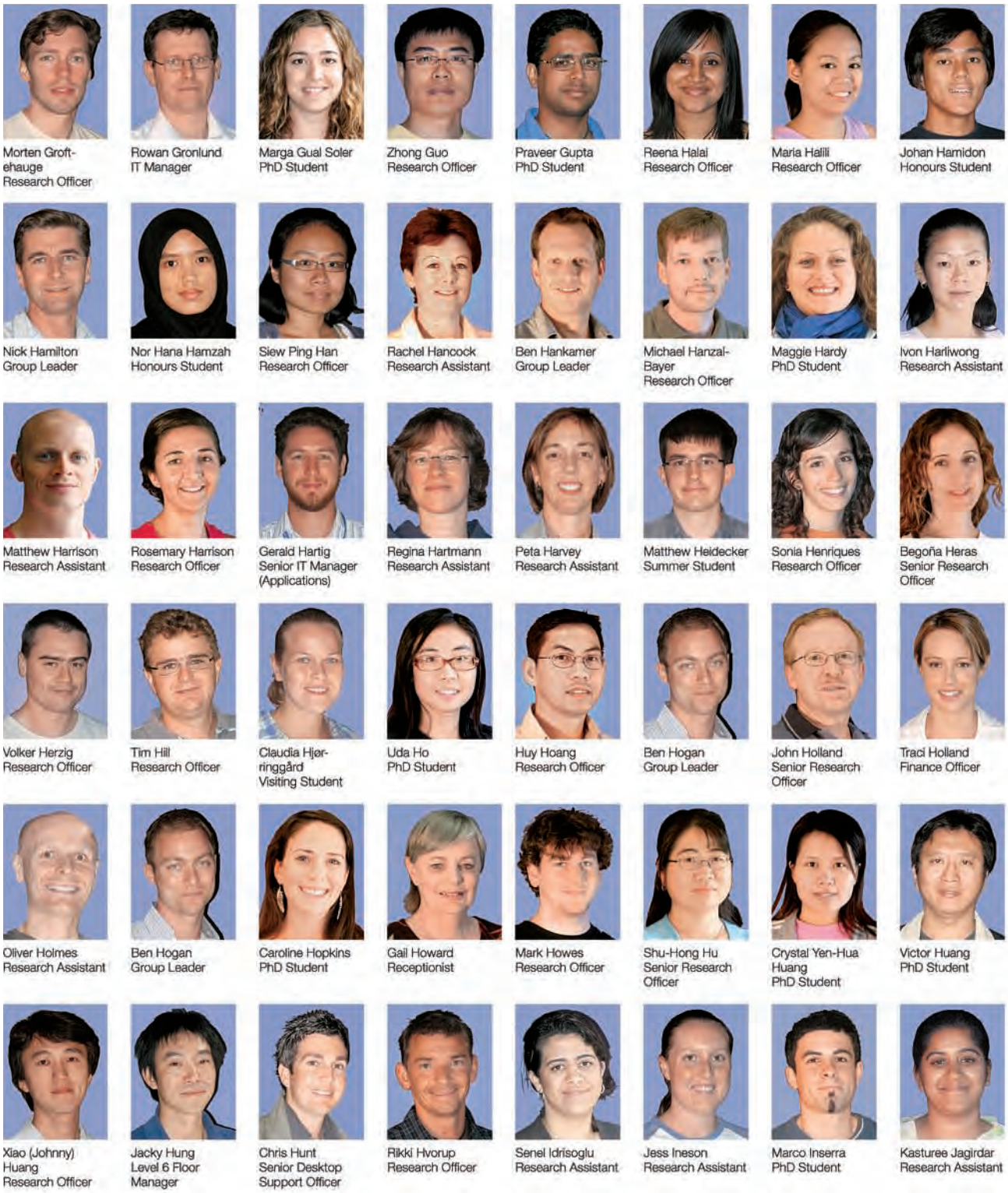

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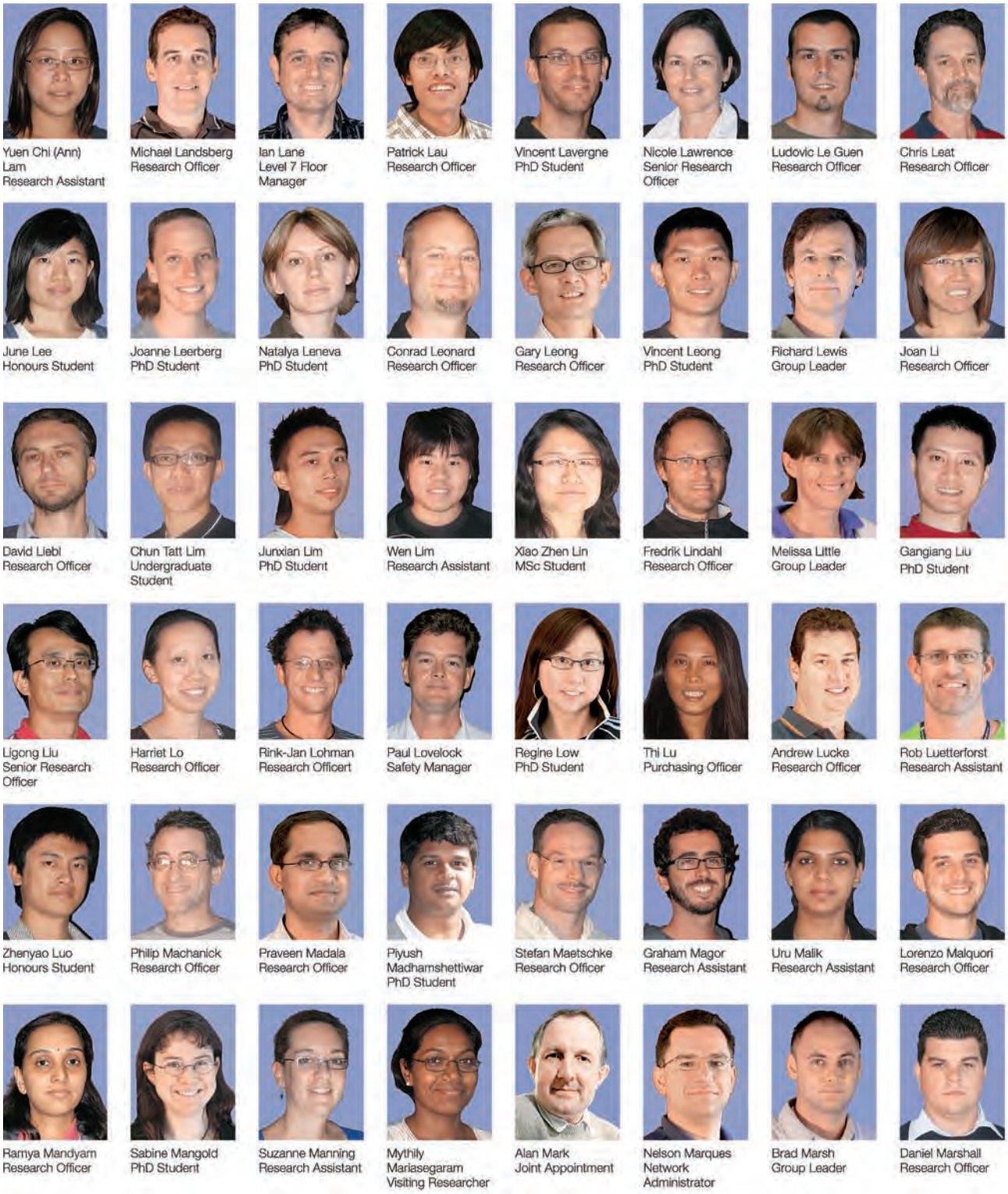

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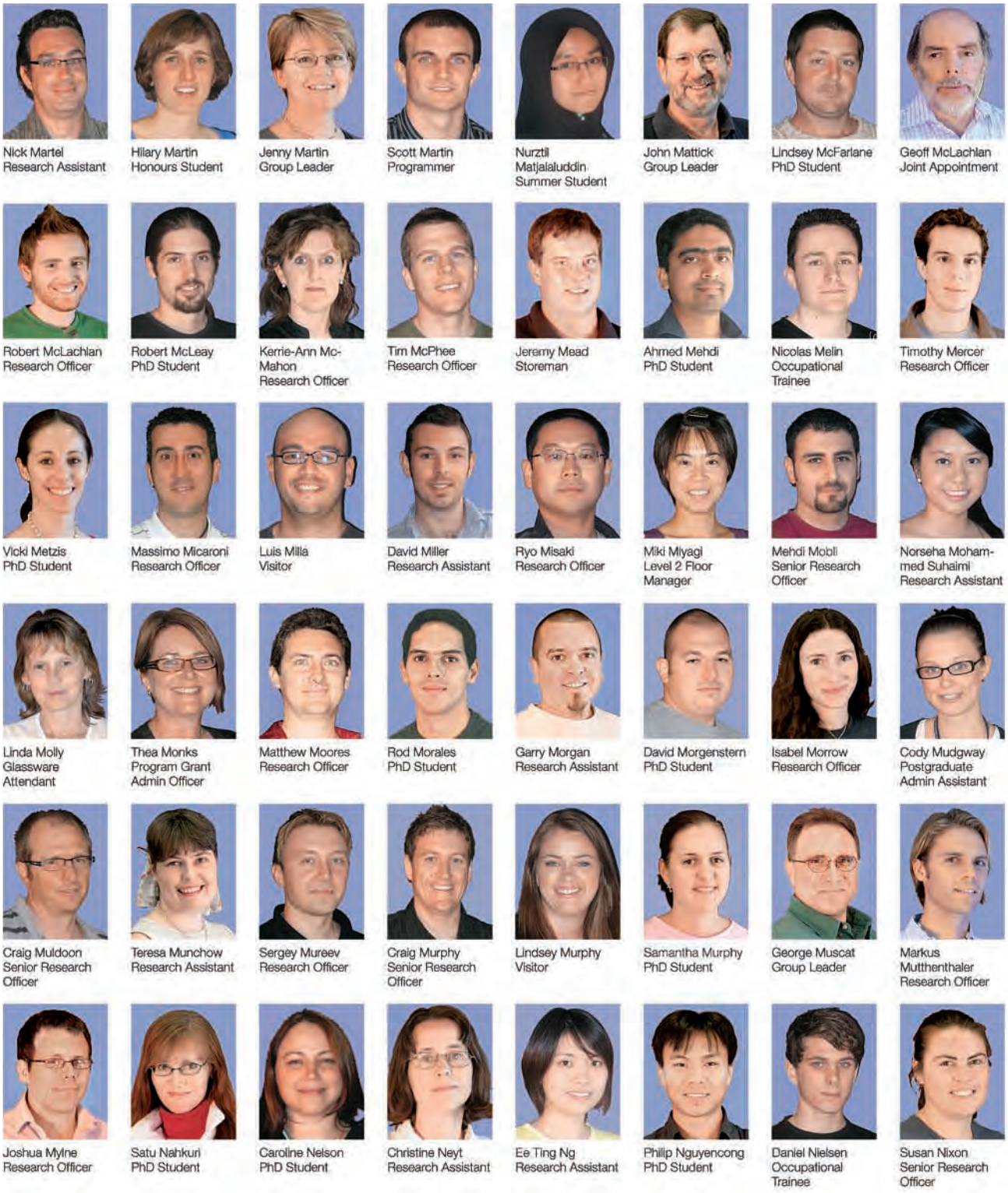

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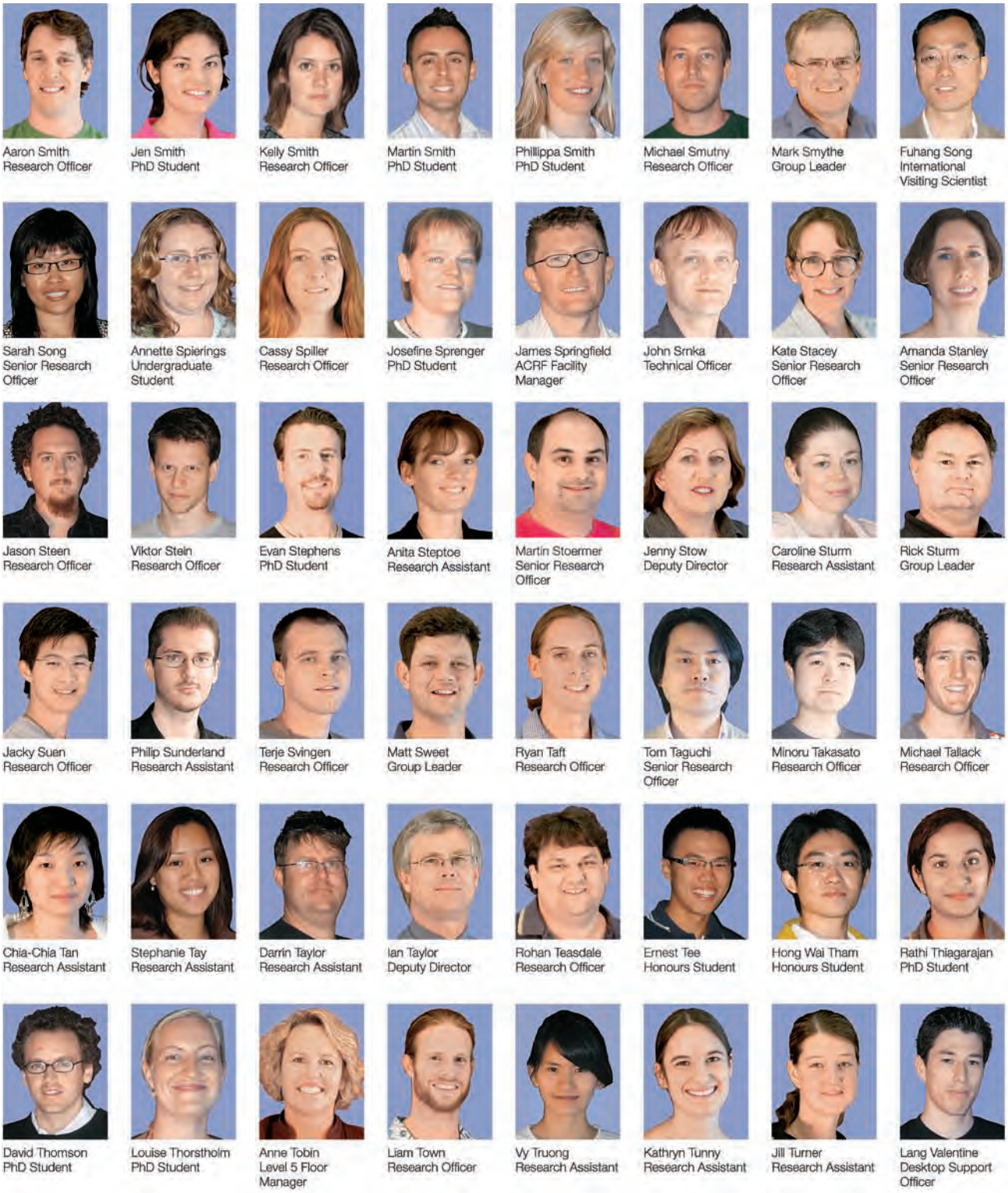

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Kathy Webb
Acting Finance Manager

Jane Weber
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Tom Whitington
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Andrew Whitten
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Carol Wicking
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Dagmar Wilhelm
Group Leader

Lorine Wilkinson
Research Officer

Kai Willadsen
Research Officer

Danielle Wilson
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David Wilson
Research Assistant

Peter Wilson
QCMG Executive Officer

Josh Wingerd
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Brit Winnen
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Benjamin Wong
Undergraduate Student

Karen Wong
Summer Student

Lanna Wong
ARC Centre of Excellence Manager

Shu Shyan Wong
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David Wood
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Scott Wood
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IMB Staff and Students


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Eugene Zhang
PhD Student


Fiona Zhang
Finance Officer


Hua Zhang
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Jenny Zhang
Research Officer


Katharina
Zimmerman
Visiting Scientist


Mark Ziza
Technical Officer


Johannes Zuegg
Senior Research
Officer

IMBcom


Kellie Broderick
Manager, Infrastructure
& Education


Kelly Coomber
Company
Accountant


Ujjwal Dua
Commercialisation
Officer


Paul Ellender
Marketing & Events
Co-ordinator


Philip Ellery
Commercialisation
Officer


Deborah Ferguson
Company
Accountant


Peter Isdale
Chief Executive
Officer


Erin Kefford
IP & Operations
Support


Tracey Mynott
Commercialisation
Consultant


Lyn Rosen
Executive Assistant


Amanda Smith
Manager, IP &
Development


Karen Soxsmith
Systems
Administrator


Carla Toland
Commercialisation
Officer


Charlie Widberg
Commercialisation
Officer

FINANCIAL STATEMENT

STATEMENT OF OPERATING INCOME AND EXPENDITURE
YEAR ENDED 31 DECEMBER 2010

INCOME	Note	2006	2007	2008	2009	2010
University of Queensland (Operating Grant)	1	10,767,311	11,087,942	11,062,918	13,383,853	10,920,370
University of Queensland Research Grants		252,252	300,436	190,291	311,370	260,901
State Government		10,175,000	11,127,168	10,857,620	14,867,120	10,824,480
SRC Grant (Australian Research Council)		1,159,047	1,182,516	1,206,166	0	0
Australian Research Council	2	5,218,279	6,010,239	5,977,542	7,637,369	8,624,071
Australian Cancer Research Foundation		0	0	0	1,250,000	1,250,000
Australian National University		0	0	0	0	55,800
Australian Nuclear Science & Technology Organisation		78,757	230,492	61,326	8,540	992
Australian Stem Cell Centre		159,780	467,335	770,065	1,342,609	425,442
Baker IDI Heart & Diabetes Institute		0	0	0	76,237	735
Bioplatforms Australia		0	0	0	0	1,029,675
Cancer Council Queensland (previously QCF)		148,700	312,000	554,000	402,000	182,000
Clive and Vera Ramaciotti Foundation		0	60,000	30,000	0	0
Community Health + Tuberculosis Australia		49,000	0	0	0	0
CRC for Chronic Inflammatory Diseases		1,326,058	1,462,776	1,214,510	0	0
Invasive Animals CRC (was Pest Animal Control)		122,210	0	47,952	0	0
CSIRO		0	0	0	0	627,789
Cystic Fibrosis UK		0	0	0	0	10,000
Dairy Australia		167,644	700,321	333,084	0	0
Dept Industry Science and Technology (Commonwealth) was DISR		0	200,000	135,000	37,245	4,853
Department of Primary Industries		0	50,000	0	0	0
Diabetes Australia Research Trust		45,000	0	50,008	60,000	0
Grain Research and Development Corporation		0	0	0	0	399,640
Human Frontiers Science Program		0	81,783	58,180	279,530	113,522
Japanese Science & Technology Agency		0	0	106,462	142,331	0
The John Trivett Foundation		0	267,817	0	0	0
Juvenile Diabetes Foundation International		178,634	147,708	110,723	167,904	136,109
The Mazda Foundation		0	0	150,000	0	0
Monash University – ARDC Subcontract (EBI Mirror)		0	0	0	0	400,000
The Murdoch Childrens Research Institute		0	347,527	235,515	379,122	10,899
National Breast Cancer Foundation		0	0	0	413,490	65,997
National Institute of Health (US)		1,176,642	969,415	561,829	503,882	432,842
National Health and Medical Research Council	2	7,888,967	11,054,142	12,445,955	15,622,119	21,197,020
National Heart Foundation		0	0	65,800	0	2,000
New Zealand Dept Science & Technology		0	81,392	40,738	0	0
Oncology Children's Foundation		0	0	0	100,000	0

Financial Statement

INCOME (continued)	Note	2006	2007	2008	2009	2010
Postgraduate Scholarships		261,263	305,255	234,520	142,619	132,703
Queensland Cyber Infrastructure Foundation Ltd		0	0	0	0	600,000
University of Alberta		0	0	0	0	20,752
University of Alabama		0	0	0	0	22,786
University of Sydney (Analytical Services)		0	0	0	0	100,000
Wellcome Trust		0	0	0	0	15,957
Commercial Income		2,018,054	4,880,234	4,585,955	2,521,961	2,269,267
Cross-Institutional contributions to LIEF or Facilities		509,472	188,000	50,000	0	230,000
University of Newcastle (re ARC Centre)		252,562	128,218	153,218	150,000	553,930
Marjory A Welford Bequest		0	0	0	0	58,799
Dr Rosamond Siemon Postgraduate Renal Research Scholarship		30,000	30,000	30,000	30,000	30,000
Rina Martina (Donation)		20,000	20,000	20,000	0	15,000
The Simon Axelsen Memorial Fund		0	0	0	0	180,000
QBP recoveries		386,092	371,257	363,065	346,442	386,301
Facilities – Analytical Services		0	0	0	0	471,896
Shared Grants		234,685	4,000	40,772	0	0
Conference Income		66,615	184,340	70,558	91,656	152,840
QBP Store		276,819	314,057	326,215	357,613	332,675
Victor Chang Cardiac Research Institute		0	0	0	0	86,000
Wesley Research Institute		20,000	93,645	98,423	101,628	0
Miscellaneous Income		399,887	357,293	391,776	186,154	338,924
TOTAL INCOME		**43,338,729**	**52,967,307**	**52,580,186**	**60,882,794**	**62,972,966**
Funds brought forward from previous year	3	**9,050,612**	**11,441,270**	**15,641,004**	**18,495,763**	**24,755,723**
TOTAL FUNDS AVAILABLE		**52,389,341**	**64,408,577**	**68,221,189**	**79,378,557**	**87,728,689**
EXPENDITURE:						
Salaries – Research		20,110,376	22,878,237	24,750,517	24,717,110	29,518,795
– Administration		1,205,466	1,349,056	1,345,709	1,548,200	1,713,594
– Infrastructure		2,673,620	2,368,795	2,862,623	3,090,792	3,179,745
Research Services		10,995,871	13,099,865	13,091,734	14,696,645	19,154,756
Education Programs	4	358,445	332,919	380,733	458,699	458,558
Administration	5	529,612	521,743	496,666	370,541	395,422
Corporate Services (UQ)	1	0	0	0	0	0
Infrastructure	6	1,295,139	1,862,212	2,160,052	1,693,759	1,616,966
Capital Equipment	7	2,569,801	5,156,825	3,438,525	6,847,087	5,923,904
IMBcom		1,209,741	1,197,920	1,198,528	1,200,000	1,200,000
TOTAL EXPENDITURE		**40,948,071**	**48,767,573**	**49,725,426**	**54,622,833**	**63,161,739**
Funds carried forward	8	**11,441,270**	**15,641,004**	**18,495,763**	**24,755,723**	**24,566,950**

Explanatory notes to Statement of Income and Expenditure

1a In-kind Contributions

Figure does not include the following salaries for affiliate appointments paid externally or by other departments:

	Location	Percentage
G. McLachlan	UQ Mathematics	90
P. Hugenholtz	UQ SCMB	80

b) Gross Income & Corporate Services Charge

The 2006 Annual Report showed University of Queensland Operating Grant Income as a gross amount and Corporate Services charge shown seperately under expenditure. Subsequent years have reverted to the previous method for better direct comparison. 2006 figures have been adjusted accordingly and now show the nett.

2 Fellowship/Projects from Government Agencies

Australian Research Council	
Projects	6,884,148
Fellowships	1,739,923
	8,624,071
National Health and Medical Research Council	
Projects	17,157,634
Fellowships	4,039,386
	21,197,020

3 Funds carried forward to 2010

University of Queensland Operating Grant	11,316,716
University of Queensland Research Grants	835,049
Postgraduate Scholarships	32,278
State Government	1,943,883
SRC Grant	-92,174
Fellowships (as approved by funding bodies)	397,160
Overseas Grants funded mid year	370,795
Contract Research	1,952,377
Project Grants (as approved by funding bodies)	7,999,639
	24,755,723

4 Education Programs

Postgraduate scholarships	406,263
Postgraduate recruitment & training	52,295
Total Education Services	**458,558**

^ Of this $883k is committed to QBP Shared Services, $154k to Core Facilities and $89k to 2010 Purchase Order Committments.

Of this $815K is the carry forward on State Govt projects, $445k is carry forward on Core and Core Facilities including $194k Purchase Order committments.

5 Administration

Annual Report	14,377
Marketing	51,706
Personnel Recruitment and Training	25,669
Visiting Scientists/Seminars	37,001
Fees	44,218
Quinquennial Review	-
Entertaining	36,777
Photocopying	57,851
Postage and Freight	3,696
Printing & stationery	31,893
Telephone	55,775
Travel Expenses	17,178
Board Fees	19,280
Total Administration	**395,422**

6 Infrastructure

Building Maintenance	107,383
Rental – Storage	12,658
Safety Equipment	43,401
Laundry	13,361
Minor Equipment & Furniture	134,232
Equipment Maintenance	325,977
Animals	335,864
Computer Services	613,778
Glass washing and replacement	55,516
Reticulated gases, RO water & dry ice	73,765
Cost Recovery	-98,969
Total Infrastructure	**1,616,966**

7 Capital Equipment

Scientific Equipment	4,934,972
Minor Equipment	988,932
Total Capital Equipment	**5,923,904**

8 Funds carried forward to 2011

University of Queensland Operating Grant	9,593,969 ^
Research O'head, Dir. Strategic, Recoveries	590,906
Postgraduate Scholarships	56,481
State Government	1,260,377 #
Fellowships (as approved by funding bodies)	221,971
Overseas Grants funded mid year	271,673
Contract Research	2,837,145
Project Grants (as approved by funding bodies)	9,734,428
	24,566,950

Glossary of terms

Actin A protein, along with myosin, responsible for muscle contraction.

Adipose Fat or fatty tissue.

Agonist A molecule that interacts with a receptor, triggering a cellular response.

Agrochemicals Chemicals used in agriculture.

Allele Different varieties of a gene that produce different traits.

Allosteric A site on a protein that isn't active.

AMPK An enzyme involved in the maintenance of cellular energy.

Amyloid A type of protein deposited in organs in certain diseases. eg. amyloid deposits are found in the brain of Alzheimer's patients.

Antagonist A molecule that blocks a chemical from binding to its receptor.

Apoptosis Programmed cell death.

Aromatase An enzyme that causes testosterone to transform into estrogen.

Arrays An ordering of samples on a slide.

Assay Qualitative or quantitative analyses of a substance performed in order to determine its components.

Atherosclerosis A disease in which cholesterol builds up on artery walls, causing the arteries to narrow.

BAC recombineering A method of introducing genetic material into an organism through a bacterial vector.

Beta-adrenergic Receptors in the nervous system that sense hormones such as adrenaline.

Bioactive Has an effect on a living organism.

Bioinformatics The use of computational resources in the study of biological information.

Biomolecule Molecules containing carbon found in living organisms.

Biophysical The intersection between physics and biology.

Bioprobes A probe containing biomolecules that measures some type of biological phenomena.

Biosynthesis The production of material from living organisms.

Chondrogenesis The development of cartilage.

Chromatin The complex of DNA and proteins that form a chromosome.

Chromosome A long coiled strand of DNA, wound around a protein.

Chromotographic Involving the separation of compounds into their constituent parts.

CNV Copy number variant. A sequence of DNA that is repeated a different number of times in different genomes.

Coculture A culture (preparation) in which more than one type of cell is grown.

Conotoxins Toxic peptides from marine cone snail venom.

Covalent A bond in which electrons are shared between atoms.

Crystallography The use of X-rays to determine the structure of crystallised molecules.

Cytokines Small proteins released by cells that affect the behaviour of other cells.

Cytoplasm All the contents of a cell, excepting the nucleus.

Cytoskeleton The protein framework of a cell.

Cytotoxicity Toxic to cells.

De novo Not previously present.

Differentiation The process by which cells become more specialised.

Diffraction The scattering of light waves as they pass through or around an object.

DNA Deoxyribonucleic acid. The chemical chain that carries the genetic instructions for making a living organism.

Dyslipidemia A disorder that occurs when there is an excess of lipids in the blood.

Effector complexes A molecule that alters the activity of a protein by binding to it.

Electron tomography A microscopy technique that samples a specimen at different angles and builds the resulting information into a 3D image.

Embryogenesis The development of an embryo.

Endocrine A system of glands that secrete hormones directly into the bloodstream.

Endocytosis Uptake of material into a cell.

Endogenous Within the body.

Endosomes An organelle involved in protein trafficking.

Enzymes A protein produced by living organisms that catalyses chemical reactions of other substances without being altered itself by the reactions.

Epifluorescence A type of microscopy using a very bright light source. This light is used to energise the sample into re-emitting light (or "fluorescing") at various wavelengths, which allows researchers to produce an image of the sample.

Epigenetic The changes in phenotype that occur without a corresponding change in genotype.

Epigenomic A cataloguing of the non-genetic changes that occur in the genome that affect gene expression.

Epithelial Of the membranous cellular tissue that covers the internal and external surfaces of the body.

Epitopes The site on the surface of a foreign substance that triggers the production of antibodies, and to which these antibodies bind.

Erythropoiesis The development of mature red blood cells.

Eukaryotes Organisms whose genetic material is enclosed in a membrane-bound nucleus. Includes all organisms except viruses and bacteria.

Ex vivo Taking place outside an organism.

Exocytosis The discharge of material from the cell.

FACS Fluorescent-activated cell sorting. A method of sorting a heterogeneous group of cells using the light scattering and fluorescent characteristics of each cell.

Flavivirus One of a family of small RNA viruses that are often transmitted by mosquitoes and ticks.

Gastrulation An embryonic stage of development where the embryo turns from a blastula (ball of cells) into three layers of cells, from which organs develop.

Gene Considered the basic unit of heredity, a gene is a region of DNA that encodes all of the information to make a protein.

Genome All DNA contained in an organism or cell.

Genotype The specific set of alleles possessed by an individual, either in whole or at one loci.

Globin The protein component of haemoglobin.

Golgi An organelle that packages and distributes chemicals within and outside the cell.

GPCRs G protein-coupled receptors, the largest family of membrane receptors.

Gram-negative A type of bacteria with a double cell wall, which lessens the effect of some antibiotics.

Haemoglobin The molecule in blood that carries oxygen around the body.

Heterocycles Compounds containing a ring of atoms of different elements.

Heteromeric Made up of different subunits.

Heterogeneous Consisting of varied constituents.

Histone deacetylase An enzyme that can catalyse the inhibition of gene transcription.

Homeostasis A condition where the body uses negative feedback processes to maintain its systems at a constant equilibrium.

Homology Similarity due to common ancestry.

Homozygous Having the same two copies of alleles at a gene.

Hormone Any of a type of chemical secreted by one tissue that has an effect on another tissue.

Hypercholesterolemia High blood cholesterol.

Immuno-precipitation The process whereby an antigen is formed in a solution using a specific antibody.

In toto Totally.

In vitro A process occurring in an artificial environment that would normally occur in an organism.

Informatics The science of using technology to better process, store and analyse information.

Ion A particle or atom with a charge.

Ion channels Protein pores in the membrane that control the flow of ions into and out of the cell.

Isothermal calorimetry A technique of measuring the heat and heat capacity of chemical reactions; often used to characterise potential drug candidates.

Keratinocytes Cells that make keratin, a substance found in hair and nails (hard keratin) and skin (soft keratin).

Kinase An enzyme that catalyses the transfer of a phosphate group from a donor to a target molecule.

Knockouts Organisms in which specific genes have been made inactive, so scientists can determine their effect.

Ligands A chemical that binds to a larger molecule/receptor.

Lipid Any of a group of heterogeneous fat or fat-like compounds that are insoluble in water.

Lipodystrophies Disorders that result in the abnormal accumulation or loss of fat in different areas of the body.

Lipogenic Related to the production of fat.

Lipopolysaccharides A molecule made up of a lipid (fat) and a polysaccharide (a type of carbohydrate) found in the cell wall of Gram-negative bacteria.

Liposomes Artificial vesicles capable of delivering drugs to target tissues.

LXR Liver X receptor, which regulates cholesterol, fat and sugar levels.

Lymphatic system The circulatory network of vessels that produce and store the cells that fight infection.

Lymphedema A condition that occurs when excess lymph fluid collects in a localised area.

Lysosome An organelle capable of digesting microorganisms and cellular debris.

Macrophage A large cell that engulfs and absorbs waste material, harmful microbes or other foreign bodies in the bloodstream and tissues.

Macropinocytosis The formation of fluid-filled macropinosomes.

Macropinosomes Large, heterogeneous, dynamic vesicles.

Mass spectrometry A technique for determining the chemical constituents and structure of a sample.

Mechanosensing Responsive to mechanical (as opposed to eg. chemical) stimuli.

Melanin Skin and hair pigment.

Melanoblast Precursor of a melanocyte.

Melanocyte A cell that produces melanin, the pigment that gives skin, hair and eyes their colour.

Membrane A thin layer of tissue surrounding a cell and separating it from the rest of the environment.

Mesoderm The middle layer of cells in the early embryo.

Metastasis Migration of cancer cells from their original site to other parts of the body.

Microarray A technique for studying how large numbers of genes interact and how a cell's regulatory network controls vast amount of genes simultaneously.

MicroRNAs Also known as MiRNA, microRNAs are RNA molecules around 20 nucleotides long that regulate gene expression.

Mimetics Artificial molecule that mimics the structure of a natural molecule.

Monoculture A culture (preparation) in which only one type of cell is grown.

Monomer A molecule that can be bound to others to form polymers (large molecules consisting of repeating smaller molecules).

mRNA Messenger RNA. The type of RNA that carries the instructions for coding proteins from DNA to the ribosomes, where proteins are assembled.

MRSA Metacillin-resistant *Staphylococcus aureus*. A species of bacteria that is resistant to broad-spectrum antibiotics and thus can cause infections that are difficult to treat.

Munc A protein essential for the process of secreting neurons.

Murine Relating to mice or rats.

Mutagenesis The process of intentionally creating mutations in an organism's DNA.

Myosins A protein, along with actin, responsible for muscle contraction.

Nanometre One billionth of a metre.

Neisseria A family of bacteria, two species of which cause diseases in humans *(N. meningitides* and *N. gonorrhoeae*).

Nephron Tubes within the kidney that act as filters.

Neuropathic Pain from nerves themselves, as opposed to injured or diseased body parts.

Neurosecretion The production and secretion of hormones by neurons.

Glossary of terms

Nevus A birthmark.

Nexin (sorting) A group of proteins, some of which play a role in sorting proteins.

NMR spectroscopy Nuclear Magnetic Resonance spectroscopy. A spectroscopic technique that analyses the disruptions to a high magnetic field to elucidate the chemical structure and molecular dynamics of a sample.

Nucleators Something that either forms into a nucleus or aids in this formation.

Nucleic acid The molecules that carry genetic information. DNA and RNA are examples of nucleic acids.

Nucleosomes The repeating subunit of chromatin.

Nucleus A large, membrane-bound, usually spherical structure within a living cell, containing the cell's hereditary material and controlling its metabolism, growth and reproduction.

Onco-MIRs A microRNA associated with cancer.

Organelle A discrete subcellular structure with a specialised function.

Organic chemistry The chemistry of compounds containing carbon.

Orthologous Any gene found in more than one species that can be traced back to the same common ancestor.

Oxidative Relating to the addition of oxygen.

Paralogous Two genetic sequences that have the same evolutionary ancestor and arose through gene duplication.

Pathogenicity The capacity to cause disease.

Pathogens Disease-causing organisms.

Pathophysiology A change in function caused by a disease or condition.

Peptides A compound of two or more amino acids.

Petameric Made up of five identical monomers.

Phagocytosis The process by which cells engulf material in order to destroy or digest it.

Pharmacology The study of drugs and their effect on organisms.

Phasevarions Genetic systems where phase variation (reversible, high-frequency on/off switching of expression) regulates the expression of multiple genes.

Phenotype The characteristics of an organism resulting from the interaction between its genotype and its environment.

Phosphorylation The addition of a phosphate group to another molecule, which often alters the activity of an enzyme.

Phototype A category into which people are placed depending on the amount of melanin in their skin.

Phylogenetic Of the evolutionary development of organisms.

PNMT Phenylethanolamine N-methyltransferase. An enzyme that catalyses the production of adrenalin.

Polymorphism The existence of multiple forms of a gene or DNA sequence.

Prenylation A process whereby hydrophobic molecules are added to a protein.

Protease Any enzyme that causes the interior peptide bonds of a protein to split.

Protein A large molecule composed of one or more chains of amino acids in a specific order. Proteins are required for the structure, function and regulation of the body's cells, tissues and organs, and each protein has a unique function. Examples are hormones and antibodies.

Protozoan A type of one-celled organism with a defined nucleus.

qPCR Real-time polymerase chain reaction. A technique that allows the detection and quantification of a sequence in a DNA sample as the analysis is occurring.

Quantitative A measurement based on numerical data.

Radioligand A radioactive substance injected into tissue that binds to receptors and allows researchers to study its behaviour.

Redox A reduction/oxidation reaction, where the oxidation number of an atom changes.

Retinoic acid A derivative of Vitamin A.

Retromer A protein complex that is involved in the transport of proteins to the Golgi.

Retrotransposon A segment of DNA that can move around the genome and amplify itself.

RNA A chemical similar to a single strand of DNA, except that RNA contains ribose instead of deoxyribose and uracil instead of thymine. RNA delivers DNA's message to the site of protein synthesis.

Scission Splitting.

Secretory Relating to secretion.

Single-nucleotide polymorphisms (SNPs) A single base of DNA which can differ in a population.

SNARE A family of proteins, the main function of which involves directing vesicles out of the cell.

SNP Single nucleotide polymorphism. A single base of DNA which can differ in a population.

Spectroscopy The study of the interaction between matter and radiation (eg. light).

Thalassaemia An inherited blood disorder where the body has difficulty producing haemoglobin.

Theranostic Therapy that tests patients to determine if they are suitable candidates for a new medication.

Transcription The formation of RNA from a DNA template.

Transcription factors Proteins that control the transfer of genetic information from DNA to messenger RNA.

Transcriptome All RNA molecules produced in a cell or organism at any one point in time.

Transferase An enzyme that transports a chemical from one molecule to another.

Transgenic An organism that has a transferred gene (transgene) incorporated into the chromosome of all its cells.

Triplex Consisting of three parts.

UTR Untranslated Region. The non-coding sections at the beginning and end of a protein-coding segment of mRNA.

UQ ROCX University of Queensland Remote Operation Crystallization and X-Ray Diffraction Facility.

Vasculature Network of conductive vessels, eg. blood vessels, lymphatic vessels.

Vesicle A closed membrane shell.

X-ray crystallography A method of determining the structure of a sample by bouncing an X-ray off a crystallised version of the sample and analysing the resulting light diffraction pattern.

2010 PUBLICATIONS

NICK HAMILTON: FISHING IN THE CELLULAR SEA

Fluorescently tagged proteins light up the interior of a cell allowing the intricate structures floating within to be seen.

GENOMICS AND COMPUTATIONAL BIOLOGY

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NICOLE CLOONAN: SHORT SEQUENCE DE NOVO ASSEMBLY

Being able to read the order (sequence) of the DNA gives us amazing insight into our genes and how they contribute to biological processes. This image depicts the de novo assembly of human chromosome 21 using short sequences. The four building blocks (nucleotides) that make up the DNA are represented by the letters A, C, G, and T.

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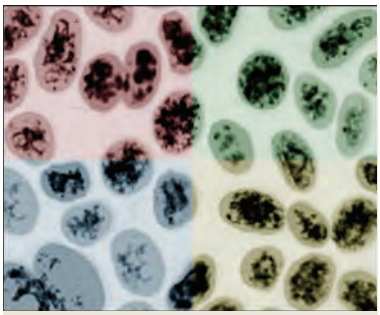

SEETHA KARUNARATNE: MOLECULAR COMPUTERS

Visualising genetic material that drives life by a simple staining technique is a fascinating experience. Each living cell has its own molecular computer which is busy all the time.

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JESS INESON: KIDNEY KALEIDOSCOPE

The image is from a section of mouse embryonic kidney at 15.5 days of development. It has been stained by immunofluorescence for two markers of early kidney development, Calbindin (red), which marks the utereic bud and Pax2 (green), an early nephron marker. Nuclei of each cell are shown in blue.

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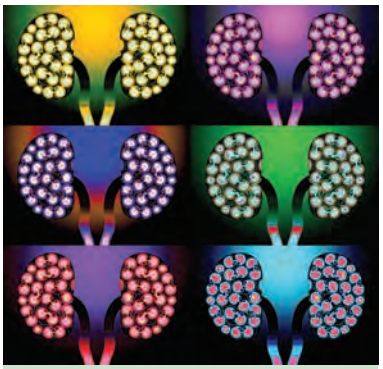

KYLIE GEORGAS: POP NEON KIDNEYS

This artwork is a pop art version of a schematic diagram of embryonic mouse kidneys. The diagram has been modified from a kidney diagram designed and drawn by Kylie Georgas for the GUDMAP website and has been enhanced and stylised for the competition.

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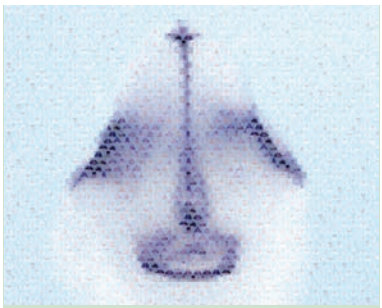

HAN SHENG CHIU: ART OF SEX SCIENCE

The art is a mosaic picture containing all of my whole-mount in situ hybridisation results on an organ called genital tubercle also known as external genitalia, with a combination of 81 different pictures of mouse genital tubercle.

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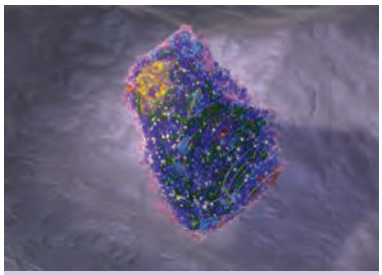

ANDREW NOSKE: APPROACHING A BETA CELL

This image is a rendering of a pancreatic beta cell imaged at high resolution in true 3D using whole cell tomography with a transmission electron microscope. As the first mammalian cell imaged in its entirety at 15-20nm resolution, it highlights how complex and crowded the internal organisation of a cell can be.

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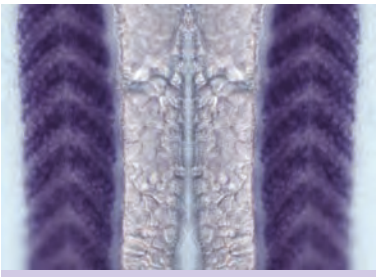

SUSAN NIXON: TRACKS

Mirror image of developing muscle in a zebrafish embryo.

Publications 2010

MOLECULAR CELL BIOLOGY (CONTINUED)

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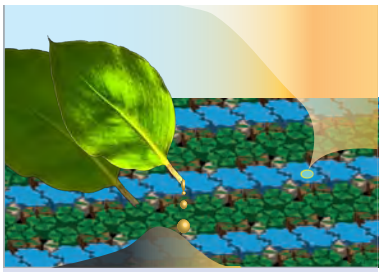

ANDREW RINGSMUTH: PHOTOFUEL FUTURE

This piece depicts the potential for photosynthetic bio-fuels to ease the impending transition from a fossil oil-based global economy to a carbon-neutral future. The limitation in energy availability caused by this peak is predicted to pose a major problem for the global economy.

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MAGGIE HARDY:
THE DOSE MAKES THE POISON

Paracelsus was among the first scientists to realise that anything can be poisonous, and harm or good to the patient depends on the dose. Recently, drugs to lower blood pressure have been developed from the venom of vipers, and medications to treat people's chronic pain could be isolated from the venom of cone snails and spiders. My PhD research is focused on isolating novel, environmentally-friendly insecticides from the venom of native Australian spiders.

Publications 2010

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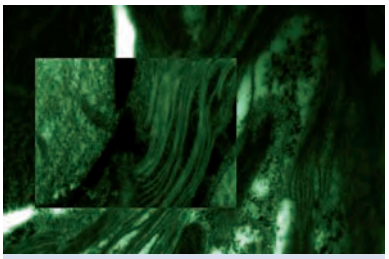

EMILY KNAUTH: STACKED UP

Plants and algae have a particular interesting internal structure, especially inside the thylakoid membrane. The structures, proteins and pigments here give these organisms their well known green colour. In particular, the thylakoid membrane shown here forms stacks which help these algae capture the maximum amount of light possible.

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NOTES

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