THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

IMB Institute for Molecular Bioscience

ANNUAL REPORT 2009

CONTENTS

COVER IMAGE: *A coneshell with the structure of the α-conotoxin, Vc1.1, determined in the laboratory.*
IMAGE COURTESY DAVID CRAIK

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

THE MULTIDISCIPLINARY NATURE of the Institute for Molecular Bioscience is one of its great strengths. Chemists, biologists, bioinformaticians and other researchers work together under one roof to address some of humanity's most difficult problems. Their expertise spans a range of areas from biomedical science, to bioinformatics, to biofuels.

While this diversity undoubtedly yields advantages, it also means the IMB defies pigeonholing. It is not solely a cancer institute, nor a medical research institute, so it may not immediately spring to mind when people think of a certain disease. On the other hand, the IMB proves that it is possible to investigate and excel in a number of areas. For example, it has become one of Australia's best cancer research centres, and is climbing the pinnacle held by international leaders.

Two developments in 2009 have augmented its authority in cancer research. The first was IMB's selection as Australia's base for contributions to the International Cancer Genome Consortium. Scientists in this network will, collectively, sequence the genomes of 25,000 tumours. This effort will result in unparalleled knowledge about the genetic changes that lead to tumours, and should result in more personalised treatments for cancer sufferers, based on the genetics of their tumours.

Professor Sean Grimmond of the IMB leads the Australian mission, which is to sequence pancreatic and ovarian tumours. He used a $5 million grant from the Queensland State Government to establish the Queensland Centre for Medical Genomics, which will undertake the sequencing. The National Health and Medical Research Council gave its largest-ever grant - $27.5m – to the Centre to ensure the success of the project.

The second major cancer-related development was the receipt of $2.5 million from the Australian Cancer Research Foundation (ACRF) to fund the ACRF Cancer Biology Imaging Facility. It will complement an existing ACRF centre at IMB, with the new centre's focus being fluorescent imaging, in which researchers tag both cancerous and healthy cells with fluorescent molecules. They can then track the cells' movements, learning more about how healthy cells mutate into cancerous cells, and about metastasis, the process by which cancer cells spread beyond the primary infection site.

During 2009, institute teams have also made important inroads into other areas of research, and this progress is detailed in the following pages.

The foundations of such achievements are dedicated institute staff and supporters, and it is a pleasure for me to thank the board members, Scientific Advisory Committee members, research and professional staff and students for ensuring 2009 was an excellent year.

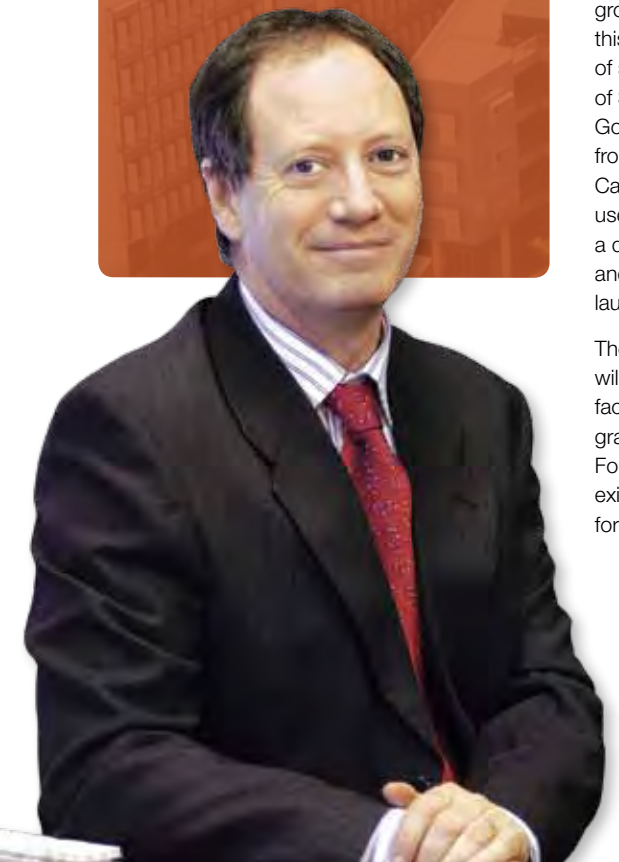
Professor Paul Greenfield, AO

Vice-Chancellor
The University of Queensland

> "Chemists, biologists, bioinformaticians and other scientists work together under the one roof to solve problems facing our society and add to the world's store of knowledge. But while this broad spectrum of research is undoubtedly an advantage, it also makes the IMB harder to pigeonhole"

DIRECTOR'S REPORT

> "2010 presents new challenges for the Institute with a major review of our State Government funding scheduled during the year. This will be the second quinquennial review of our State Government funding. Our first review took place in 2005 and we were successful in securing State Government support to 2014"



2009 HAS BEEN an outstanding year for the Institute, with announcements of large grants to fund new infrastructure and facilities, record success in the domestic competitive grant schemes for our researchers and a number of prestigious accolades and prizes for our Group Leaders.

The Chair has already mentioned in his report the outstanding work Professor Sean Grimmond and others have put into securing Australia's place in the International Cancer Genome Consortium, which aims to sequence the genomes of 50 different types of tumours from 25,000 individuals. The node of this international consortium that will be located within the IMB will be known as the Queensland Centre for Medical Genomics. The Centre will give medical researchers around the world a better understanding of the genetic changes that drive pancreatic and ovarian cancers, enabling them to better predict outcomes, provide more effective treatments for sufferers and create prevention strategies for risk groups. Funding for the establishment of this new Centre has come from a number of sources including the NHMRC grant of $27.5 million, a Queensland State Government grant of $5 million, money from The University of Queensland and the Cancer Council of NSW. The Centre will use technologies from Applied Biosystems, a division of Life Technologies Coporation, and (SGI) Silicon Graphics. We will be launching this new facility in early 2010.

The ACRF Cancer Biology Imaging Facility will also be launched in early 2010. This facility has been funded by a $2.5 million grant from the Australian Cancer Research Foundation and will combine with the existing ACRF Dynamic Imaging Facility for Cancer Biology 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.

Professor Rob Parton had a spectacular start to the year with an announcement in late January that he had been successful in his application for an NHMRC Australia Fellowship. Rob's five-year fellowship, worth $4 million, will allow him to investigate a microscopic vehicle with the potential to deliver treatments directly into cells. A week or two after his NHMRC Fellowship success, Rob was made a Fellow of the Australian Academy of Sciences – an honour that is bestowed by scientific peers and acknowledges world-class research and discovery.

At the 2009 Lorne Genome conference Professor John Mattick was awarded the Julian Wells medal for his research work on non-coding RNA, acknowledgement of his outstanding contribution to our understanding of the organisation and expression of the genome. Later in the year Professor Peter Koopman was awarded the 2009 Lemberg Medal by the Australian Society for Biochemistry and Molecular Biology. Associate Professor Ben Hankamer spent two months in the United States on an Eisenhower Fellowship looking at industrial applications for his biofuel technology, and Professor David Craik was awarded an Honorary Doctorate *(honoris causa)* from the University of Kalmar in Sweden.

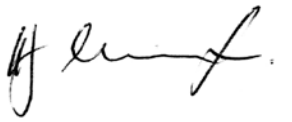
In June, Professor Jenny Martin was presented with an ARC Laureate Fellowship by Senator Kim Carr, Minister for Innovation, Industry, Science and

Research. The Laureate scheme has evolved from the ARC Federation Fellowship Scheme and is aimed at building research capacity in Australia. A couple of months later Professor Kirill Alexandrov was advised that he had been awarded a prestigious ARC Future Fellowship, which aims to promote research in areas of critical national importance by giving outstanding mid-career researchers incentives to conduct their research in Australia.

These are just some of the highlights from a year of outstanding performance by both our research and support staff. IMB researchers distinguished themselves by achieving a 59 percent success rate in this year's NHMRC competitive grant round – the best result at the University – as well as success in other competitive grant schemes such as the Smart State Fellowship scheme (Dr Mathias François) and the UQ Research Excellence Awards (Dr Josh Mylne).

Two new Group Leaders arrived from overseas this year. Professor Matt Cooper joined us from Cambridge in February to take up his NHMRC Australia Fellowship at the IMB in the Chemistry and Structural Biology Division, and Dr Ben Hogan joined us from the Netherlands in early December to take up a Group Leader position in the Division of Molecular Genetics and Development. Welcome to both Matt and Ben and we look forward to working with them in the coming year.

2010 presents new challenges for the Institute with a major review of our State Government funding scheduled during the year. This will be the second quinquennial review of our State Government funding. Our first review took place in 2005 and we were successful in securing State Government support to 2014. We do not underestimate the challenges that face us with this second review but I am confident that the IMB's performance across a range of key performance indicators will illustrate that we are making an important contribution to the future health and prosperity of the State.



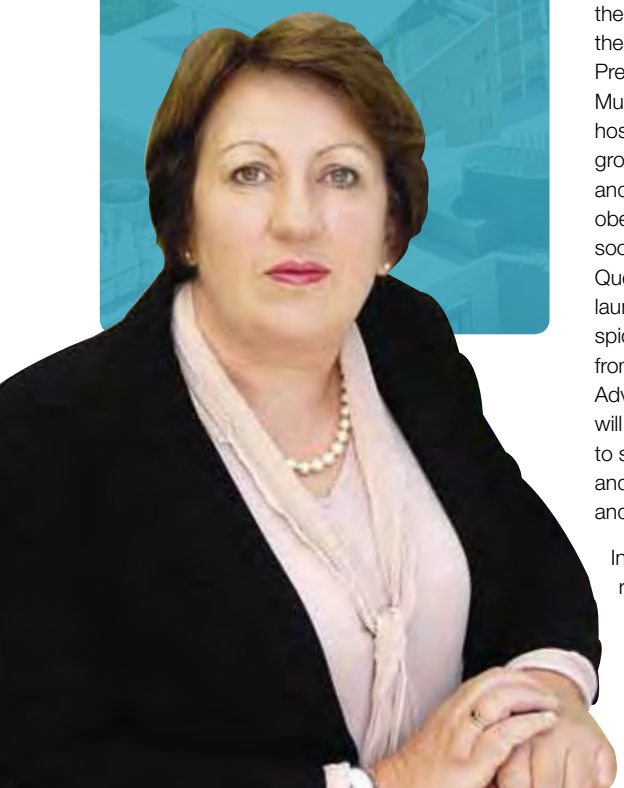
Professor Brandon Wainwright
IMB Director

DEPUTY DIRECTOR (Research) REPORT

2009 HAS BEEN a fruitful year for the Institute for Molecular Bioscience. IMB's people and research have continued to impact significantly across multiple scientific disciplines. IMB researchers have authored important papers in world-leading journals, and received auspicious awards, fellowships and invitations to speak at international conferences. New discoveries have gone into our development and commercialisation pipelines. Finally, IMB has continued to seed new research programs and new Centres in its areas of research strength and in response to public need.

Dr Kate Stacey, from the Sweet group, led a team that had a paper published in *Science* at the beginning of the year. Dr Stacey and her team discovered the genetic mechanism that lies behind a cell's ability to 'commit suicide' through apoptosis if infected with a virus. This information is important in understanding how cells fight viral infection, and may also have implications for treatment of lupus.

> "IMB continued to be successful in securing major funding to support our medical research efforts"



IMB researchers were part of an international team that discovered how genes are controlled in mammals. The team, known as the FANTOM4 Consortium, found that gene expression is influenced by a network of regulatory elements, rather than a few master regulator genes. Professor John Mattick and Professor Sean Grimmond, along with PhD students Ryan Taft and Geoff Faulkner, each made important contributions to the series of papers that were published on this discovery.

IMB continued to be successful in securing major funding to support our medical research efforts. Professors Greenfield and Wainwright have already outlined IMB's record grant from the National Health and Medical Research Council, which together with Queensland State Government funding has served to establish the Queensland Centre for Medical Genomics headed by Professor Sean Grimmond. A $2.5 million grant from the Australian Cancer Research Foundation is being used to establish the ACRF Cancer Biology Imaging Facility at IMB, due to be opened in early 2010. Both of these new Centres acknowledge IMB's ability to make a real contribution in the fight against cancer. In the latter half of 2009, IMB also established the Centre for Diabetes Research and Prevention, headed by Professor George Muscat, which in partnership with hospitals, the University and community groups, will focus research, clinical studies and public outreach efforts to tackle obesity and diabetes as major health and societal problems of obesity and diabetes. Queensland Treasurer Andrew Fraser launched Arachnoserver, a database of spider toxins developed by researchers from IMB and the Queensland Facility for Advanced Bioinformatics. The database will allow scientists from all over the world to share knowledge about spider toxins and work towards developing therapeutics and insecticides using spider venom.

Individual staff members were also recognised nationally. Professor Melissa Little was selected for the NHMRC Research Council, a position which will allow her to help steer the course of medical research in this country. Professors Wainwright and Grimmond were invited to serve on committees for the International Cancer Genome Consortium where they will have carriage over global research on cancer genomes. Professor Kirill Alexandrov received an ARC Future Fellowship, which he will use to study protein prenylation.

IMB staff and students have been hard at work creating new programs and initiatives too. The IMB Science Ambassador Program was launched, turning out its first 'graduates' in 2009. This program was initiated by Ms Maggie Gentz, one of IMB's graduate students, along with staff members Dr Amanda Carozzi and Bronwyn Adams, to train young scientists in public relations and to help communicate IMB's research outcomes to the public. This provides our graduate students and postdocs with fantastic training in the very important task of conveying the excitement, importance and relevance of our research back to the people for whom we work, the general public. Our quest to make discoveries that will benefit and improve the lives of people in Queensland, Australia and beyond also requires commercialisation, and IMBcom continues to help us in this area. In 2009, IMBcom reported new deals with international companies on the back of IMB research. You can read more about these on page 68.

Finally, one of the responsibilities of research, particularly given our location at The University of Queensland, is to train the next generation of scientists. I am very pleased to report IMB has recorded, year on year, growth in the number of graduate students trained. In 2009, 15 PhD students graduated from our program. This is an outstanding result given the trend across Australia at present shows declining numbers of PhD students. We are implementing a number of initiatives in this area to ensure this success continues and I hope to report further good news in graduate training in the future.

Professor Jenny Stow
IMB Deputy Director (Research)

DEPUTY DIRECTOR (Systems & Administration) REPORT

THE PRIOR REPORTS demonstrate the scientific strength of the IMB. This strength is due, in no small part, to the Institute's team of support staff. These include technical staff, IT staff, finance and administration staff, marketing, postgraduate student administration, central sterilising, mail and stores. This team is dedicated and hardworking, and I would like to thank staff for supporting our researchers throughout 2009.

There was some turnover of senior staff during the year. IMB has been an institute long enough that some of our new appointments were drawn from the ranks of IMB alumni, who have returned with the benefit of experience gained elsewhere. Safety Manager Charles Nelson left for new challenges after 18 years with The University of Queensland. He was replaced by Dr Paul Lovelock, who has played several roles at IMB in the past: postgraduate student, researcher and floor manager. We welcome him back into the IMB community from his most recent appointment, which was as Safety Manager at the Queensland Brain Institute (QBI). The ensuing vacancy at QBI was in turn filled by IMB's Level 3 Floor Manager, Dr Ross Dixon. The Level 3 Floor Manager position was thus taken over by Christine Fraser, while Dr James Springfield, IMB's Digital Imaging Officer, took on an expanded role as Manager of the new ACRF Facility at IMB.

We also had some temporary departures among senior staff. Felicity Ray, HR Consultant, went on maternity leave for a year. Joanne French, who worked previously at IMB, came back part-time to fill in for Felicity, with IMB's HR Officer Caraine Gomez ably filling the HR Consultant role the rest of the time. Finance Manager Angela Gardner received a grant from the Australia Council to spend time writing poetry in Ireland. Angela is a recognised poet who has previously won prizes for her work; she took advantage of the opportunity to spend a total of six months overseas working on her art and poetry. Kathy Webb from UQ's School of Geography, Planning and Environmental Management was seconded to IMB in Angela's absence.

2009 also saw the establishment of two new research support facilities, each requiring refurbished dedicated space: the ACRF Cancer Biology Imaging Facility, which represents a significant expansion of the previous ACRF-supported facility, now occupies space on Level 6, while the Queensland Centre for Medical Genomics and its high-throughput DNA sequencing facility is located on Level 5. We also took the opportunity to create a new dedicated space for our IT Desktop Support Group, making them more available to their customer base. Some laboratory groups were also relocated out of necessity during this time. The relative ease of most of these rearrangements underscores the success of the philosophy of flexibility and adaptability which underpinned the design of the Queensland Bioscience Precinct. I am confident it will continue to be an enjoyable place for researchers to work and allow the installation of cutting-edge equipment into the future.

We had many visitors throughout the year come to view our facilities, and also to hear about IMB's research. Visitors ranged from school students to government ministers, and represented both Australia and 26 other countries. In total, over 3000 people visited the IMB in 2009.

Dr Ian Taylor
Deputy Director
(Systems and Administration)

> "IMB has been an institute long enough that some of our appointments were drawn from the ranks of IMB alumni, who have returned with the benefit of experience gained elsewhere"

A cure for CANCER?

It's one of the most sought-after goals in medical research but the reality is there will not be one sweeping cure for cancer. 'Cancer' is not one illness, but rather a group of diseases that cause uncontrolled cell growth, where cells divide and multiply at a much greater rate than normal and invade surrounding tissues. Different types of cancer have varying triggers, and what cures one cancer may in fact aggravate others.

For researchers, this means each type of cancer may need a separate treatment, although the common properties of different cancers mean some strategies could work across a range of cancers. IMB scientists are tackling the problem from a number of angles: defining the origins of cancer, investigating the routes through which it spreads, developing treatments, improving current treatments through more accurate drug delivery and studying strategies for prevention.

Cancer research requires not only dedicated and passionate scientists, but also cutting-edge equipment and secure funding. In 2009, IMB received two large grants that will propel cancer research forward at the Institute with the establishment of two new centres: the ACRF Cancer Biology Imaging Facility and the Queensland Centre for Medical Genomics. Both centres will focus on cancer, but will use different methods.

The ACRF Facility will contain state-of-the-art fluorescent microscopes, which will allow researchers to tag molecules with fluorescent proteins and track their progress. Facility users will study how healthy cells turn into cancerous cells and spread throughout the body. The ACRF Cancer Biology Imaging Facility is the second facility at IMB to be funded by the Australian Cancer Research Foundation. The initial imaging facility was opened in 2005, but the advent and increasing importance of fluorescent imaging convinced the Foundation it was worth providing the IMB with a further $2.5 million to buy new fluorescent microscopes and establish the most advanced imaging facility in the Southern Hemisphere. It will officially open in early 2010.

The first ACRF facility at IMB has been instrumental in cancer-related research. Professor Brandon Wainwright was one of the leaders of a team that discovered the origins of the often-fatal brain tumour medulloblastoma. Professor Peter Koopman and Dr Mathias François identified a gene critical for the development of the lymphatic system, the route through which tumours spread. Professor Jenny Stow is studying e-cadherin, a protein that suppresses tumours, for its potential as an anti-cancer drug. And Associate Professor Rick Sturm is examining the genetics of pigmentation to discover how people with different-coloured skin and hair respond to sun

Senel Idrisoglu with a SOLiD sequencing system. The QCMG will have eleven of these sequencers when it officially opens in 2010.

exposure in order to develop skin cancer risk profiles for individuals.

Meanwhile, the Queensland Centre for Medical Genomics (QCMG) will sequence the genomes of tumours and compare them with similar non-cancerous tissue to determine the genetic changes that trigger tumour development. The Centre will begin by sequencing pancreatic and ovarian tumours as part of the International Cancer Genome Consortium (ICGC). This is a massive undertaking in which laboratories from around the world will sequence 25,000 tumours from 50 different types of cancer.

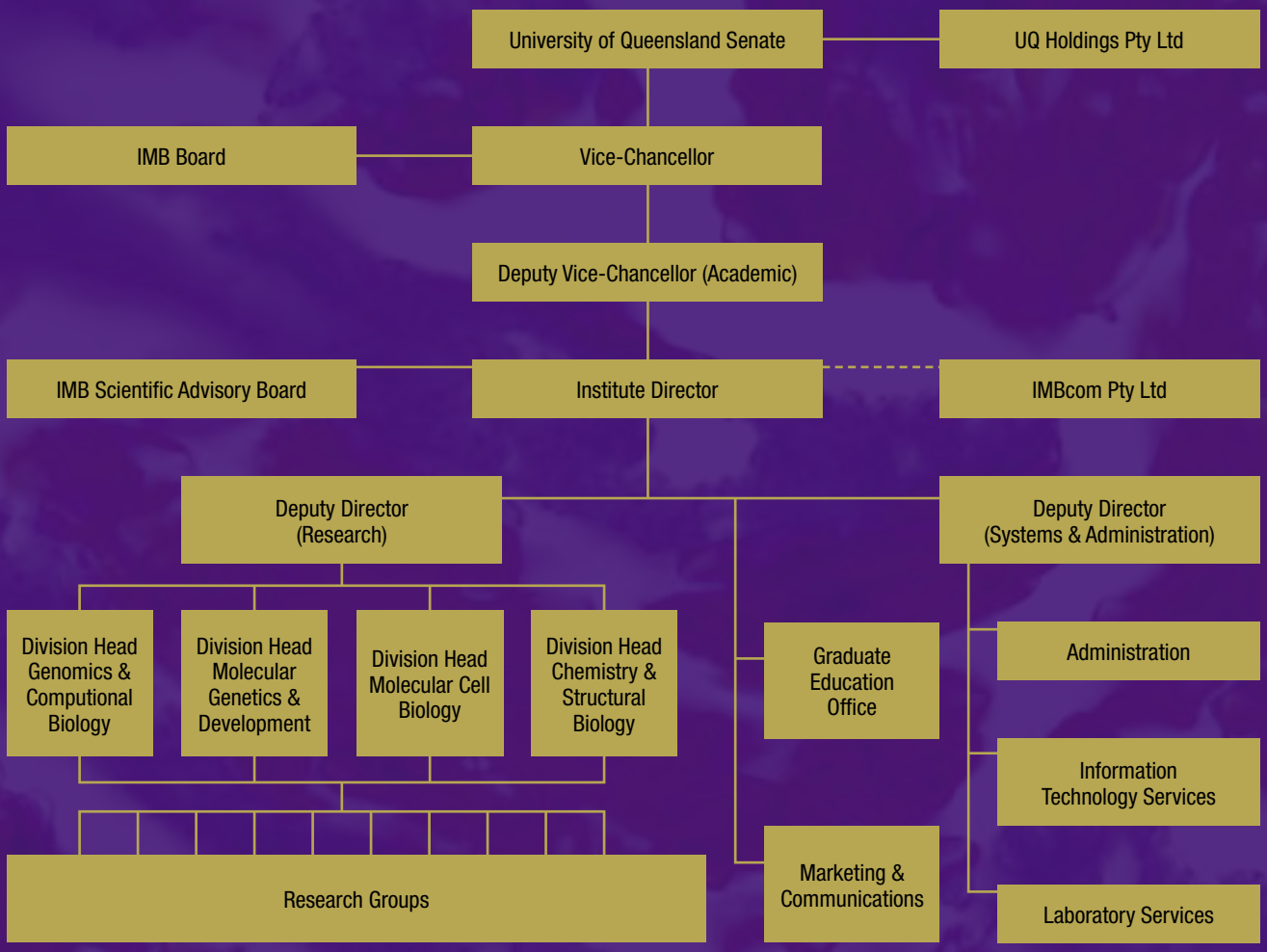
The QCMG was established with a $5 million grant from the Queensland Government, and funding for the project will come from a $27.5 million grant from the National Health and Medical Research Council (NHMRC). This is the largest-ever grant awarded by the NHMRC, which speaks volumes about both the importance of the research and the agency's confidence in IMB's ability to lead the project. Professor Sean Grimmond is Director of the QCMG and will spearhead Australia's involvement in the ICGC, which also includes vital contributions from the Peter MacCallum Cancer Centre and the Garvan Institute of Medical Research.

As Professor Paul Greenfield said in his message at the beginning of this report, IMB's breadth of research makes the Institute difficult to classify, and means it perhaps isn't immediately included when people think of cancer research centres. But the range of research conducted can be a bonus for those working on cancer. For example, Professor Rob Parton is studying nanovesicles, tiny shells that bud off from the surface of cells and can be engineered to target specific sites in the body. These discoveries highlight the potential of nanovesicles to deliver drugs, such as chemotherapy, in a targeted fashion that wouldn't affect healthy cells. Another IMB research area closely linked to cancer is bioinformatics. The QCMG generates a petabyte – a quadrillion bytes – of data per month, meaning it needs innovative ways of processing and storing data.

The IMB might not be thought of as a cancer research institute, but this diversity of research, along with the two new centres that will be launched in 2010, has positioned the institute as one of the leading cancer research hubs in Australia.

A cure for cancer may not be a reality yet, but it is drawing ever closer.

2009 IMB ORGANISATIONAL CHART



2009 IMB HIGHLIGHTS

► IMB research discovers how dangerous DNA can cause cell suicide

A team led by Dr Kate Stacey discovered how cells sacrifice themselves for the greater good if they are infected with a virus, with viral DNA being the key to responding to the infection.

The cell is able to recognise foreign DNA because DNA in mammalian cells is contained within a structure known as the nucleus. The presence of DNA outside the nucleus, which occurs with viral DNA, is a sure sign something is wrong, and may indicate the presence of a viral invader. The research was published in top scientific journal *Science*.

► Research boosted by rapid protein production

UQ researchers led by Professor Kirill Alexandrov have developed a novel cell-free protein production system that will allow more effective research into the molecular basis of disease and the development of new therapies. Proteins are involved in almost all biological processes, so the ability to manufacture large numbers of proteins to specification is very important for scientific research and medicine.

"We have created a universal initiation sequence, so proteins can be produced in any organism. It's a tool that allows us to put proteins rapidly through different systems to see which is better at making the protein."

► New researcher uses nanotechnology to probe effectiveness of antibiotics

Professor Matt Cooper, previously based in the United Kingdom, joined the IMB on an Australia Fellowship in February. Professor Cooper will use his $4 million NHMRC fellowship to establish a research program in the development of antibiotics and antifungals that are active against drug-resistant pathogens, in particular those responsible for hospital-acquired infections.

INTERNATIONAL TEAM CRACKS MAMMALIAN GENE CONTROL CODE

An international consortium of scientists, including researchers from IMB, probed further into the genome than ever before, discovering how genes are controlled in mammals as well as the tiniest genetic element ever found.

Their discoveries were published in three milestone papers in leading journal *Nature Genetics.* PhD student Ryan Taft led one paper, on which Professor John Mattick was the senior author, while Professor Sean Grimmond was a senior author on another paper led by Dr Geoff Faulkner.

> "This knowledge will help us determine, for example, why some cells turn cancerous, or how to control stem cells for use in regenerative medicine"

"We have shown that instead of having one or a few 'master regulator' genes that control growth and development, there is a sophisticated network of regulatory elements that subtly influence the ways in which genes are expressed in different cells in the body," Professor John Mattick said.

This information will be very useful to medical and biological researchers, according to Professor Sean Grimmond: "We can use it to discover how cells transform from rapidly-growing 'blank slate' cells to mature cells with a specific function. This knowledge will help us determine, for example, why some cells turn cancerous, or how to control stem cells for use in regenerative medicine."

IMB 2009 highlights

SPIDER SECRETS DECODED IN WORLD-FIRST DATABASE

Queensland scientists have developed a world-first database that catalogues the venom components from hundreds of spiders.

Queensland Treasurer and Minister for Employment and Economic Development Andrew Fraser launched the database, saying scientists worldwide were now better able to investigate how spider toxins could be put to good use as natural insect sprays or pain killers.

► National honour for IMB scientist

Professor Rob Parton became the only newly-elected Queensland-based researcher to be selected as a Fellow of the Australian Academy of Science, one of the highest scientific honours in Australia.

Professor Parton was selected for his work on the cell surface, which has a range of applications including the potential to improve drug delivery and better understand prostate cancer.

► UQ scientist to help guide future of Australian medical research

Professor Melissa Little became one of only two Queenslanders to be appointed to a the National Health and Medical Research Council's (NHMRC) Research Committee. The Committee advises on medical and public health research in Australia, as well as making recommendations on research grant applications and funding.

► Accelerating the discovery of drugs from venoms

A new method developed to identify and characterise individual molecules in the venom of animals such as the cone snail has the potential to accelerate the discovery of life-saving drugs.

A team from the IMB and Rockefeller University in New York have devised the method, which will speed up the sequencing of mini-proteins known as peptides and allow them to be screened for medical uses.

► Finding a pathway to new virus drugs

IMB researchers took an important step in the characterisation of a viral infection pathway, which may potentially lead to the development of new drugs targeting a broad range of viruses including HIV and Ebola virus.

Dr Michael Landsberg, in conjunction with four other scientists, recently solved the 3D structure of a key controlling enzyme in the pathway of enveloped virus infection. A number of viruses appear to hijack this pathway to facilitate their own spread from infected to healthy cells within an organism.

► The smallest turn – an alpha-helical bond mimetic

A new approach has been developed to mimic helices that occur frequently within proteins and peptides and often present an interaction site for other proteins. A team led by Professor Paul Alewood developed the approach; such a mimetic will underpin new peptidomimetic drugs of the future.

GRANTS

RECORD FUNDS FOR CANCER FIGHT

A new IMB centre will give hope to patients with two of Australia's most fatal cancers. Researchers used a $5 million grant from the Queensland State Government to establish the Queensland Centre for Medical Genomics, which will be based at the IMB and run by Professor Sean Grimmond.

The Centre will seek to unlock the genetic causes of ovarian and pancreatic cancer, and has already attracted extra funding, including $27.5 million from the National Health and Medical Research Council, the largest grant the NHMRC has ever awarded.

IMB RESEARCHER WINS PRESTIGIOUS AUSTRALIA FELLOWSHIP

Professor Rob Parton will use a $4 million Australia Fellowship from the National Health and Medical Research Council (NHMRC) to investigate a microscopic vehicle with the potential to deliver treatments directly into cells.

"A serious problem with many treatments today, especially for cancer, is that they kill healthy cells as well as diseased cells," Professor Parton said. "Targeted drug delivery systems, in which the drugs are enclosed in a vehicle that is targeted towards specific sites in the body, can avoid this problem."

► Multi-million dollar world-leading cancer imaging facility at IMB

A $2.5 million grant from the Australian Cancer Research Foundation (ACRF) will be used to establish a world-class cancer imaging centre at The University of Queensland's Institute for Molecular Bioscience (IMB).

The ACRF Cancer Biology Imaging Facility will be the most advanced imaging research facility in the Southern Hemisphere when it opens in early 2010. It will allow researchers to study the progression of cancer cells and their interactions with healthy cells.

► $10 million for IMB research into superbug drugs, sexual development and brain tumours

Researchers from the Institute for Molecular Bioscience won nearly $11 million in grants from the NHMRC for 19 projects ranging from developing drugs targeting superbugs to studying disorders of sexual development and examining brain tumours.

► $6 million in research grants for IMB

IMB researchers received a $6.4 million boost from the Australian Research Council for 11 projects ranging from using genes to predict skin cancer risk to developing a more efficient system to recombine proteins. Professor Kirill Alexandrov received The University of Queensland's largest Discovery Projects grant - $1.5 million to study posttranslational modifications of proteins critical for a multitude of normal cellular functions.

► Pain research receives $6.4 million boost

Professor Richard Lewis received $6.36 million from the NHMRC to develop new drugs to treat chronic pain.

"The goal of our research is to improve treatments for pain, especially persistent pain, which remains a poorly managed global health burden," Dr Lewis said. "We are investigating the venom from animals such as cone shells to develop a new class of pain killers that can treat persistent pain."

► International fellowship for biofuels researcher

Associate Professor Ben Hankamer won an Eisenhower Fellowship to meet with political and business leaders from the U.S. in an effort to fast-track algal biofuel development. These prestigious fellowships were awarded to people identified as international leaders in areas of energy, technology and supply, with only two fellowships assigned to Australia.

The fellowship allowed Dr Hankamer to tailor an initial six-week program of meetings with researchers, Senators and Members of Congress from both sides of the biofuels debate, and top CEOs from industry organisations including microalgae producers, biofuel producers and the transport industry.

IMB 2009 highlights

► IMB looks to the future of research with ARC fellowship

Improvements in technologies for diagnostics and drug development is one of the possible outcomes of an ARC Future Fellowship awarded to Professor Kirill Alexandrov. He will use it to create fluorescent protein molecules that will allow researchers to watch complex biochemical processes in living organisms.

► IMB links up for better research

Professor Richard Lewis leads a team that received $424,000 from the ARC's Linkage Infrastructure, Equipment and Facilities scheme to establish an advanced molecular discovery and characterisation facility in conjunction with RMIT University.

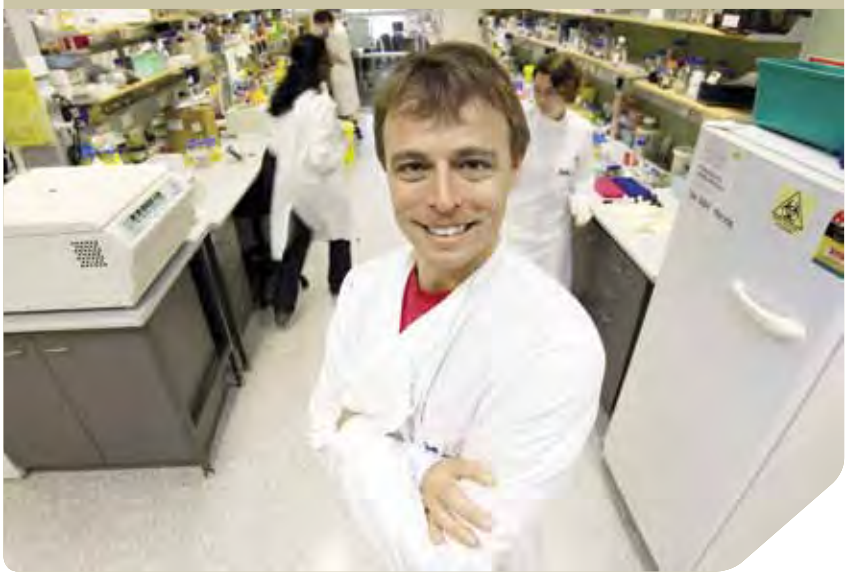
Professor Lewis said the facility would accelerate the discovery of drugs from natural products by providing dedicated, state-of-the-art facilities for testing the suitability of molecules from organisms such as cone snails for use as potential pharmaceuticals.

DELVING INTO JUNK DNA YIELDS FELLOWSHIP

Dr Marcel Dinger received a $150,000 Queensland Government Smart Futures Fellowship to examine stretches of the genome that don't contain genes.

He will screen sections of non-coding RNA to determine their function.

He is part of a team of researchers led by Professor John Mattick, who believe non-coding RNA plays a role in directing development in complex organisms such as humans. The research has the potential to greatly improve knowledge about the molecular basis of development and disease.



IMB RESEARCHER AWARDED PRESTIGIOUS AUSTRALIAN LAUREATE FELLOWSHIP

Professor Jenny Martin received a $3.1 million Laureate Fellowship from the Australian Research Council (ARC), which she will use to develop a new class of antibacterial drugs that may avoid the problems of antibiotic resistance.

"Bacteria develop resistance because antibiotics work by killing most bacteria, leaving only the resistant bacteria alive," Professor Martin said. "My research will address this by developing compounds that won't kill bacteria, but rather will inactivate a specific bacterial machinery responsible for causing disease."

► Vietnam brings a new research generation to UQ

An IMB PhD student is one of five researchers who will share in a $1 million University of Queensland scholarship package. IMB's scholarship winner, Ms Duong Minh Tam, will work to advance knowledge of the role of a gene, Sox18, in the development of the human lymphatic system. Lymphatic vessels are the route through which tumours spread throughout the body, so Ms Duong's research has the potential to enable treatments that will reduce the cancer death rate.

Ms Duong's research may also have the potential to explain why the lymphatic vessels sometimes develop abnormally, causing diseases such as Hypotrichosis-Lymphedema-Telangiectasia and secondary lymphedema, and suggesting targets for treatments for these diseases.

RESEARCH AWARD TO FUND PLANT-GROWN DRUGS

Dr Joshua Mylne was presented with a Research Excellence Award to fund his work into using plants to produce pharmaceuticals. He is adapting a natural machinery found in plants to manufacture small circular proteins for use as therapeutic drugs.

Small proteins (peptides) can target cancer-causing enzymes with pinpoint precision, but they are costly to manufacture and are susceptible to breakdown. Circular peptides produced in plants solve both these problems.

AWARDS

► Fertile ground for research bears medal

Professor Peter Koopman was recognised by the Australian community of biochemists and molecular biologists by being awarded the 2009 Lemberg Medal. The medal is presented by the Australian Society for Biochemistry and Molecular Biology (ASBMB) to a distinguished Australian molecular biologist.

Professor Koopman was one of the discoverers of the Sry gene, which determines gender in mammals, and is a world expert in the genetics of male and female development. He has identified many genes associated with these developmental pathways.

► Award for junk DNA research

Professor John Mattick was presented with the Julian Wells Medal at the Lorne Genome Conference in March, an acknowledgement of his achievements and years of service to Australian genome science. Professor Mattick's research focuses on showing that there is another layer of information in the genomes of humans and other complex organisms, beyond the conventional protein-coding genes.

The medal is presented to an Australian scientist who has made a significant contribution not only to genome science but also to the development of this field in Australia, as well as to the Lorne Genome Conference.

IMB 2009 highlights

► IMB gene researchers leading the State

IMB researchers proved the Institute is home to some of the best minds in the State when they won two of the three categories at the Queensland Premier's Awards for Health and Medical Research, held as part of Medical Research Week in June.

Dr Mathias François won first prize in the Postdoctoral Researcher Award for his work demonstrating that the gene SOX18 triggers the development of the lymphatic vessels in mice. Dr Nicole Cloonan was runner-up in the same category for her research into personalised medical genomics, particularly in the field of cancer. Dr Geoff Faulkner won first prize in the postgraduate student section for research on retrotransposons undertaken while he was a PhD student.

► Student awards

Reena Halai, a PhD student from the Craik group, won no less than five awards in three months in 2009. She won a travel bursary to attend the American Peptide Symposium, where she was awarded the Young Scientific Investigator poster award. Ms Halai repeated the feat at the HOPE meeting, where she won both a travel award and Best Poster Presenter. She also won a travel award to the 8th Australian Peptide Conference.

Lindsey McFarlane (Wilhelm group) came first in the IMB division of UQ's Three-Minute Thesis competition with his talk on his PhD, which involves introducing RNA into cells in order to interfere with protein production, effectively silencing target genes. Mr McFarlane is studying how to silence genes in carp, in order to genetically manipulate the fish into only being able to produce sons. This would eventually cause the carp to breed themselves out.

Rhonda Kan from the Wainwright group was runner-up with a description of her research into basal cell carcinomas. Both Ms Kan and Mr McFarlane went on to compete at the UQ Institutes semi-final, where Mr McFarlane won the People's Choice award.

The Queensland branch of the Australian Society of Medical Research held its Postgraduate Student Conference in late May to coincide with Medical Research Week. Rehan Villani from the Wainwright group won first prize for her poster oral, with an abstract titled, "The role of Patched in adult skin and basal cell carcinoma development", while Kylie Alexander won third prize with her abstract, "Macrophages are novel and critical participants in bone healing".

Rodrigo Morales from the Alewood group won 'Best protein-focused abstract', an award bestowed by the Queensland Protein Group, for his presentation titled "Role of the N-terminal AVITG for the structure and pharmacological function of the Prokineticin Bv8 in the SH-SY5Y neuroblastoma cell line".

Kevin Chen, a PhD student from the Martin group, was awarded first prize in the poster competition at the Crystal 26 meeting of the Society for Crystallographers in Australia and New Zealand. His poster was titled "A structural genomics approach to the structure determination of macrophage proteins".

COMMERCIALISATION

► IMBcom and PROLOR Biotech enter into non-exclusive technology licence

PROLOR Biotech Inc took out a non-exclusive licence to UQ's human growth hormone (hGH) receptor cell line. Developed by Professor Mike Waters, the line is significantly cheaper and more reliable than other hGH assays, and does not use animals for testing.

► Queensland's IMBcom and Sequenom enter into an exclusive technology licence

IMBcom made a deal with Sequenom to take out an exclusive licence to UQ's Foetal Cell Isolation and Enrichment Technology. This technology allows diagnostic screening of a foetus using cells from a pap smear, eliminating the need for invasive techniques such as amniocentesis. This technology potentially improves the safety margin when testing for sex determination, genetic defects, paternity profile and DNA fingerprinting.

► IMBcom partners with Wyeth and Cyclogenix

IMBcom has entered into licence agreements with Cyclogenix Ltd., a U.K.-based company, and Wyeth Pharmaceuticals, one of the world's largest pharma companies.

IMBcom has granted Cyclogenix licences to cyclotide peptide technologies developed by the IMB. In turn, Cyclogenix has entered into licence and research agreements with Wyeth, which will have rights to the novel drug discovery platform for use in generating therapeutic peptides.

IMB ADVISORY BOARD




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 moved to CSIRO before winning a three-year fellowship to the U.S. In 1975 he 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. From 2002 to 2007, he served as UQ Senior Deputy Vice-Chancellor, before becoming Vice-Chancellor in 2008. Professor Greenfield has extensive experience as a Board Director and has consulted and worked widely with industry. His interests lie in biotechnology, environmental management, and R & D management and commercialisation. He is currently Chair of the Scientific Advisory Group of the South East Queensland Healthy Waterways Partnership. He is also Chair of the Riversymposium Strategic Planning Committee, the Thiess International Riverprize Committee and the International Water Centre. In 2006 he was appointed an Officer in the Order of Australia for his contribution to environmental management, biotechnology and tertiary education, and in 1995, he won the Chemeca Medal, 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 continues his research into the use of genomic approaches to dissect the basis of common genetic disease. In 2008 he led a team that discovered the origins of the often-fatal brain tumour, medulloblastoma.

PROFESSOR FRANK GANNON

Frank Gannon is the Director General of Science Foundation Ireland. From 1994-2007, Frank 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 he has published over 200 research articles. He serves on a number of scientific advisory boards at institutes throughout the world.

DR RUSSELL HOWARD

Dr Howard is CEO and founder of Oakbio Inc., a cleantech company working on developing water processing systems. He is also a founder and former CEO of Maxygen, a company focused on optimisation and development of significantly-improved proprietary versions of several marketed protein pharmaceuticals. Originally trained in biochemistry and chemistry at the University of Melbourne, Dr Howard spent over 20 years studying infectious diseases, primarily malaria. Before joining Maxygen, Dr Howard served at research institutes, biotechnology companies and a pharmaceutical company both in Australia and overseas. In addition to numerous patents, Dr Howard has over 140 publications in peer-reviewed journals.

IMB Advisory Board

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 five 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 of North Queensland. 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.

BOB McCARTHY (until July 2009)

Bob McCarthy was the Director-General of the Queensland Department of Tourism, Regional Development and Industry until his retirement in July 2009. He led a staff totaling more than 800 people, and was responsible for delivering the Smart Industry Policy, which will improve productivity levels across key Queensland priority industries, and rolling out the Centres of Enterprise initiative, which will build the economic strength of regional areas by focusing on their particular industry strengths. As Director-General, Mr McCarthy chaired or co-chaired several state and national committees including Queensland Water Infrastructure Board, Aviation Australia, the Knowledge Based Research and Business (KBRB) CEO Steering Committee, the Aviation Industry Advisory Board, and the Tourism Queensland Board. He was also the Queensland Government's Champion for Napranum, a remote settlement located 13 kilometres south of Weipa.

Mr McCarthy has extensive experience and understanding of agribusiness and resource management and structural change, and regional economic development gained from over 30 years working in the private sector and state and federal governments. He has previously held positions as Director-General of the Department of Natural Resources, Mines and Water, and Deputy Director-General of the Department of State Development and Innovation.

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 Council. He is Assistant Director of the Walter and Eliza Hall Institute, where he also serves as Head of the Cancer and Haemotology Division. 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 200 journal articles and has 17 patents.

PROFESSOR DAVID SIDDLE (until March 2009)

Professor Siddle was the Deputy Vice-Chancellor (Research) of The University of Queensland from 2002 until 2009. He was responsible for enhancement of the University's research and research training profile, and development of research collaborations. Areas under his direct management were the six research Institutes (including IMB), the Research and Research Training Division, the Graduate School and UQ Biological Resources. He joined UQ in September 2001 as the University's Pro-Vice-Chancellor (Research). Previously he was Pro-Vice-Chancellor (Research) at the University of Sydney 1997-2001 and Dean, Postgraduate Studies at the University of Queensland 1993-1997. Professor Siddle was a Director of the Australian Synchrotron Company and Australian Synchrotron Holding Company; AHURI Queensland Research Centre Ltd; CRCMining and the Australian Genome Research Facility Ltd. Professor Siddle is an experimental psychologist with interests in the areas of orienting, attention and conditioning. He has published two books and more than 100 book chapters and journal articles, and was editor of *Biological Pyschology* for five years. He has worked at the University of London and the University of Southampton, both in the United Kingdom, and the University of Ottawa in Canada. He has held positions at Macquarie University, the University of Tasmania, and the University of Sydney in Australia, as well as The University of Queensland.




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 and the UQ Graduate School. Professor Terry's position was previousy titled Vice-Chancellor (Teaching and Learning) and she came to the role after serving a half-time role as Pro-Vice-Chancellor (Teaching and Learning). She completed a Bachelor of Arts and a PhD in Pyschology 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 became Head of School in 2000. Professor Terry accepted the position of Executive Dean, Faculty of Social and Behavioural Sciences in 2006, before being appointed Pro-Vice-Chancellor in 2007.

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 pyschology. She 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.*

DR JANE WILSON

Dr Wilson is a professional company director with a background in medicine and finance. She has a Masters degree in Business Administration from the Harvard Business School where she studied agribusiness and the health sector. Dr Wilson is Chair of IMBcom Pty Ltd, and a Director of 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 University of Queensland Senator. She is also involved in a number of charitable and cultural organisations.

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 the Faculty. 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 5 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 medical research (electrocardiology). He has extensive experience in collaborative research, in conjunction with Government agencies, utilities, and private industry. He is currently a member of a number of advisory boards, and is a Director of the Queensland Parallel Supercomputer Foundation.

IMB SCIENTIFIC ADVISORY COMMITTEE

Top row: Prof. Nicos Nicola, Prof. Chris Abell, Prof. David Galas, Prof. Nancy Jenkins, Prof. Rob Krumlauf.
Second row: 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

Chair and Director
Cancer Research UK
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

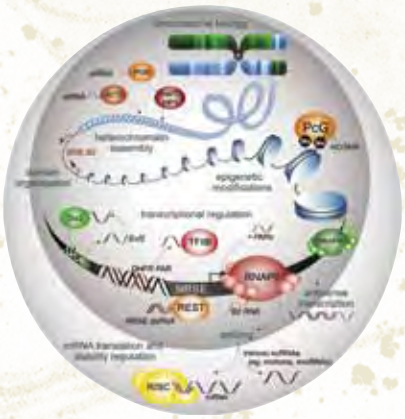
Max Planck Institute of Molecular Cell Biology, Dresden, Germany

IMB RESEARCHERS

The IMB is a highly collaborative environment where researchers from different fields combine to contribute to strategic research programs investigating the basis of growth and development at the genetic, molecular, cellular and organ levels.

Only by understanding the complex molecular and cellular events that occur throughout a normal human life can scientists understand abnormalities responsible for many common human diseases and to find treatments for them.

Division of GENOMICS & COMPUTATIONAL BIOLOGY



In 2009 our research in genomics, computational biology and bioinformatics was led by seven Group Leaders (Dr Tim Bailey, Professor Kevin Burrage, Professor Sean Grimmond, Professor John Mattick, Professor Mark Ragan, Associate Professor Rohan Teasdale, Dr Nick Hamilton) and two affiliates (Professor Jane Hunter, Professor Geoff McLachlan). Our year began with a review of the Division by IMB Scientific Advisory Committee members Professor David Galas (Institute for Systems Biology) and Professor Jill Mesirov (Broad Institute).

Fellowships, promotions and awards: Professor John Mattick was awarded the 2009 Julian Wells Medal of the Lorne Genome Conference. Sean Grimmond was promoted to Professor, and Rohan Teasdale to Associate Professor.

Centres and facilities: The Queensland Centre for Medical Genomics was established within IMB to anchor Australia's contribution to the International Cancer Genome Consortium. More information on the Centre can be found in the Chair's report on page 2, the Director's report on page 3, the feature 'A Cure for Cancer?' on page 7, and Professor Grimmond's report on page 25.

Also in 2009, the Facility for Life Science Automation (LISA) was established within IMB under the leadership of Rohan Teasdale. LISA represents an investment of more than $2 million in robotics and libraries, providing genome-wide RNAi screening capacity and automation services at UQ.

Funding was secured in 2009 to establish the National Computational Infrastructure Specialised Facility in Bioinformatics, and the EMBL Australia EBI Mirror, at UQ in partnership with the Commonwealth and State governments, CSIRO, Queensland Cyber Infrastructure Foundation and Queensland Facility for Advanced Bioinformatics. By mid-2010 these new facilities will provide computing capability to the Australian bioscience and biotechnology communities through merit allocation, and a dynamic mirror of the major EBI data services. Novel value-added data resources, based on Australian technologies and focused in needs of the Australian and national bioscience research communities, will be added as the EBI Mirror is developed.

The ARC Centre of Excellence in Bioinformatics, headquartered at IMB, entered its penultimate year. This Centre links 16 research groups in five Australian and four international institutions to develop genome-scale bioinformatics. Six of our Division's research leaders are associated with the Centre (Bailey, Hamilton, Mattick, McLachlan and Teasdale, with Ragan as Director). Its 2009 Winter School in Mathematical and Computational Biology attracted more than 200 registrants, a record. Planning commenced on continuation of this national bioinformatics focus beyond 2010.

Grant funding and research: In 2009 our Group Leaders held multi-year external competitive grants with a total value in excess of $61.8 million including research awards, fellowships and infrastructure. Of this, more than $37.9 million represents new awards or renewals beginning in 2009. Nine grants are held collaboratively with Group Leaders from other IMB Divisions, with all three other Divisions involved. A further $10.9 million in fellowship and infrastructure funding was secured to begin in 2010. Major awards beginning in 2009 include $27.5 million from NHMRC to Sean Grimmond and colleagues for Australian participation in the ICGC, and $2.5 million from the Australian Cancer Research Foundation to establish the ACRF Cancer Biology Imaging Facility led by Professor Jenny Stow and involving Sean Grimmond, John Mattick and Rohan Teasdale from our Division. Strategic collaborations were begun or extended with all three other bioscience research institutes at UQ (AIBN, QBI and the Diamantina), with RIKEN (Japan), the University of Washington, and many other Australian and international research institutions.

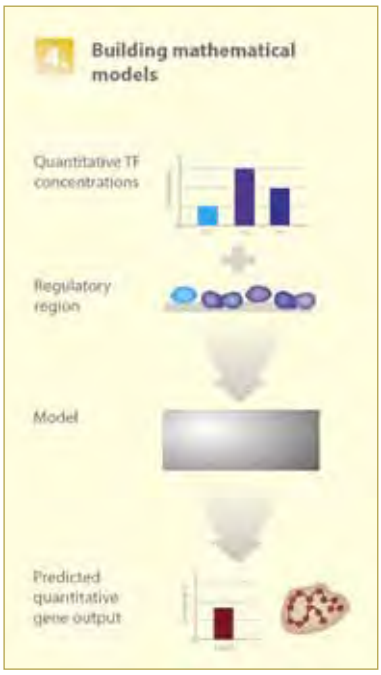
Major publications: In 2009 our Group Leaders and adjuncts continued to publish in prestigious journals including *Nature Genetics* (three papers; Bailey, Grimmond, Mattick and Teasdale groups), *Nature Reviews Genetics* (Mattick group), *Genome Research* (one from Mattick group, another from Ragan group), *Proceedings of the National Academy of Sciences USA* (one from Geoff McLachlan with Scientific Advisory Board member Jill Mesirov; another with Kevin Burrage), and *Philosophical Transactions of the Royal Society of London B* (editorship of theme issue and two papers, Ragan group). Nick Hamilton's iCluster software was featured on the cover of the August 2009 issue of *Traffic*.

Commercialisation: Agreements were signed in 2009 among IMBcom, University of California San Diego Tech Transfer, and the University of Washington on revenue-sharing for Tim Bailey's MEME software. QFAB secured a major CSIRO contract, and was part of the successful bid establishing the Wound Management Innovation CRC.

Collaboration and outreach: In 2009 Kevin Burrage continued his 50-50 appointment between our Institute and Oxford University, and four students from Oxford's systems biology program were based at IMB for 1-2 months each. Our Group Leaders were keynote or plenary speakers at conferences in China, France, UK (Mattick), Australia, Germany, USA (Grimmond, Mattick) and Japan (Grimmond, Ragan). John Mattick was an invited speaker at the Adelaide Festival of Ideas, and Mark Ragan was an invited speaker in a session of CreateWorld with nature photographer and publisher Steve Parish. Jane Hunter was appointed Deputy Chair of Australian Academy of Sciences National Committee on Data in Science, and Mark Ragan served on the Steering Committee of Australian National Data Service. We hosted distinguished visitors including the Malaysian Minister of Science, Technology and Innovation Datuk Dr Maximum Ongkili; a delegation from Genome British Columbia including CEO Pierre Meulien and head of bioinformatics Dr Steve Jones; and AgResearch New Zealand CEO Dr Andrew West.

Pattern recognition and modelling in computational biology

TIMOTHY L. BAILEY



My research involves developing and applying computational methods to extract knowledge and understanding of biological processes from the huge quantities of raw data made possible by automated biology. The current focus of my research is on understanding how the cell regulates the expression of genes. My approach is to develop computer algorithms for discovering patterns in high-throughput data related to control of gene expression, and to build models of regulation based on those patterns. Knowing how gene expression is regulated is essential to understand cellular processes such as reproduction and metabolism. It will also enhance our understanding of development and pathology in higher organisms, and may also lead to advancements in biotechnology.

In 2009 we attacked the problem of building models of transcriptional regulation on several fronts. We published the first method for utilising high-throughput chromatin modification data for predicting tissue-specific binding of transcription factors. We will continue exploring this topic because we believe it is the most promising way to achieve accurate predictions of the binding of transcription factors to DNA under all conditions in all tissues. The team published a study on the potential of phylogenetic data ("comparative genomics") to improve prediction of DNA binding, albeit in a non-tissue-specific way. We undertook several projects to predict transcriptional regulation networks in neural precursor cells, in conjunction with researchers at the Queensland Brain Institute (Richards lab), and in erythrocytes, together with researchers at IMB (Perkins lab). This year we also developed new algorithms for discovering DNA binding motifs of transcription factors from high-throughput data (chromatin immunoprecipitation followed by deep sequencing). We addressed the question of identifying the biological role of a given transcription factor using a form of "motif enhancement analysis" that leverages comparative genomics. Finally, we studied ways to optimise predictive models of transcription, and investigated explanations for individual transcription factors working to both enhance and repress transcription rate.

In the coming year, we will continue to investigate the transcriptional networks governing neural and erythrocyte development. We are currently exploring algorithms that incorporate chromatin modification data to predict cis-regulatory modules—clusters of DNA binding sites that may be distal from the regulated gene.

In addition, we will intensify our study of the prediction of the nuclear organisation of regulatory molecules. We will also continue work on the possible role of DNA-RNA triplex formation in genetic regulation.

KEY PUBLICATIONS

Bailey, T.L., Boden, M., Buske, F.A., Frith, M., Grant, C.E., Clementi, L., Ren, J., Li, W.W., and Noble, W.S. (2009). MEME Suite: tools for motif discovery and searching. *Nucleic Acids Research* **37**: W202–W208.

Bauer, D.C., and Bailey, T.L. (2009). Optimizing static thermodynamic models of transcriptional regulation. *Bioinformatics* **25**: 1640–1646.

Boden, M., Dellaire, G., Burrage, K., and Bailey, T.L. (2009). A Bayesian network model of proteins association with promyelocytic leukemia (PML) nuclear bodies. *Journal of Computational Biology* In Press.

The Fantom Consortium. (2009). The transcriptional network that controls growth arrest and differentiation in a human myeloid leukemia cell line. *Nature Genetics* **41**: 553–562.

Hawkins, J., Grant, C., Noble, W., and Bailey, T.L. (2009). Assessing phylogenetic motif models for predicting transcription factor binding sites, Conference on Intelligent Systems for Molecular Biology (ISMB2009). *Bioinformatics* **25**: i339–i347.

Whitington, T., Perkins, A.C., and Bailey, T.L. (2009). High-throughput chromatin information enables accurate tissue-specific prediction of transcription factor binding sites. *Nucleic Acids Research* **37**: 14–25.

LAB MEMBERS

Research Fellow: Dr Mikael Boden

Research Officers: Dr John Hawkins, Dr Philip Machanick

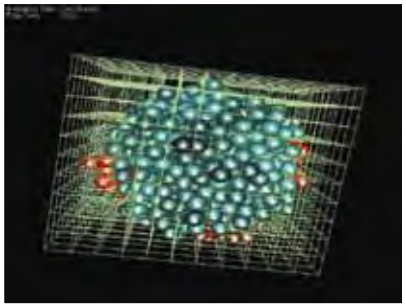
PhD Students: Denis Bauer, Tom Whitington, Robert Mcleay, Fabian Buske

Programmer: James Johnson

DIVISION OF GENOMICS & COMPUTATIONAL BIOLOGY

Modelling and visualising cellular processes

KEVIN BURRAGE



A rectangular discretisation of the space occupied by the cell colony. This discretisation is used to efficiently locate nearest neighbours, done by querying neighbouring volumes as opposed to querying the entire colony itself. In collaboration with Mr David Woolford.

This group works on developing simulations and visualisation methodologies for understanding the behaviour of complex cellular processes, both on the plasma membrane, in the cytosol and at the genetic regulatory level. The simulation models take into account stochastic effects, while the visualisation focuses on two or three-dimensional display.

In microscopic systems formed by living cells, the small numbers of reactant molecules can result in dynamic behaviour that is discrete and stochastic rather than continuous and deterministic. Our research introduces new classes of discrete stochastic methods that more accurately and effectively reflect the underlying cellular models.

We are also focusing on some new methods for both large-scale kinetics and spatial methods that more faithfully capture complex kinetics and transport processes within the cell.

RESEARCH PROJECTS

- Developing new Monte-Carlo Simulation techniques in conjunction with Professor John Hancock at the University of Texas and researchers at Oxford University (Dan Nicolau Jr.) that allow us to model the behaviour of lipid rafts and to investigate the effects of anomalous diffusion and the linking of kinetics on the plasma membrane with cascading reactions such as MAPK
- Modelling the effects of transcriptional and translational delays in genetic regulatory systems
- Building mathematical models from imaging data, with the Teasdale, Hamilton and Parton labs
- Developing spatial models that capture complex chemical kinetics within the cell

KEY PUBLICATIONS

Burrage, P.M., Burrage, K., Kurowski, K., Lorenc, M., Nicolau Jr., D.V., Swain, M., and Ragan, M.A. (2009). A parallel plasma membrane simulation. In: Proceedings of 1st International Workshop on High Performance Computational Systems Biology (HiBi 2009), Trento, Italy, 14-16 October 2009 (J. Guerrero, Ed.) pp. 105-112. IEEE Computer Society. ISBN: 978-0-7695-3809-9

Bustamam, A., Sehgal, M.S., Hamilton, N., Wong, S., Ragan, M.A., and Burrage, K. (2009). An efficient parallel implementation of Markov clustering algorithm for large-scale protein-protein interaction networks that uses MPI. In: Proceedings of the 5th IMT-GT International Conference on Mathematics, Statistics and Their Applications (ICMSA-2009), Bukittinggi, Indonesia, 9-11 June 2009 (I.M. Arnawa, M. Muhafzan & S. Bahri, Eds), pp. 94-101. Department of Mathematics, Andalas University, Indonesia. ISBN: 978-602-95343-0-6.

Lesmono, D., Tonkes, E., and Burrage, K. (2009). Opportunistic timing and manipulation in Australian Federal Elections. *European Journal of Operational Research* **192**: 677-691.

MacNamara, S., and Burrage, K. (2009). Krylov and steady-state techniques for the solution of the chemical master equation for the mitogen-activated protein kinase cascade. *Numerical Algorithms* **51**: 281-307.

Leier, A., Marquez-Lago, T.T., and Burrage, K. (2008). Generalized binomial Tau-leap method for biochemical kinetics incorporating both delay and intrinsic noise. *Journal of Chemical Physics* **128**: 205107.

MacNamara, S., Bersani, A.M., Burrage, K., and Sidje, R.B. (2008). Stochastic chemical kinetics and the total quasi-steady-state assumption: application to the stochastic simulation algorithm and chemical master equation. *Journal of Chemical Physics* **129**: 095105.

MacNamara, S., and Burrage, K. (2008). Krylov and steady-state techniques for the solution of the Chemical Master Equation for the Mitogen-activated protein kinase cascade. *Numerical Algorithms* **51**: 281-307.

McNamara, S., Burrage, K., and Sidje, R.B. (2008). Application of the Strang splitting to the chemical master equation for simulating biochemical kinetics. *International Journal of Computational Science* **2**: 402-421.

MacNamara, S., Burrage, K., and Sidje, R.B. (2008). Multiscale modeling of chemical kinetics via the master equation. *SIAM Journal: Multiscale Modelling and Simulation* **6**: 1146.

Nicolau Jr., D.V., and Burrage, K. (2008). Stochastic Simulation of Chemical Reactions in Spatially Complex Media. *Computers and Mathematics with Applications* **55**: 1007-1018.

Nicolau Jr., D.V., Burrage, K., Nicolau, D.V., and Maini, P.K. (2008). 'Extremotaxis': Computing with a bacterial-inspired algorithm. *BioSystems* **94**: 47-54.

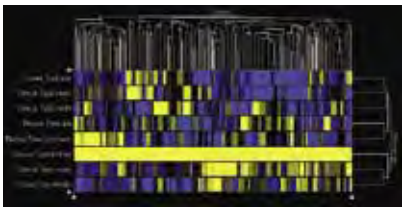
LAB MEMBERS

Research Officers: Dr Shoaib Sehgal, Dr Shev MacNamara, Dr John Belward, Dr Fawang Liu

PhD Students: Shev MacNamara, Alhadi Bustamam, Duncan Mortimer

Queensland Centre for Medical Genomics

SEAN GRIMMOND



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

In 2009 the IMB's Expression Genomics laboratory expanded into the Queensland Centre for Medical Genomics, through the support of Queensland State Government and Federal Government funding into personal genomics. The laboratory is focused on globally surveying genomic, transcriptomic and epigenomic information using next-generation sequencing and array-based approaches, and then using these data to define the underlying molecular networks controlling biological processes (such as cell division and differentiation) and pathological states (pancreatic, ovarian and breast cancer). These systems-wide studies 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 cancer development and progression

Next-generation sequencing technology has heralded new opportunities for cancer genomic research. It is now feasible to survey the entire sequence content of an individual tumour and define the accumulation of somatic mutations and structural variations. We have recently established Australia's largest genome sequencing centre at the IMB and are undertaking the systematic surveying of complete transcriptome complexity, genome sequence content/genome structure and epigenomic signatures in a large cohort of individual pancreatic cancers (in collaboration with A. Biankin, Gavan Institute) and ovarian cancers (in collaboration with D. Bowtell, Peter Mac Cancer Institute) as part of the International Cancer Genome Consortium (ICGC). 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, and survey transcriptome content during the cell cycle.

Studying temporo-spatial transcriptome dynamics at histological resolution:

In collaboration with the Little lab, we have used microarray and in situ-based expression profiling to develop a detailed molecular atlas of urogenital development (http://kidney.scgap.org).

RESEARCH PROJECTS

Predicting the function of onco-miRs through mRNA-mRNA networks

Defining the complete repertoire of genetic damage driving development and progression of breast cancer in a mouse model

Studying temporo-spatial transcriptome dynamics at histological resolution

KEY PUBLICATIONS

Cloonan, N., *et al.* (Grimmond, S.M. senior author) (2009). RNA-MATE: a recursive mapping strategy for high-throughput RNA-sequencing data. *Bioinformatics* **25**: 2615-2616.

FANTOM Consortium (including Grimmond, S.M.) (2009). The transcriptional network that controls growth arrest and differentiation in a human myeloid leukemia cell line. *Nature Genetics* **41**: 553-562.

Faulkner, G.J., *et al.* (including Grimmond, S.M. as equal senior author) (2009). *Nature Genetics* **41**: 563-571.

Kolle, G., *et al.* (including Grimmond, S.M. as senior author) (2009). Identification of human embryonic stem cell surface markers by combined membrane-polysome translation state array analysis and immunotranscriptional profiling. *Stem Cells* **27**: 2446-2456.

Taft, R.J., *et al.* (2009). Tiny RNAs associated with transcription start sites in animals. *Nature Genetics* **41**: 572-578. Erratum in: *Nature Genetics* **41**: 859.

LAB MEMBERS

Senior Research Officers: Dr Peter Wilson, Dr Nicole Cloonan, Dr Nicola Waddell

Research Officers: Dr Brooke Gardiner, Dr Gabriel Kolle, Dr Geoff Faulkner, Dr Karin Kassahn, Dr Katia Nones, Dr Craig Nourse, Dr Peter Rohde, Dr Conrad Leonard

Research Assistants: Anita Steptoe, Suzanne Manning, David Miller, Milena Gongora, Shivangi Wani, Ehsan Nourbakhsh, Ivon Harliwong, Senel Idrisoglu, Jason Steen, Dave Tang, Darrin Taylor, Qinying Xu

PhD Students: Rathi Thiagarajan, Keerthana Krishnan, Mellissa Brown

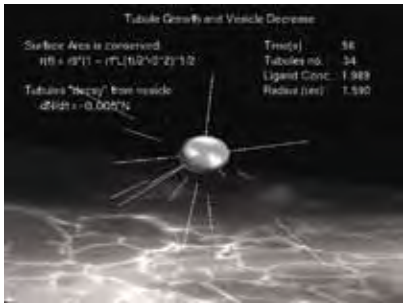
Honours Student: Yunshan Xiao

DIVISION OF GENOMICS & COMPUTATIONAL BIOLOGY

Modelling, visualisation and classification of live cell imaging

NICK HAMILTON

High throughput bio-image visualisation.



Modelling and interference from video microscopy imaging of cells.

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 and tools needed to enable the full benefit of these rich new data sources to be realised.

Recent research has focused on automated classification, clustering and visualisation of high-throughput microscopy imaging. Towards this, the Automated Subcellular Phenotype Classifier (ASPiC) was developed by combining novel image statistics created in the group with machine-learning methodologies to enable rapid classification of high-throughput imaging with near-perfect accuracy. Building on this, the iCluster methodology currently being developed allows the clustering, differentiation and visualisation of high-throughput image sets to enable sense to be made of the vast sets being generated. A recent highlight has been the creation of a more sensitive statistical test to enable the automated detection of subtle differences between treated and untreated cells.

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 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.

RESEARCH PROJECTS

- Automated classification of bio-imaging via machine learning
- Clustering and information visualisation methodologies for high-throughput bio-data sets
- Statistical testing and content-based searching of bio-imaging
- Modelling endosomal systems from live cell video microscopy imaging
- Segmentation and quantification of 2D, 3D and 4D live cell imaging

KEY PUBLICATIONS

Hamilton, N.A. (2009). Quantification and its applications in fluorescent microscopy imaging. *Traffic* **10**: 951-961.

Woodcroft, B.J., Hammond, L., Stow, J.L., and Hamilton, N.A. (2009). Automated organelle-based colocalization in whole-cell imaging. *Cytometry Part A* **75A**: 941-950.

Hamilton, N.A., and Teasdale, R.D. (2008). Visualising and clustering high throughput sub-cellular localization imaging. *BMC Bioinformatics* **9**: 81.

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

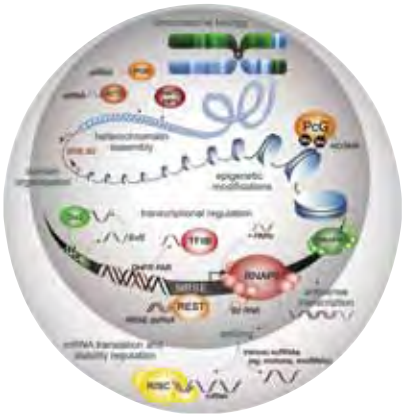
Research Officers: Daniel Marshall, Oliver Caincross, Matthew Moores

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

DIVISION OF GENOMICS & COMPUTATIONAL BIOLOGY

RNA regulation in human evolution, development, cognition and disease

JOHN MATTICK



We are exploring the thesis that the evolution and genetic programming of human development and cognition has been fundamentally misunderstood for the past 50 years, because of the assumption that most genetic information is transacted by proteins. It is now only a tiny fraction of the human genome that encodes proteins and the number and repertoire of protein-coding genes has remained largely static from simple worms to humans, despite huge differences in developmental and cognitive complexity. On the other hand the extent of non-protein-coding DNA sequences, traditionally thought of as being mainly junk, has increased markedly with increased complexity. Moreover it is now evident that these sequences are transcribed in a dynamic manner, mainly to produce non-protein-coding 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.

In conjunction with collaborators in the United States, Europe and Japan, and using a range of experimental, deep sequencing and bioinformatic techniques, we are working to characterise and understand the functions of this hidden transcriptome, 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 recently 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 a new class of tiny RNAs associated with transcription start 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. The outcomes of our research will be to expand our understanding of human development, brain function and disease, with important consequences and applications in medicine.

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 PUBLICATIONS

Mattick, J.S. (2009). The genetic signatures of noncoding RNAs. *PLoS Genetics* **5**: e1000459.

Mattick, J.S. (2009). Deconstructing the dogma: a new view of the evolution and genetic programming of complex organisms. *Annals of the New York Academy of Sciences* **1178**: 29-46.

Mattick, J.S., *et al.* (2009). RNA regulation of epigenetic processes. *Bioessays* **31**: 51-59.

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

Nahkuri, S., *et al.* (2009). Nucleosomes are preferentially positioned at exons in somatic and sperm cells. *Cell Cycle* **8**: 3420-3424.

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.

Mercer, T.R., *et al.* (2008). Specific expression of non-coding RNAs in mouse brain. *Proceedings of the National Academy of Sciences USA* **105**: 716-721.

LAB MEMBERS

Senior Research Officers: Dr Lynn Fink, Dr Marcel Dinger

Research Officers: Dr Timothy Mercer, Dr Marjan Askarian Amiri, Dr Lorenzo Malquori

Research Assistant: Ke-Lin Ru

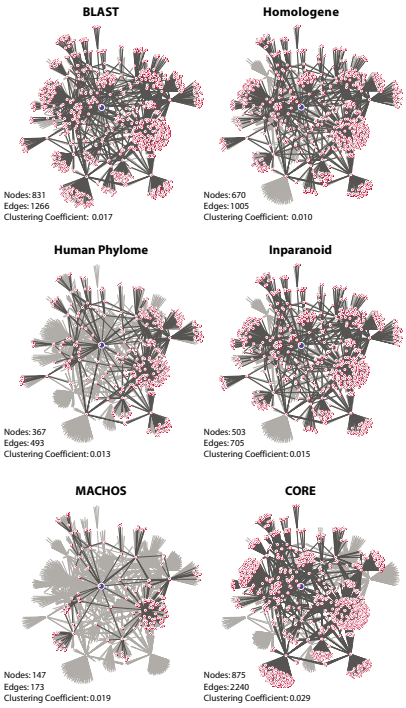
PhD Students: Satu Nahkuri, Darren Korbie, Chol Hee Jung, Paulo Amaral, Michael Clark, Selene Fernandez Valverde, Pierre Cattenoz, Martin Smith, Dennis Gascoigne, Vikram Ratnu, Ryan Taft

Visiting Researchers: Dr Larry Croft, Dr Mythily Mariasegaram, Dr Johanna Vendelin, Dr Harald Oey, Dr Hatice Akarsu

DIVISION OF GENOMICS & COMPUTATIONAL BIOLOGY

Computational genomics

MARK RAGAN



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.

The 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: **http://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
- Integrating bioinformatic information using Semantic Web technologies

KEY PUBLICATIONS

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.

Wong, S., and Ragan, M.A. (2008). MACHOS: Markov Clusters of Homologous Subsequences. *Bioinformatics* **24**: i77-i85.

Beiko, R.G., Harlow, T.J., and Ragan, M.A. (2005). Highways of gene sharing in prokaryotes. *Proceedings of the National Academy of Sciences USA* **102**: 14332-14337.

LAB MEMBERS

Research Officers: Dr Pamela Burrage, Dr Melissa Davis (QFAB), Dr Karin Kassahn, Dr Stefan Maetschke

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

Manager, ARC Centre of Excellence in Bioinformatics: Lanna Wong

Scientific Programmer: Chikako Ragan

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

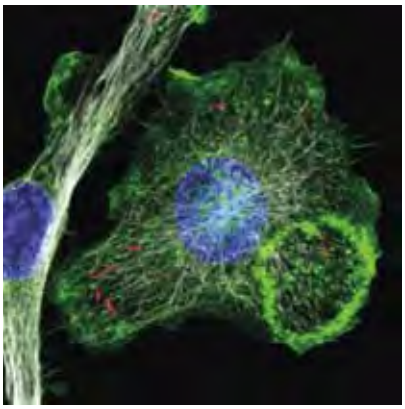
Masters Student: Kshitji Jain

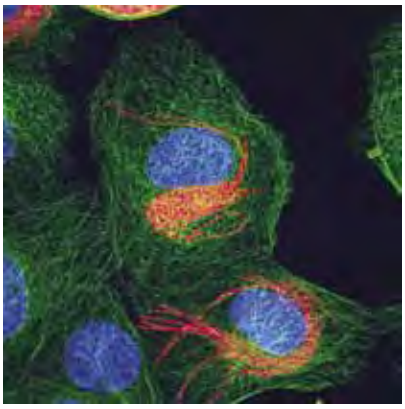
Research Trainee: Cindy Yan (Queensland University of Technology)

DIVISION OF GENOMICS & COMPUTATIONAL BIOLOGY

Endosomal dynamics: regulated endocytosis, host-pathogen interactions and protein trafficking

ROHAN TEASDALE





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. We have implicated this complex, using real-time microscopy and molecular interaction techniques, in the sorting of numerous membrane receptors, including EGFR, within the endosomal system.

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. Our recent work has focused on characterising macropinocytic pathways and the molecular machinery associated with macropinosomes. We have determined that the regulation of phosphoinositides is central to macropinocytosis and leads to the recruitment of key effector proteins including the PtdIns(3)P-binding PX-domain family of proteins. This emerging protein family performs a range of critical biochemical actions within the mammalian endosome and we are keenly interested in the roles these proteins play. Currently we are undertaking a systems biology approach to examine the distinct stages of macropinocytosis.

Numerous infectious pathogens exploit specific endocytic pathways 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.

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

Fink, J.L., Karunaratne, S., Mittal, A., Gardiner, D., Hamilton, N., Mahony, D., Kai, C., Suzuki, H., Hayashizaki, Y., and Teasdale, R.D. (2008). Towards defining the nuclear proteome. *Genome Biology* **9**: R15.

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.

Kerr, M., Lindsay, M., Luetterforst, R., Hamilton, N., Simpson, F., Parton, R., Gleeson, P.A., and Teasdale, R.D. (2006). Visualisation of macropinosome maturation by the recruitment of sorting nexins. *Journal of Cell Science* **119**: 3967-3980.

LAB MEMBERS

Senior Research Officer: Dr Zheng Yuan

Research Officers: Dr Markus Kerr, Dr Stefan Maetschke, Dr Andrea Bugarcic, Dr Michael Hanzal-Bayer

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

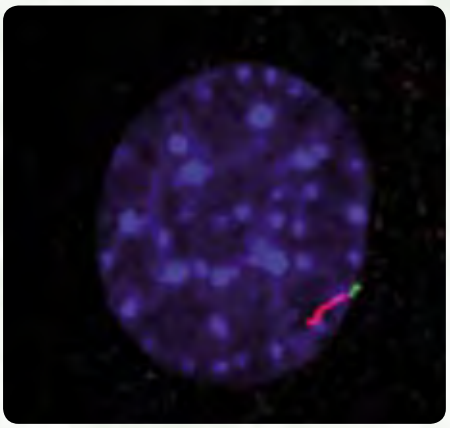
PhD Students: Josefine Sprenger, Jack Wang

IMB RESEARCHERS

The IMB is a highly collaborative environment where researchers from different fields combine to contribute to strategic research programs investigating the basis of growth and development at the genetic, molecular, cellular and organ levels.

Only by understanding the complex molecular and cellular events that occur throughout a normal human life can scientists understand abnormalities responsible for many common human diseases and to find treatments for them.

Division of MOLECULAR GENETICS & DEVELOPMENT



The overarching aim of the division is to dissect the molecular mechanisms that underlie development, and to understand where defects occur in these mechanisms to produce disease. Researchers from the division have made a number of seminal contributions to their fields over the years. In 2009, Dr Kate Stacey's *Science* paper, describing the process by which DNA in the cytoplasm triggers macrophage cell death, was a particular highlight.

Division of MOLECULAR GENETICS & DEVELOPMENT

For most of the year, the division comprised nine group leaders overseeing approximately 100 research staff. Dr Ben Hogan became our tenth group leader when he joined the IMB in December 2009. Dr Hogan came to us from the Hubrecht Institute for Developmental and Stem Cell Biology in the Netherlands; his research focuses on the development and function of the vascular system, particularly the lymphatic vessels. The lymphatic system is important for normal health, and is implicated in diseases such as lymphedema and cancer, but its development and function are poorly understood. To study these issues, Dr Hogan uses the zebrafish as a model system, and is a world expert in zebrafish development.

Other research interests in the division are: 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 performed admirably in research funding rounds in 2009. Divisional researchers received over $6 million of the $10 million awarded to IMB from the National Health and Medical Research Council. Particularly gratifying was the fact two of our newer group leaders (Dr Wilhelm and Dr Hogan) were successful in their funding applications, and that some of our postdoctoral researchers were lead Chief Investigators on other successful grants. The ability of its younger researchers to gain funding in their own right bodes well for the future of the division. Funding for researchers begins with PhD scholarships, and most of the postgraduate students in the division are supported by scholarships, including Koopman group student Duong Minh Tam, who was one of five Vietnamese scholars to share in a $1 million scholarship package from UQ.

The division's researchers were recognised with awards throughout the year. Professor Peter Koopman was presented with the 2009 Lemberg Medal at the Combio conference. The medal is awarded by the Australian Society for Biochemistry and Molecular Biology to a distinguished Australian molecular Biologist. Dr Mathias François from the Koopman group was awarded first prize at the Queensland Premier's Awards for Health and Medical Research. Dr François won for his part in research that proved the development of the lymphatic vessels in mice is triggered by the gene SOX18. Our students were also successful in being recognised in 2009. Elanor Wainwright from the Wilhelm group won the Amgen Award for best honours student at the IMB, while Wicking group student Natalie Butterfield was named on the Dean's List for Outstanding Research Higher Degree Theses. Lindsey McFarlane from the Wilhelm group and Rhonda Kan from the Wainwright group won first and second prizes respectively at the IMB heat of UQ's Three-Minute Thesis competition. Lindsey went on to take the People's Choice Award at the Research Institutes semi-final.

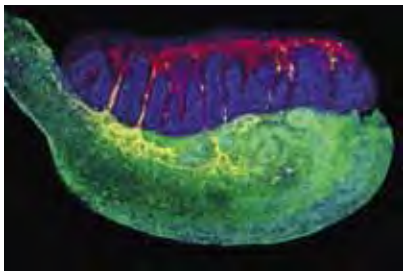
Molecular Genetics and Development researchers continued to engage on a national and international level. Professor Melissa Little was appointed to the NHMRC's Research Committee, which advises on medical and public health research in Australia and makes recommendations on research grant applications and funding. Researchers gave talks in Australia and overseas, and in turn hosted both national and international speakers at the IMB. These included Professor John Bateman from the Murdoch Children's Research Institute and Dr Paul Gregorevic from the Baker Institute, both in Melbourne, Professor Wolfgang Weninger from the Centenary Institute of Cancer Medicine and Cell Biology at the University of Sydney, and Professor Andrew McMahon from the Harvard Stem Cell Institute in Boston. They presented at IMB's Friday Seminar Series, which gave the entire institute a chance to hear their talks. The division ran a fortnightly seminar series at which our students and postdoctoral researchers presented their work to a wide audience of fellow researchers.

An important milestone in the history of the Division was reached with the completion of a two-day review of our operations by two members of the IMB Scientific Advisory Board: Professor Robb Krumlauf, Director of the Stowers Institute for Medical Research in Kansas City, USA, and Professor Nancy Jenkins, co-Director of the Institute for Molecular and Cellular Biology in Singapore. The reviewers were evidently impressed with the IMB and with the calibre of staff and students within the Molecular Genetics and Development Division. They noted the high standard of equipment and systems within the Institute as a whole, and congratulated its members on ongoing success of its research staff. The review also provided an opportunity for the reviewers to provide high-level strategic advice in terms of organisation, administration and research directions. Overall the review was seen as a positive and energising experience by the Group Leaders in the Division, and will be useful in setting our research agenda for the next five years.

DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

How genes regulate embryo development

PETER KOOPMAN



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).

Our group studies genes controlling the formation of various organs in the developing embryo. In particular we are striving to understand the events that regulate the development of functional male and female gonads and the formation of the blood and lymphatic vessels.

The gene SRY, which acts as a single switch to initiate the male pathway of development, was discovered over a decade ago. However, the genetic and cellular events leading to testis development and male sex determination remain elusive. Our lab specialises in identifying and characterising sex development genes using techniques such as microarray screening and transgenic mouse models, and examining the potential contribution of these genes to human disorders in sex development.

We are also interested in how germ cells come to develop as sperm in males or eggs in females. The recent discovery in our lab that retinoic acid controls germ cell meiosis entry in the female gonad has provided a pivotal point to understanding this process.

A third major focus in our group includes investigating the function of Sox genes during embryo development. Specifically we are investigating the role of SOX18, which we 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.

The study of embryo development provides insight into mechanisms of disease and cancer, and provides a molecular and cellular basis for 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

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

Wilhelm, D., Palmer, S., and Koopman, P. (2007). Sex determination and gonadal development in mammals. *Physiological Reviews* **87**: 1-28.

Bowles, J., Knight, D., Smith, C., Wilhelm, D., Richman, J., Mamiya, S., Yashiro, K., Chawengsaksophak, K., Wilson, M.J., Rossant, J., Hamada, H., and Koopman, P. (2006). Retinoid signaling determines germ cell fate in mice. *Science* **312**: 596–600.

Wilhelm, D., and Koopman, P. (2006). The makings of maleness: Towards an integrated view of male sexual development. *Nature Reviews Genetics* **7**: 620-631.

LAB MEMBERS

Senior Research Officer: Dr Josephine Bowles

Research Officers: Dr Mathias François, Dr Terje Svingen, Dr Kallayanee Chawengsaksophak, Dr Kenichi Kashimada, Dr Juan Carlos Polanco, Dr Cassy Spiller, Dr Antoine Rolland

Research Assistants: Tara Davidson, Deon Knight, Allen Feng, Ee Ting Ng, Kelly Sweeney, Danielle Wilson, Cameron Curtis

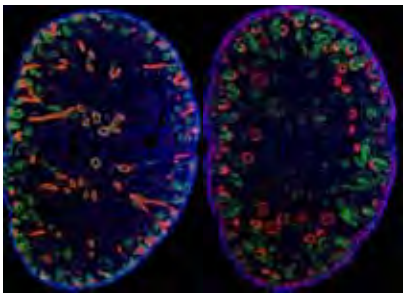
Admin Assistant: Mei Goh

PhD Students: John Abramyan, Tam Duong, Lindsey McFarlane

DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Kidney development, damage, repair and regeneration

MELISSA LITTLE



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 cost the health system $1.8 billion dollars in 2006. This cost is likely to escalate to $4.7 billion by 2010. 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

- Creating an atlas of gene expression during kidney development and disease
- Investigating the link between the processes of development and normal repair in the kidney
- Characterising the molecular basis of nephron formation
- Looking for stem cells in the adult kidney
- Reinitiating kidney development to repair an adult kidney
- Characterising the process of vascular development in kidney

KEY PUBLICATIONS

Brunskill, E., Aronow, B., Georgas, K., Rumballe, B., Valerius, M.T., Aronow, J., Kaimal, V., Jegga, A.G., Grimmond, S., McMahon, A.P., Patterson, L.T., Little, M.H., and Potter, S. (2008). Atlas of gene expression in the developing kidney at microanatomic resolution. *Developmental Cell* **15**: 781-791. (Front cover)

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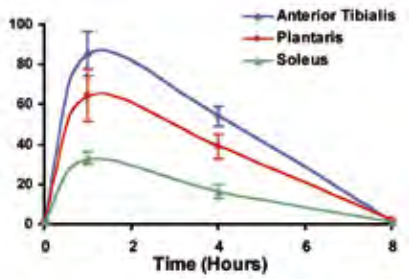
DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Nuclear hormone receptors, and metabolic disease

GEORGE MUSCAT



β2-adrenergic agonist increases NR4A2/ Nurr1 mRNA expression in slow oxidative (soleus) and fast glycolytic (tibialis anterior & plantaris) skeletal muscle.

Nuclear Hormone Receptors (NRs) function as ligand-dependent DNA-binding proteins that translate nutritional, metabolic and pathophysiological signals into gene regulation. NRs control metabolism in an organ-specific manner. The importance of NRs in human health is underscored by the curative efficacy of medicinals that target dysfunctional hormone signalling in the context of inflammation, cancer, endocrine and metabolic diseases. Proteins that belong to the NR superfamily on the basis of sequence identity but lack established ligands are denoted as orphan NRs. The orphans provide a platform for the unearthing of new signalling cascades that may have therapeutic utility.

The group focuses on understanding the molecular role of NRs in the regulation of metabolism and body composition in transgenic mouse models. Moreover, we exploit these animal models and studies to gain insights into obesity, type II diabetes and cancer, and translate this research into several human diseases including melanoma, breast cancer, obesity and type 2 diabetes.

Orphan NRs are expressed in skeletal muscle, a peripheral tissue that accounts for ~40 percent of the total body mass and energy expenditure, and is a major site of fatty acid and glucose oxidation. Accordingly, muscle has an important role in insulin sensitivity, the blood lipid profile, and energy balance. Consequently, the tissue has a significant role in metabolic disease. Surprisingly, the function of orphan NRs in skeletal muscle metabolism has not been examined. In this context, our group has provided evidence for crosstalk between beta-adrenergic and Nuclear Receptor (NR) 4A signalling in muscle to control oxidative metabolism (1-3). Secondly, we have utilised established mouse models (eg. the staggerer sg/sg line) to demonstrate that dysfunctional NR1F/RORa expression leads to reduced adiposity and resistance to diet-induced obesity (4). Thirdly, in the context of understanding crosstalk between NRs and other transcription factor signalling pathways in obesity, Dr Gary Leong and I have utilised the Ski transgenic mouse model to investigate the role of c-ski and NR crosstalk in regulating body composition (6). Collaboratively, with Aaron Smith and Richard Sturm, we have shown regulatory crosstalk between melanocortin 1 receptor (MC1R) and NR4A signaling in melanocytic cells in the context of the red hair phenotype and melanoma susceptibility (7).

In the context of human health and translation, we, in collaboration with Dr Leong, are profiling the expression of the NRs, coregulators and metabolic genes (using custom Taqman Low Density Arrays) in overweight and obese children before and after the implementation of a nutrition and lifestyle program. Furthermore, we are also involved in an NBCF-funded large collaborative research program to completely profile NR and coregulator expression in several human cohorts, including (pre- and post-menopausal) normal breast, estrogen receptor (ER) positive and negative breast cancers. This will enable identification of new target genes that may be therapeutically exploited for the treatment of breast cancer.

RESEARCH PROJECTS

- Examining the role of the ROR and COUP-TF subgroups in lipid homeostasis
- Elucidating the role of the NR4A subgroup in skeletal muscle oxidative metabolism, adrenergic signalling and melanocortin signalling
- Determining the role and function of the Ski gene in body composition
- Profiling NR and cofactor expression in breast cancer

KEY PUBLICATIONS

1. Pearen, M.A., *et al.* (2009). Expression profiling of skeletal muscle following acute and chronic beta2-adrenergic stimulation: implications for hypertrophy, metabolism and circadian rhythm. *BMC Genomics* **10**: 448-468.

2. Myers, S.A., *et al.* (2009). Beta-adrenergic signaling regulates NR4A nuclear receptor and metabolic gene expression in multiple tissues. *Molecular and Cellular Endocrinology* **309**: 101-108.

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4. Lau, P., *et al.* (2008). The orphan NR, RORalpha, regulates gene expression that controls lipid metabolism: sg/sg mice are resistant to diet induced obesity. *Journal of Biological Chemistry* **283**: 18411-18421.

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6. Leong, G.M., *et al.* (2009). The Ski proto-oncogene regulates body composition and suppresses lipogenesis. *International Journal of Obesity* **34**: 524-536.

7. Smith, A.G., *et al.* (2008). Melanocortin 1 receptor signaling markedly induces the expression of the NR4A nuclear receptor subgroup in melanocytic cells. *Journal of Biological Chemistry* **283**: 12564-12570.

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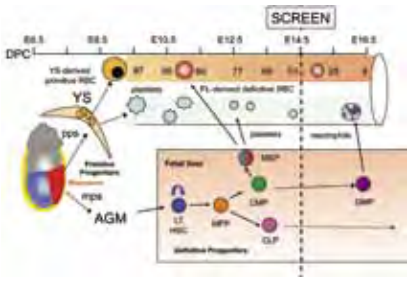
Blood development

ANDREW PERKINS



Blood Development: Blood is derived from the mesoderm of gastrulating embryos in two waves. The primitive wave derives from the posterior primitive streak (pps). Stem cells migrate onto the yolk sac (YS) from 6 days of mouse development (or ~3 weeks in man) and give rise to nucleated primitive red cells and platelets. Stem cells from the mid primitive streak (mps) migrate a little later to the YS and the AGM where they are dormant until the foetal liver (FL) develops from the gut tube from 11 days of mouse development. In the FL they proliferate and give rise to lineage restricted blood progenitor cells and mature blood cells. Shortly before birth HSCs migrate to the bone marrow where they reside for the rest of life.

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 generation of haematopoietic stem cells in the mammalian embryo.

RESEARCH PROJECTS

- Studying transcriptional hierarchies active during ES cell differentiation into mesoderm-derived tissues
- Investigating the transcriptional regulation of erythropoiesis
- Studying the roles of KLFs in human diseases
- Using chemical mutagenesis to discover new genes that regulate HSC generation and behaviour

KEY PUBLICATIONS

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

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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.

Hodge, D., Coghill, E., Keys, J., Maguire, T., Hartmann, B., McDowall, A., Weiss, M., Grimmond, S., and Perkins, A.C. (2006). A global role for EKLF in definitive and primitive haematopoiesis. *Blood* **107**: 3357-3370.

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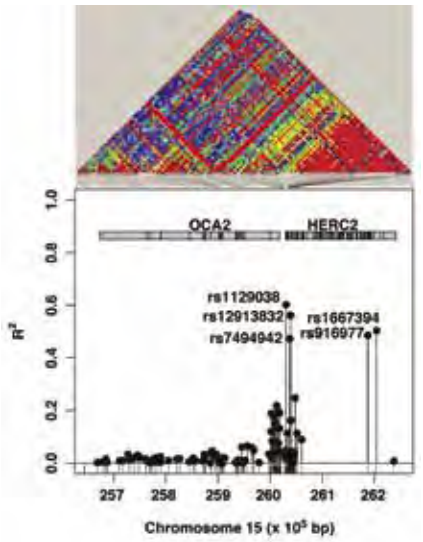
DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Molecular genetics of human pigmentation

RICK STURM



The genetic basis underlying normal variation in the pigmentary traits of skin, hair and eye colour has been the subject of intense research directed at understanding the diversity seen both between and within human populations. A combination of approaches has been used by workers in the field, including comparative genomics of candidate genes and identification of regions of the human genome under positive selection, together with genome-wide and specific allele association studies. 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 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.

Functional testing of variant pigmentation gene alleles in our laboratory has begun to connect phenotype correlations with biological differences. Variant *MC1R* alleles show direct correlations between the biochemical signalling properties of the encoded receptor and the red hair fair skin pigmentation phenotype. We have established a range of clonal melanocyte cultures derived from donor skin tissue characterised for three causal SNPs within *SLC45A2*, *SLC24A5* and *OCA2*, and have assessed their impact on melanin content as well as tyrosinase enzyme activity. From a culmination of genetic and functional studies, it is apparent that a number of genes impacting melanosome biogenesis or the melanin biosynthetic pathway are candidates to explain the diversity seen in human pigmentation.

RESEARCH PROJECTS

- Understanding skin cancer risk phenotypes through studying the interaction of genes involved in skin, hair and eye colour
- Investigating eye colour as a genetic trait
- Undertaking parallel genetic and cellular analysis of 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

Cook, A.L., *et al.* (2009). Analysis of cultured human melanocytes based on polymorphisms with the SLC45A2/MATP, SLC24A5/NCKX5 and OCA2/P loci. *Journal of Investigative Dermatology* **129**: 392-405.

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Smith, A.G., Luk, N., Newton, R.A., Roberts, D.W., Sturm, R.A., and Muscat, G.E.O. (2008). MC1R signalling markedly induces the expression of the NR4A nuclear receptor subgroup in melanocytic cells. *Journal of Biological Chemistry* **283**: 12564-12570.

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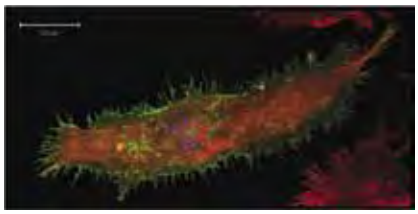
DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Pathogen surveillance, innate immunity and inflammation

MATT SWEET



Cell surface expression of a novel macrophage-specific protein.

The major research themes of this group are innate immunity and inflammation. In mammals, cells of the innate immune system use several families of pattern recognition receptors (PRRs) to detect specific structural components displayed by invading microorganisms. The Toll-like Receptors (TLRs) are the most widely studied of the PRRs. TLRs, as well as other PRRs, enable the innate immune system to contain and destroy invading microorganisms, and to activate an appropriate acquired immune response. We study TLR-dependent and TLR-independent mechanisms by which macrophages sense and respond to invading pathogens by focusing on recognition of whole pathogens (e.g. *Salmonella* Typhimurium, Uropathogenic *E. coli*), as well as individual microbial components (e.g. lipopolysaccharide, bacterial CpG-containing DNA). PRRs also detect endogenous host ligands that are present in inflammatory disease settings, for example in response to cell damage. Thus, PRRs are essential for host defence against invading microbes, but also contribute to the pathology of many inflammatory diseases.

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), and the functions of TLR target genes, which ultimately promote inflammation and antimicrobial responses. Research highlights for 2009 include: (1) the identification of the cellular detection system for foreign cytoplasmic DNA (a protein known as AIM2), as well as a negative regulator of the pathway (a related protein called p202); (2) the identification of a specific histone deacetylase (HDAC7) that acts as a signalling molecule in TLR-driven inflammatory pathways; (3) the identification of key species differences in TLR response pathways; and (4) the characterisation of a potent and selective inhibitor of a specific prostaglandin synthase that drives inflammation. Our immediate research goals are to further define the role of individual histone deacetylases in promoting inflammation, and to characterise novel TLR-activated anti-microbial pathways in human macrophages. Our ultimate objectives are to develop new approaches to targeting inflammatory diseases, and to generate key insights into the mechanisms used by the host innate immune system to destroy invading microbes.

RESEARCH PROJECTS

- Characterising the role of specific histone deacetylases in Toll-like Receptor-mediated inflammatory responses
- Human macrophage anti-microbial responses against *Salmonella* Typhimurium and Uropathogenic *E. coli*
- 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
- Characterisation of novel inhibitors of prostaglandin synthases for anti-inflammatory applications

KEY PUBLICATIONS

Roberts, T.L., Idris, A., Dunn, J.A., Kelly, G.M., Burnton, C.M., Hodgson, S., Hardy, L., Garceau, V., Sweet, M.J., Ross, I.L., Hume, D.A., and Stacey, K.J. (2009). HIN-200 proteins regulate caspase activation in response to foreign cytoplasmic DNA. *Science* **323**: 1057-1060.

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Schroder, K., Spille, M., Pilz, A., Lattin, J., Bode, K.A., Burrows, A.D., Ravasi, T., Weighardt, H., Stacey, K.J., Decker, T., Hume, D.A., Dalpke, A., and Sweet, M.J. (2007). Differential effects of CpG DNA on IFNb induction and STAT1 activation in murine macrophages versus dendritic cells: alternatively activated STAT1 negatively regulates toll-like receptor signaling in macrophages. *Journal of Immunology* **179**: 3495-3503.

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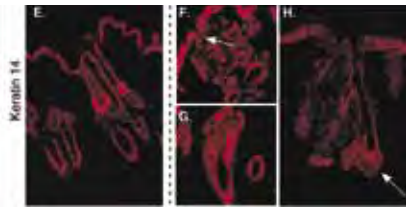
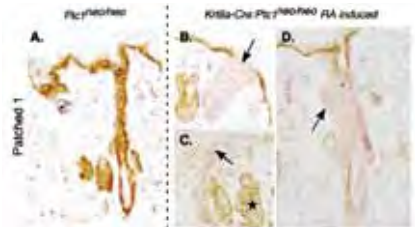
DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Tissue repair and cancer

BRANDON WAINWRIGHT



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



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.

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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Developmental genes and human disease

CAROL WICKING

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, suggesting a conservation of the molecular development of these structures. We are investigating the molecular aspects of limb and face development with a particular focus on the role of the hedgehog signalling pathway in these processes.

We primarily use the mouse as a model system and have conditionally deleted the hedgehog receptor patched in the limb and face at varying stages of development. In the limb this has led to patterning defects as well as uncovering a novel role in the very earliest stages of skeletal development. In 2009 we completed the analysis of the patterning defects, thus contributing to our understanding of how digit number and identity are determined. These studies are important because the limb has long been considered a paradigm for organogenesis, and findings in this system can often be extrapolated to other organs.

Over the past several years the primary cilium has emerged as a novel cellular compartment required for hedgehog signalling. The primary cilium is a single non-motile microtubule-based organelle that protrudes from the surface of virtually every vertebrate cell. Aberrant formation of the cilium leads to a range of human disorders known as ciliopathies, and studies in mice have revealed a firm link between cilia and hedgehog signalling. In collaboration with Emma Whitelaw at QIMR, we have identified a mouse with an N-ethyl-N-nitrosourea (ENU) induced point mutation in a cilia-related gene. Analysis of this mouse is yielding valuable insight into the role of the primary cilium in hedgehog signalling and disease.

RESEARCH PROJECTS

- Conditional knockout of the hedgehog receptor patched in the developing mouse limb causes novel patterning defects
- 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
- Identification and analysis of genes regulated by the transcription factor Gli3 in the developing limb
- Using an ENU-induced mutation in the mouse to investigate the role of the primary cilium in hedgehog signalling and disease

KEY PUBLICATIONS

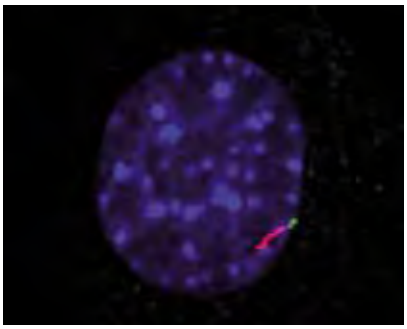
Butterfield, N.C., Metzis, V., McGlinn, E., Bruce, S.J., Wainwright, B.J., and Wicking, C. (2009). Patched1 is a crucial determinant of asymmetry and digit number in the vertebrate limb. *Development* **136**: 3515-3524.

Town, L., McGlinn, E., Fiorenza, S., Metzis, V., Butterfield, N.C., Richman, J.M., and Wicking, C. (2009). The metalloendopeptidase gene *Pitrm1* is regulated by hedgehog signalling in the developing mouse limb and is expressed in muscle progenitors. *Developmental Dynamics* **238**: 3175-3184.

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.

McGlinn, E., Richman, J.M., Metzis, V., Town, L., Butterfield, N.C., Wainwright, B.J., and Wicking, C. (2008). Expression of the NET family member *Zfp503* is regulated by hedgehog and BMP signaling in the limb. *Developmental Dynamics* **237**: 1172-1182.

Msx1 gene expression in the embryonic mouse limb.



Immunofluorescence analysis to detect the primary cilium in cultured cells.

Bennetts, J.S., Rendtorff, N.D., Simpson, F., Tranebjaerg, L., and Wicking, C. (2007). The coding region of *TP53INP2*, a gene expressed in the developing nervous system, is not altered in a family with autosomal recessive non-progressive infantile ataxia on chromosome 20q11-q13. *Developmental Dynamics* **236**: 843-852.

Simpson, F., Lammerts van Bueren, K., Butterfield, N., Bennetts, J.S., Bowles, J., Adolphe, C., Simms, L.A., Young, J., Walsh, M.D., Leggett, B., Fowles, L.F., and Wicking, C. (2006). The PCNA-associated factor KIAA0101/p15PAF binds the potential tumour suppressor product p33ING1b. *Experimental Cell Research* **312**: 73-85.

LAB MEMBERS

Research Officers: Dr Natalie Butterfield, Dr Steve Bruce

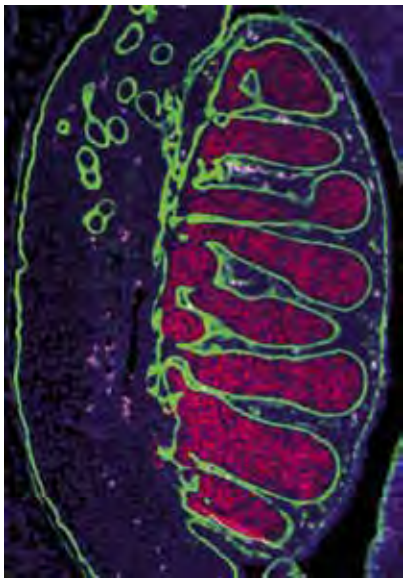
Research Assistants: Rachael Barry, Andrew Courtney

PhD Students: Liam Town, Vicki Metzis

DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Towards a new understanding of the reproductive system: from non-coding RNAs to disease

DAGMAR WILHELM



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.

In addition, 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 processing and functional mechanisms of small RNAs in fish?

RESEARCH PROJECTS

- Characterisation of the role of miR-202 during embryonic development
- Identification and analysis of novel microRNAs involved in gonad development
- Functional characterisation of uaRNAs during embryonic development
- Studying the cellular and molecular regulation of foetal ovary development
- Characterisation of RNAi in fish

KEY PUBLICATIONS

Wilhelm, D. (2007). R-spondin1 – the long-missing, female-determining gene? *BioEssays* **29**: 314-318.

Wilhelm, D., Hiramatsu, R., Mizusaki, H., Widjaja, L., Combes, A.N., Kanai, Y., and Koopman, P. (2007). SOX9 regulates prostaglandin D synthase gene transcription in vivo to ensure testis development. *Journal of Biological Chemistry* **282**: 10553-10560.

Wilhelm, D., Palmer, S., and Koopman, P. (2007). Sex determination and gonadal development in mammals. *Physiological Reviews* **87**: 1-28.

Wilhelm, D., and Koopman, P. (2006). The making of maleness: Towards an integrated view of male sexual development. *Nature Reviews Genetics* **7**: 620-631.

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 Assistants: Vy Truong, Huijun Chen, Alexandra Schulz, Elanor Wainwright

PhD Student: Lindsey McFarlane

Occupational Trainee: Antje Fitzner

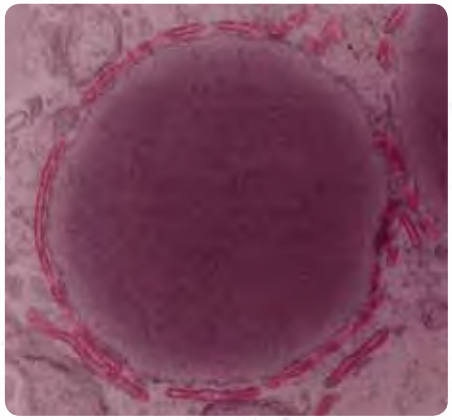
Undergraduate Students: Joanna Rakoczy, Tahlia Whiting, Caillan Crowe-McAuliffe

IMB RESEARCHERS

The IMB is a highly collaborative environment where researchers from different fields combine to contribute to strategic research programs investigating the basis of growth and development at the genetic, molecular, cellular and organ levels.

Only by understanding the complex molecular and cellular events that occur throughout a normal human life can scientists understand abnormalities responsible for many common human diseases and to find treatments for them.

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 Genomics and Computational Biology); 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. A major funding achievement in 2009 was the successful application to the Australian Cancer Research Foundation to establish the ACRF Cancer Biology Imaging Facility. Led by Professor Jenny Stow, this $2.5 million grant will fund a major expansion of the IMB's armamentarium in light and confocal microscopy and image analysis. This technology is at the forefront of systems cell biology and complements the IMB's expertise in electron microscopy, its collaboration with the Centre for Microscopy and Microanalysis, and its expertise in high-throughput screening and computational image analysis. We anticipate that the ACRF Cancer Biology Imaging Facility will provide a unique resource for all divisions of the Institute, and for colleagues in the UQ and national scientific communities.

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 and on the Research Grants committee of the HFSP; 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 co-chair of the 2009 Hunter Cellular Biology Meeting and the 2009 Gordon Research Conference on Cell Contact & Adhesion.

Group leaders of the Division received a variety of honours during 2009. Professor Parton was awarded a prestigious Australia Fellowship of the NHMRC and elected Fellow of the Australian Academy of Science. Professor Kirill Alexandrov received a senior Future Fellowship of the ARC. Alpha Yap was promoted to full Professor at The University of Queensland and Professor Stow was the Davson Distinguished Lecturer for the American Physiological Society. The presence of the Division was also apparent at many major national and international conferences in 2009. These include ComBio2009 (Parton, Alexandrov, Teasdale), Hunter Cellular Biology Meeting (Alexandrov, Parton, Stow, Collins), Gordon Research Conferences (Yap) and Keystone Meetings (Yap).

The Division hosted several distinguished national and international visitors who presented IMB Seminars in 2009. These included Professor Mark Marsh (University College London, U.K.), Assistant Professor James Bear (Howard Hughes Medical Institute and University of North Carolina, Chapel Hill, U.S.A.), Professor Leann Tilley (Latrobe University, Victoria) and Professor Herbert Waldemann (Max-Planck Institute, Dortmund, Germany). 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 Dr 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. A successful innovation for 2009 was the inclusion in the Forum programme of an external lecturer chosen and sponsored by students and post-doctoral fellows in the Division. Dr Andrew Brooks, Carolin Offenhauser and Dr Markus Kerr formed the organising committee that hosted Professor David James (Garvan Institute – and an alumnus of IMB) who presented a research seminar in the Forum and conducted mentoring sessions with junior staff of the Division. This will undoubtedly form a valuable part of the annual CBF schedule in years to come.

Biochemistry of protein prenylation

KIRILL ALEXANDROV

Over the past 15 years, it has become increasingly clear that post-translational modification with isoprenoids is a widespread phenomenon, affecting up to two percent of proteins in eukaryotic cells. In all cases that have been studied, such a modification has been shown to be crucial for protein function by modulating protein–lipid or protein–protein interactions. Most of the prenylated proteins are GTPases that have key functions in signal-transduction pathways. 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 human pathologies. Currently, one of the main focuses in prenylation research is to elucidate the causal relationship between those defects and the clinical outcome in patients.

Our aim is to understand the molecular mechanisms underlying regulation of protein prenylation both on mechanistic and systemic levels. We use a combination of biophysical methods such as fluorescent spectroscopy and X-ray crystallography with methods of cell and chemical biology to obtain a global model of prenylation regulation in eukaryotic cells.

RESEARCH PROJECTS

- Proteome-wide analysis of protein prenylation and its variation in human diseases
- Understanding of the mechanisms regulating protein prenylation machinery
- Identification of small molecules modulating prenylation and localisation of RabGTPases
- Quantitative analysis of protein:protein protein:small molecule interactions using a novel in vitro protein expression system

KEY PUBLICATIONS

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.

Nguyen, U.T., Guo, Z., Delon, C., Wu, Y., Deraeve, C., Fränzel, B., Bon, R.S., Blankenfeldt, W., Goody, R.S., Waldmann, H., Wolters, D., and Alexandrov, K. (2009). Analysis of the eukaryotic prenylome by isoprenoid affinity tagging. *Nature Chemical Biology* **4**: 227-235.

Guo, Z., Wu, Y.W., Das, D., Delon, C., Cramer, J., Yu, S., Thuns, S., Lupilova, N., Waldmann, H., Brunsveld, L., Goody, R.S., Alexandrov, K., and Blankenfeldt, W. (2008). Structures of RabGGTase-substrate/product complexes provide insights into the evolution of protein prenylation. *EMBO Journal* **27**: 2444-2456.

Wu, Y., Tan, K.-T., Waldmann, H., Goody, S.R., and Alexandrov, K. (2007). Quantitative analysis of the interaction of prenylated Rab proteins with REP and GDI explains the requirement for both regulators in Rab function. *Proceedings of the National Academy of Sciences USA* **104**: 12294-12299.

Pylypenko, O., Rak, A., Durek, T., Kushnir, S., Dursina, B.E., Thomae, N.H., Constantinescu, A.T., Brunsveld, L., Watzke, A., Waldmann, H., Goody, R.S., and Alexandrov, K. (2006). Structure of doubly prenylated Ypt1:GDI complex and the mechanism of GDI-mediated Rab recycling. *EMBO Journal* **25**: 13-23.

Novel selective inhibitor of Rab prenylation bound to the active site of RabGGTase.

Surface representation of structure of β-subunit of RabGGTase.

LAB MEMBERS

Research Officers: Dr Daniel Abankwa, Dr Sergey Mureev, Dr Viktor Stein, Dr Andrew Goodall

Research Assistants: Martina Franke, Virajitha Rajagopalan, Veronika Schreiber, Regina Hartmann

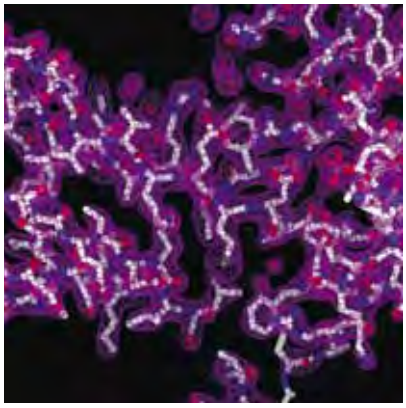
PhD Students: Oleksiy Kovtun, Zakir Tnimov, Marta Kubala

DIVISION OF MOLECULAR CELL BIOLOGY

Cellular trafficking at atomic resolution

BRETT COLLINS

Crystals of the retromer subunit VPS26B.



Electron density for the VPS26B subunit of retromer.

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 are 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.

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

Malintan, N.T., Nguyen, T.H., Han, L., Latham, C.F., Osborne, S.L., Wen, P.J., Joo, L.S., Sugita, S., Collins, B.M., and Meunier, F.A. (2009). Abrogating Munc18-1-SNARE interaction has limited impact on exocytosis in PC12 cells. *Journal of Biological Chemistry* **284**: 21637-21646.

Collins, B.M. (2008). The structure and function of the retromer protein complex. *Traffic* **9**: 1811-1822.

Collins, B.M., Norwood, S.J., Kerr, M.C., Mahony, D., Seaman, M.N.J., Teasdale, R.D., and Owen, D.J. (2008). Structure of Vps26B and mapping of its interaction with the retromer protein complex. *Traffic* **9**: 366-279.

Miller, S.E., Collins, B.M., McCoy, A.J., Robinson, M.S., and Owen, D.J. (2007). A SNARE-adaptor interaction is a new mode of cargo recognition in clathrin-coated vesicles. *Nature* **450**: 570-574.

Collins, B.M., Skinner, C.F., Watson, P.J., Seaman, M.N.J., and Owen, D.J. (2005). Vps29: a phosphoesterase fold that acts as a protein-protein interaction scaffold for assembly of retromer. *Nature Structural & Molecular Biology* **12**: 594-602.

Collins, B.M., Watson, P.J., and Owen, D.J. (2003). The structure of the GGA1-GAT domain reveals the molecular basis for ARF binding and membrane recruitment of GGAs. *Developmental Cell* **4**: 321-332.

Collins, B.M., McCoy, A.J., Kent, H.M., Evans, P.R., and Owen, D.J. (2002). Molecular architecture and functional model of the endocytic AP2 complex. *Cell* **109**: 523-535.

LAB MEMBERS

Research Officers: Dr Suzanne Norwood, Dr Ramya Mandyam

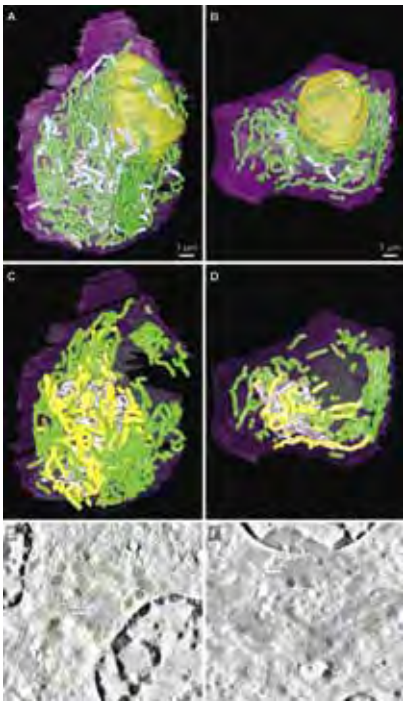
Research Assistants: Jasmine Davis, Natasha Chaudhary

PhD Students: Daniel Shaw, Rajesh Ghai

DIVISION OF MOLECULAR CELL BIOLOGY

Structure-function studies of the pancreatic beta cell – mapping insulin biosynthesis and trafficking in situ in 3D at the nanoscale

BRAD MARSH



The beta cells of the endocrine pancreas are the sole source of insulin in mammals; their malfunction or death manifests as the set of diseases broadly referred to as *diabetes*. Diabetes is one of Australia's national health priority areas and *type 1 diabetes* in particular has been identified as one of Australia's fastest-growing chronic childhood diseases that often results in premature death through health complications. Currently, *type 1 diabetes* cannot be prevented, and a cure remains to be found.

Our research is aimed at quantitatively mapping beta cell organisation in 3D under healthy versus disease conditions, and across multiple scales - from molecule to cell to tissue - using a high-resolution 3D imaging approach called 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 the nanometre scale. 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.

Over the past 18 months, we have worked to combine our various ET methods - which allow us to map large cellular volumes from beta cells in pancreatic islet tissue - with complementary biochemical approaches and correlative light microscopy studies of cell lines to elucidate the fundamental molecular mechanisms that regulate the cellular machinery underpinning the transport, sorting and packaging of protein traffic in mammalian cells.

KEY PUBLICATIONS

Dobrucki, W.L., Marsh, B.J., and Kalinowski, L. (2009). Elucidating structure-function relationships from molecule-to-cell-to-tissue: from research modalities to clinical realities. *Journal of Physiology and Pharmacology* **60** (Supp 4): 83-93.

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.

LAB MEMBERS

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

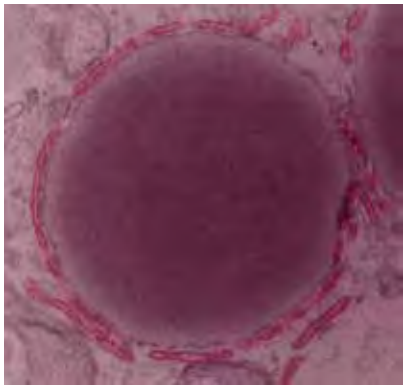
Research Assistant: Garry Morgan

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

DIVISION OF MOLECULAR CELL BIOLOGY

The cell surface in health and disease

ROB PARTON



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 have particularly focused our attention on caveolae, a specialised domain of the cell surface with a distinct structure. Caveolae have been implicated in regulation of cell growth and in maintaining the balance of lipids in the cell. In addition, caveolae and caveolins, the major proteins of caveolae, have been implicated in a number of disease states including tumour formation, atherosclerosis, and muscular dystrophy. To study caveolae function and, in particular, the link between lipid regulation and cancer, we are using caveola-null mice, cells lacking caveolins, 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. We have recently discovered a family of caveolar coat proteins that regulate caveola formation and function. 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

- Characterisation of the structure and function of a new family of caveolar coat proteins
- 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 and caveolin-3 in muscle: analysing the role of caveolin-3 and 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 *E. coli*: characterisation of novel nanovesicles and their use as drug delivery vehicles

KEY PUBLICATIONS

Bastiani, M., Liu, L., Hill, M.M., Jedrychowski, M.P., Nixon, S.J., Lo, H.P., Abankwa, D., Luetterforst, R., Fernandez-Rojo, M., Breen, M.R., Gygi, S.P., Vinten, J., Walser, P.J., North, K.N., Hancock, J.F., Pilch, P.F., and Parton, R.G. (2009). MURC/Cavin-4 and cavin family members form tissue-specific caveolar complexes. *Journal of Cell Biology* **185**: 1259-1273.

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.

Fernandez, M.A., Albor, C., Ingelmo-Torres, M., Nixon, S.J., Ferguson, C., Kurzchalia, T., Tebar, F., Enrich, C., Parton, R.G., and Pol, A. (2006). Caveolin-1 is essential for liver regeneration. *Science* **313**: 1628-1632.

Kirkham, M., Fujita, A., Chadda, R., Nixon, S.J., Kurzchalia, T.V., Sharma, D.K., Pagano, R.E., Hancock, J.F., Mayor, S., and Parton, R.G. (2005). Ultrastructural identification of uncoated caveolin-independent early endocytic vehicles. *Journal of Cell Biology* **168**: 465-476.

LAB MEMBERS

Senior Research Officer: Dr Sally Martin

Research Officers: Dr Manuel Fernandez, Dr Susan Nixon, Dr Lars Kuerschner#, Dr Harriet Lo

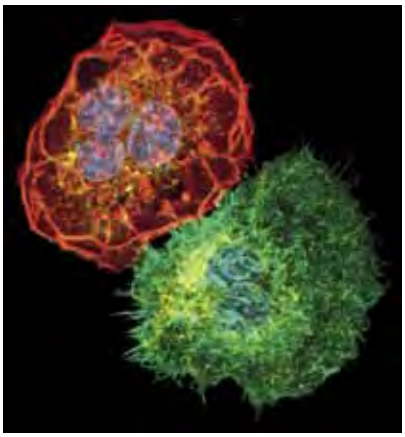
Research Assistants: Rachel Hancock*, Charles Ferguson, James Rae, Satomi Okano, Nicole Schieber*, Kwang-Jin Cho#

PhD Students: Mark Howes, Michele Bastiani, Samantha Murphy, Carol Kistler, Nick Ariotti, Natalya Leneva#

part of year
* part-time

Protein trafficking in human disease

JENNY STOW



Our research group studies protein trafficking in human and animal cells. Trafficking underlies all cellular functions and is associated with all human diseases. Our current aim is to uncover the genes, molecules and subcellular compartments that function in trafficking and protein secretion. The secretion of cytokines allows cells of the immune system to communicate and to mount inflammatory responses. We are studying the secretion of pro-inflammatory cytokines from macrophages. Understanding cytokine trafficking and secretion may lead to the development of new therapeutic strategies for chronic inflammatory diseases. Trafficking regulators including Rab and SNARE proteins are mutated in a range of human diseases, and our collaborative projects with other Centres aim to reveal resulting cellular defects and to devise future therapeutic interventions. Gene expression arrays, FACS and biochemical approaches are used in our work. Gene knockouts or mutations in mice are used in our discovery pipeline. Since trafficking is a highly dynamic process, this research has been greatly enhanced by the development of fluorescent probes and microscopic techniques for 3D and 4D imaging in living cells. Live cell imaging, combined with other forms of microscopy, has become a major core technology for the research in our group. As cell trafficking pathways are usurped by invading bacteria in infectious diseases, our studies also focus on the phagocytosis and endocytosis of various bacterial pathogens, with the aim of identifying targets for new antimicrobials. Finally, in epithelial cells we study the polarised trafficking of membrane and adhesion proteins. E-cadherin is an essential cell-cell adhesion protein, a determinant of cell and tissue polarity and a vital tumour suppressor. A main goal of this work is to understand how E-cadherin trafficking functions in morphogenesis and cancer progression.

RESEARCH PROJECTS

- Characterisation of secretory pathways for cytokines and antimicrobial proteins in macrophages
- New targets for regulating cytokine secretion in arthritis and inflammatory bowel disease
- Characterisation of the structure and function of recycling endosomes in secretory and endocytic pathways
- Gene expression, mutations and functions of Rabs and SNAREs in secretory pathways
- Granule and lysosomal-mediated secretion in immune cells
- Phagocytosis and trafficking of bacterial pathogens
- Imaging live cells to create 3D and 4D maps of trafficking pathways: fluorescence imaging, computer modelling and animation

KEY PUBLICATIONS

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. *Proceedings of the National Academy of Sciences USA* **105**: 3351-3356.

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.

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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 Marion Desclozeaux, Dr Ryo Misaki, Dr Jason Kay

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

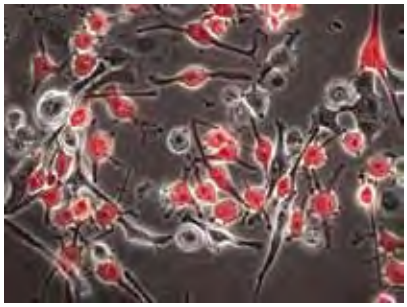
Research Coordinator: Dr Fiona Wylie

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

DIVISION OF MOLECULAR CELL BIOLOGY

Role of growth hormone and related cytokines in growth, cancer, diabetes and obesity

MIKE WATERS



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

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 six 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., *et al.* (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., *et al.* (2008). How growth hormone controls growth, obesity and sexual dimorphism. *Trends in Genetics* **24**: 41-47.

Rowlinson, S.W., *et al.* (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., *et al.* (2008). Altered metabolism of growth hormone receptor mutant mice: a combined NMR metabonomics and microarray study. *PLoS ONE* **3**: e2764.

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Rowland, J.E., *et al.* (2005). In vivo analysis of growth hormone receptor signalling domains and their associated transcripts. *Molecular and Cellular Biology* **25**: 66-77.

LAB MEMBERS

Research Officers: Dr Andrew Brooks, Dr Tim McPhee, Dr Johanna Barclay, Dr Daniel Blackmore

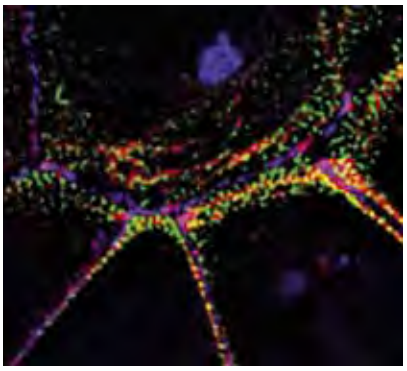
Research Assistants: Kathryn Tunny, Tania Brooks

PhD Students: Caroline Nelson, Yash Chhabra

Visiting Fellow: Mayumi Ishikawa

Cadherin adhesion and tissue organisation in health and disease

ALPHA YAP



Cells are the building blocks of our bodies. Interactions between different cells are important to shape our developing bodies, and 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.

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

Den Elzen, N., Buttery, C.V., Maddugoda*, M.P., Ren*, G., and Yap, A.S. (2009). Cadherin adhesion receptors orient the mitotic spindle during symmetric cell division in mammalian epithelia. *Molecular Biology of the Cell* **20**: 3740-3750. (*Equal contributions)

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.

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Shewan, A.M., Maddugoda, M., Kraemer, A., Stehbens, S.J., Verma, S., Kovacs, E.M., and Yap, A.S. (2005). Myosin 2 is a key target for Rho kinase necessary for the local concentration of E-cadherin at cell-cell contacts. *Molecular Biology of the Cell* **16**: 4531-4542.

LAB MEMBERS

Senior Research Officer: Dr Eva Kovacs

Research Officers: Dr Gang Albert Ren, Dr Michael Smutny, Dr Aparna Ratheesh

Research Assistants: Suzie Verma, Hayley Cox

PhD Students: Angela Jeanes, Robert McLachlan, Sabine Mangold, Vincent Leong

Honours Student: Selwin Wu

IMB RESEARCHERS

The IMB is a highly collaborative environment where researchers from different fields combine to contribute to strategic research programs investigating the basis of growth and development at the genetic, molecular, cellular and organ levels.

Only by understanding the complex molecular and cellular events that occur throughout a normal human life can scientists understand abnormalities responsible for many common human diseases and to find treatments for them.

Division of CHEMISTRY AND STRUCTURAL BIOLOGY

Top: David Craik (second from left) receives an Honorary Doctorate from the University of Kalmar in Sweden.

Above: Jenny Martin receives ARC Laureate Fellowship in Canberra.

In 2009 the Division's research in *chemistry*, *structural biology* and *pharmacology* was lead by ten Group Leaders (Professors David Fairlie, Jenny Martin, Paul Alewood, David Craik, Richard Lewis, Rob Capon, Glenn King, and Matt Cooper; Associate Professors Mark Smythe and Ben Hankamer) and 5 Affiliates (Professors Alan Mark, Bostjan Kobe, Istvan Toth, Paul Young, and Kirill Alexandrov).

Division of CHEMISTRY & STRUCTURAL BIOLOGY

Fellowship & Award Highlights: Professor Martin won a prestigious ARC Laureate Fellowship ($3.1M, 2010-2014). Professor Cooper took up an NHMRC Australia Fellowship ($4M, 2009-2013). Professor Craik was awarded an Honorary Doctorate from the University of Kalmar (Sweden) and an NHMRC Principal Research Fellowship. Professors Lewis and Alewood were coinvestigators on an NHMRC Program grant ($6.4M, 2010-2014) to develop peptides for the treatment of pain. Drs Vetter (Lewis Group) and Rosengren (Craik Group) won NHMRC Career Development Awards. Dr Josh Mylne won a University of Queensland Research Excellence Award. Professor Alexandrov was awarded an ARC Future Fellowship, Professor Kobe a new joint NHMRC program grant ($9.1M, 2010-2014) on bacterial pathogenesis, Professor Toth won the 2009 RACI Adrian Albert Award and Professor Young the 2009 Asia Pacific Medical Virology Excellence Award.

ARC & NHMRC Project Grants: The Division's Group Leaders were lead investigators in six new ARC Discovery grants ($3.3M, 60% success) and four new NHMRC project grants ($2.3M, 50% success) for commencement in 2010. Postdoctoral researcher Dr Richard Clark was CIA on another NHMRC project grant. New ARC grants will discover new toxins from cone snails (Alewood), study interactions between cone snail venom and a receptor in nerve cell signalling (Clark), design drugs to bind GPCRs on cell surfaces and study intracellular signalling (Fairlie, Cooper), convert helical turns from proteins into small bioactive molecules (Fairlie), use spider venom to develop insecticides (King), investigate structures of photosynthetic proteins (Hankamer), and study post-translational modifications of proteins critical for cell functions (Alexandrov). New NHMRC grants will develop new pain drugs from Australian marine natural products (Capon), and from cone snail venoms (Craik, Clark), study inhibition of metabolic syndrome in diet-induced obese rats (Fairlie) and modify drugs to combat resistant *Staphylococcus aureus* (Cooper).

Research Activities: The Division continued research programs in: (i) the design of organic compounds, including those that target enzymes, membrane and cellular signalling proteins; (ii) the chemical discovery of biologically active natural products (proteins, peptides, organic) from venomous invertebrates, plants, bacteria and marine organisms; (iii) the determination of crystal and solution structures of proteins and protein-ligand complexes using x-rays and NMR spectroscopy; and (iv) mechanistic studies using enzymology, biochemistry, and molecular (cells) and experimental (animals) pharmacology for small molecules that intervene in mammalian physiology and disease. The Division discovered small molecules with anti-viral, anti-inflammatory, anti-parasitic, anti-cancer, anti-neurodegenerative and anti-obesity properties. Some new Division research initiatives in 2009-2010 are:

Infectious Disease The Division has made significant new commitments to studying infectious diseases. Professor Martin's ARC Laureate Fellowship will focus on designing antibacterial drugs that act on oxidoreductase enzymes associated with disulfide bond formation and virulence factors. Professor Cooper's NHMRC Australia Fellowship will focus on development of antibacterial drugs. Professor Kobe's joint NHMRC program grant involves a different team working on pathogenesis, treatment and prevention of bacterial infections. Professors Fairlie and Young have three NHMRC project grants that are producing picomolar fusion inhibitors of Respiratory Syncitial Virus, nanomolar protease inhibitors of West Nile virus, and sub-micromolar fusion inhibitors of Dengue virus.

Natural Product Drug Discovery New grants to Professors Alewood and Lewis (conotoxins), King (spider peptides), Capon (marine and bacterial natural products) and Craik (cyclic peptides from plants, cone snails) will provide new probes for studying biological processes and may result in leads for drug development.

Diabetes and Obesity Professor Martin commenced an NHMRC program ($10.6M, 2009-2013) with Garvan Institute researchers to investigate pathways to diabetes prevention. Professor Fairlie commenced NHMRC-funded research on anti-inflammatory drugs that regulate lipid signalling in obese rats.

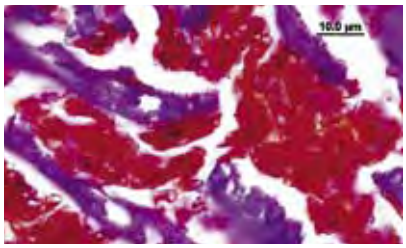
Biofuels and Microalgal Reactors Associate Professor Ben Hankamer led the Solar Bio-Fuels Consortium investigating structural biology, protein and genetic engineering, and environmental conditions associated with different microalgal cell lines that produce hydrogen and other biofuels. This is an applied scientific research program targeted at fast-track commercialisation and rapid industry uptake.

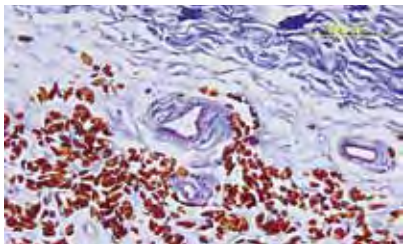
Other Highlights: Professor Martin was appointed a Member of ARC College of Experts. Professor Capon was elected to UQ Academic Board. Professor Fairlie's research on helical turns was highlighted in Chemical Engineering News. Professor Glenn King's research on toxins was featured on the TV program Catalyst and Channel 7 news. The Division (in conjunction with RMIT) received $424k from ARC-LIEF to establish a drug screening facility. Professor Kobe's group developed a bioinformatic tool (Predikin) that showed the best performance in the kinase section of the 2009 DREAM4 Peptide Recognition Prediction challenge, an international competition of computational specificity prediction methods. In 2009, most of the Division's Group Leaders each gave multiple invited plenary lectures and seminars around the world, including North America, Europe, South America and South East Asia.

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

Design and discovery of bioactive peptides and proteins

PAUL ALEWOOD





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. This has led to the development of three new classes of drugs addressing chronic pain and congestive heart failure.

RESEARCH PROJECTS

- Identification and characterisation of novel peptides from Australian animals that target ion channels, transporters and 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

Beatrix, M., Ueberheide, D.F., Alewood, P.F., and Chait, B.T. (2009). Rapid, sensitive analysis of cysteine rich peptide venom components. *Proceedings of the National Academy of Sciences USA* **106**: 6910-6915.

Mobli, M., Dantas de Araújo, A., Lambert, L., Pierens, G., Windley, M.J., Nicholson, G.M., Alewood, P.F., and King, G.F. (2009). Direct visualisation of disulfide bonds using NMR. *Angewandte Chemie* **48**: 9312-9314.

Vernall, A.J., Cassidy, P., and Alewood, P.F. (2009). A single α-helical turn stabilized by replacement of an internal hydrogen-bond with a covalent ethylene bridge. *Angewandte Chemie International Edition* **48**: 5675-5678.

Jin, A.H., Daly, N.L., Nevin, S.T., Wang, C.I., Dutertre, S., Lewis, R.J., Adams, D.J., Craik, D.J., and Alewood, P.F. (2008). Molecular engineering of conotoxins: the importance of loop size to alpha-conotoxin structure and function. *Journal of Medicinal Chemistry* **51**: 5575-5584.

Yan, W.X., Armishaw, C., Goyette, J., Yang, Z., Cai, H., Alewood, P., and Geczy, C.L. (2008). Mast cell and monocyte recruitment by S100A12 and its hinge domain. *Journal of Biological Chemistry* **283**: 13035-13043.

Lewis, R.J., Schroeder, C.I., Ekberg, J., Nielsen, K.J., Loughnan, M., Thomas, L., Adams, D., Drinkwater, R., Adams, D.J., and Alewood, P.F. (2007). Isolation and structure-activity of mu-conotoxin TIIIA. A Potent Inhibitor of Tetrodotoxin-Sensitive Voltage-Gated Sodium Channels. *Molecular Pharmacology* **71**: 676-685.

Armishaw, C.J., Daly, N., Nevin, S., Adams, D.J., Craik, D.J., and Alewood, P.F. (2006). Alpha-selenoconotoxins: A new class of potent alpha 7 neuronal nicotinic receptor antagonists. *Journal of Biological Chemistry* **281**: 14136-14143.

Sharpe, I., Gehrmann, J., Loughnan, M., Thomas, L., Adams, D., Atkins, A., Craik, D.J., Adams, D., Alewood, P.F., and Lewis, R.J. (2001). Two new classes of conopeptides inhibit the alpha1-adrenoceptor and the noradrenaline transporter. *Nature Neuroscience* **4**: 902-907.907.

LAB MEMBERS

Research Manager: Dianne Alewood

Senior Research Officers: John Holland, Lachlan Rash

Research Officers: Aline Dantas, Andrea Vernal, Tom Durek, Jean Jin, Markus Muttenthaler, Marion Loughnan

Research Assistants: Zoltan Dekan, Julie Klint

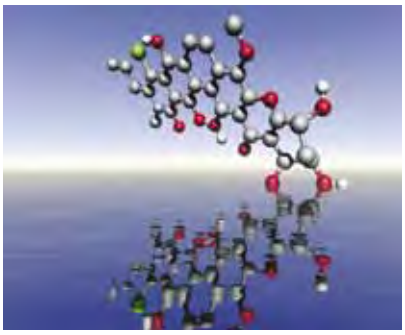
PhD Students: Rod Morales, Jen Smith, Kalyani Akondi, Simone Vink

Visiting Students: Klaus Nissen (University of Copenhagen), Alexis Depauw (University of Montpellier), Yesica Garcia Ramos (University of Barcelona), Amir Seddik (Utrecht University)

Visiting Fellows: Mehdi Varidi (University of Mashhad), Sulan Luo (Hainan University)

Biodiscovery: from biodiversity and biology, to bioactives and beyond

ROB CAPON



My research group focuses on the detection, isolation, characterisation, identification and evaluation of novel bioactive metabolites from Australian marine and terrestrial biodiversity. These metabolites span all known biosynthetic structure classes, including many molecules new to science, and their study requires the use of sophisticated chromatographic, spectroscopic and chemical technologies. Natural products uncovered during our investigations represent valuable new leads in the search for drugs with application in the fields of human and animal health and crop protection, and as molecular probes to better interrogate and understand living systems. To best capture and develop IMB and broader UQ biodiscovery capabilities, we have established the Biodiscovery@UQ network (www.biodiscovery.imb.uq.edu.au). Biodiscovery@UQ is a thematic networking initiative aimed at facilitating interdisciplinary access to bioactive natural extracts and chemistry, improving basic and applied science outcomes, and showcasing excellence in UQ biodiscovery-related research.

RESEARCH PROJECTS

- **Natural Products Chemistry:** the isolation and purification, and spectroscopic and chemical analysis, of secondary metabolites from marine and terrestrial plants, animals and microbes, with a view to better exploring and understanding "natural" chemical space.
- **Synthetic Organic Chemistry:** the synthesis of new bioactive natural products, to confirm, test and refine novel pharmacophores, to build knowledge of and prioritise new drug lead candidates, with a view to better exploring and understanding "synthetic" chemical space.
- **Microbial Metabolism:** the acquisition and fermentation of microbial biodiversity, to express silent secondary metabolite gene clusters, to better explore and make use of the full spectrum of "natural" chemical space defined by the microbial genome.
- **Chemical Ecology:** the detection, identification and evaluation of invasive pest (i.e. cane toads, insects) defensive secretions, toxins and pheromones, to improve our understanding of chemical ecology, to develop safe, effective and species-selective control solutions.
- **Biological Targets:** through a network of collaborators we have interests in developing new drug leads to target such indicators as infectious and neurodegenerative diseases, cancer, diabetes, obesity, pain and inflammation.

KEY PUBLICATIONS

Fremlin, L.J., Piggott, A.M., Lacey, E., and Capon, R.J. (2009). Cottoquinazoline A and cotteslosins A-B: Metabolites from an Australian marine-derived strain of *Aspergillus versicolor. Journal of Natural Products* **72**: 666-670.

Hayes, R.A., Piggott, A.M., Dalle, K., and Capon, R.J. (2009). Microbial biotransformation as a source of chemical diversity in cane toad steroid toxins. *Bioorganic and Medicinal Chemistry Letters* **19**: 1790-1792.

Raju, R., Piggott, A.M., Conte, M., Aalbersberg, W.G.L., Feussner, K., and Capon, R.J. (2009). Naseseazines A-B: A new dimeric diketopiperazine framework from a marine-derived actinomycete, *Steptomyces* sp. *Organic Letters* **11**: 3862-3865.

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Ratnayake, R., Fremlin, L.J., Lacey, E., Gill, J.H., and Capon, R.J. (2008). Acremolides A-D, lipodepsipeptides from an Australian marine-derived fungus, *Acremonium sp. Journal of Natural Products* **71**: 403-408.

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Zhang, H., Major, J.M., Lewis, R.J., and Capon, R.J. (2008). Phorbasins G-K: new cytotoxic diterpenes from a southern Australian marine sponge, *Phorbas* sp. *Organic and Biomolecular Chemistry* **6**: 3811-3815.

LAB MEMBERS

Personal Assistant: Nadine Coleman

Research Officers: Dr Frank Fontaine, Dr Angela Salim, Dr Andrew Piggott, Dr Hua Zhang

Research Assistant: Melissa Conte

PhD Students: Leith Fremlin, Mohammed El-Nagger, Walter Balansa, Raju Ritesh, Soumini Vijayasarathy, Fabien Plisson, Zeinab Khalil

Undergraduate Students: Michael Auld, Nathan Boase, Noor Daud, Tara Thambimuthu

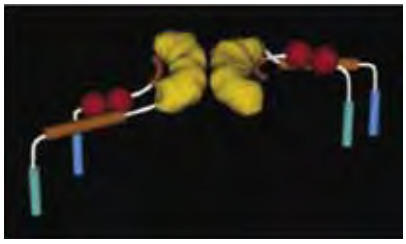
International Occupational Trainees: Kenneth Johansen (Denmark), Monika Hermann (Germany), Nicole Mueller (Austria), Helene Prevot (France), Flavie Rolland (France)

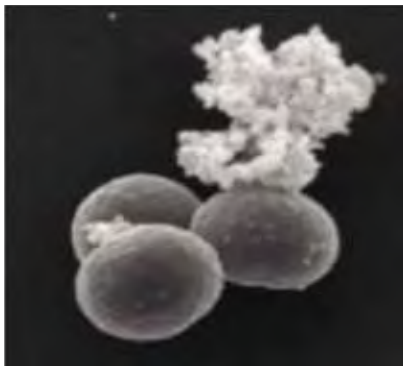
International Visiting Scientist: Dr David Myers (USA)

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

Chemical and biophysical tools for health management: diagnosis and therapy

MATT COOPER





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 are also developing cell-specific 'tags' to deliver drugs to the right target, focusing initially on antibiotics and then extending the approach to anti-cancer drugs.

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
- Dengue virus bioinformatics and antibodies for rapid early onset diagnosis of infection
- Integrated antibody and small molecule discovery for theranostic intervention against flaviviruses

KEY PUBLICATIONS

Label-free Biosensors: Techniques and Applications Ed. M.A. Cooper, *Cambridge University Press*, 2009, ISBN-13: 9780521711517.

Cooper, M.A. (2009). Signal transduction profiling using label-free biosensors. *Journal of Receptor and Signal Transduction Research* **29**: 224-233.

Natesan, M., Cooper, M.A., Tran, J., Rivera, V.R., and Poli, V.R. (2009). Quantitative detection of *Staphylococcal enterotoxin* B by Resonant Acoustic Profiling. *Analytical Chemistry* **81**: 3896-3902.

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Godber, B., *et al.* (2006). Direct quantification of analyte concentration by resonant acoustic profiling. *Clinical Chemstry* **51**: 1962-1972.

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Astrahan, P., *et al.* (2004). A novel method of resistance for influenza against a channel-blocking antiviral drug. *Proteins: Structure, Function, and Genetics* **55**: 251-257.

Cooper, M. (2002). Optical Biosensors in Drug Discovery. *Nature Reviews Drug Discovery* **1**: 515-528.

Cooper, M., *et al.* (2001). Direct and sensitive detection of a human virus by rupture event scanning. *Nature Biotechnology* **19**: 833-837.

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 Officer: Dr Craig Muldoon

Administrative Officer: Jan Pinder

Senior Research Officers: Dr Bernd Becker, Dr Rajaratnam Premraj, Dr Johannes Zuegg, Dr Tomislav Karoli, Dr Mark Butler

Research Officer: Dr Yujing Gong

Research Assistants: Soumya Ramu, Yuen Chi (Ann) Lam, Xiao (Johnny) Huang

Undergraduate Students: Noor Daud, Nor Hana Hamzah, June Lee

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

NMR and protein structure in drug design

DAVID CRAIK

A coneshell with the structure of the α-conotoxin, Vc1.1, determined in our laboratory.

Our group uses NMR spectroscopy to determine the structures of proteins that are important in drug-design programs 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. The proteins we study come from a range of animal and plant sources but are often involved in host defence. Examples include the conotoxins (venom components from marine snails) and the cyclotides (novel circular proteins from plants).

We have an interest in the discovery and structural characterisation of novel protein topologies. In particular 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 either by "grafting" new biologically-active epitopes onto them, or by stabilising them by cyclisation. We also study the protein-folding problem, i.e., how do proteins fold into the complex shapes that determine their functions?

Highlights of 2009 included our discovery that one class of circular proteins, known as cyclotides, forms discrete pores in membranes that are crucial for their insecticidal activity. These pores explain how cyclotides affect cells in insect guts. This work was published in the *Journal of Biological Chemistry*. We also characterised key cyclic peptide-processing enzymes (asparaginyl endoprotease and peptide disulfide isomerase) and identified potential common processing mechanisms of circular proteins across divergent plant families. In the conotoxin field we discovered that a crucial cluster of residues in conotoxin Vc1.1 mediates its activity at a specific subtype of the nicotinic acetylcholine receptor. This work is helping us to develop new drug leads for the treatment of pain.

Our group organised the 1st International Conference on Circular Proteins, which was held on Heron Island in October 2009. The conference was very successful and attracted leading experts on circular proteins from a dozen countries.

Some of the other projects on which we are currently working are outlined below:

We use computer modelling and NMR spectroscopy to design novel proteins that are stabilised for drug-design applications. We then synthesise them using solid-phase peptide synthesis or recombinant molecular biology methods. We currently have molecules under development for the treatment of multiple sclerosis, cardiovascular disease, cancer and chronic pain.

Our group discovered a family of proteins called cyclotides that are exceptionally stable and appear to be a natural combinatorial protein template. We undertake fieldwork in Australia and overseas for the collection of plant species so that we can explore the diversity and evolution of this novel protein family.

By unravelling the necessary elements for the processing and cyclisation of natural cyclic peptides we are working towards being able to transfer the precursors and processing machinery into a wide range of crop plants for pharming and crop protection initiatives.

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.

With our collaborator, Professor Marilyn Anderson of La Trobe University, we are studying the structure-activity relationships of naturally-occurring proteins involved in plant defense against insect attack.

RESEARCH PROJECTS

- Bioengineering circular proteins
- Discovering new circular proteins
- Studying the structure-activity relationships of toxins
- Development of new drugs for pain
- Development of new anticancer drugs
- Investigating plant proteinase inhibitors
- Elucidating the biosynthesis of circular proteins
- Development of structure-function relationships of relaxin family peptides

KEY PUBLICATIONS

Gunasekera, S., Foley, F.M., Clark, R.J., Sando, L., Fabri, L.J., Craik, D.J., and Daly, N.L. (2009). Engineering stabilized VEGF-A antagonists: Synthesis, structural characterization and bioactivity of grafted analogues of cyclotides. *Journal of Medicinal Chemistry* **51**: 7697-7704.

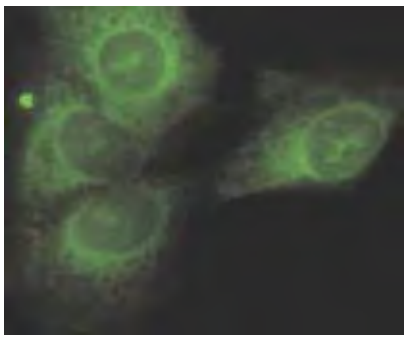
Halai, R., Clark, R.J., Nevin, S., Jensen, J.E., Adams, D.J., and Craik, D.J. (2009). Scanning mutagenesis of a-conotoxin Vc1.1 reveals residues crucial for activity at the α9α10 nicotinic acetylcholine receptor. *Journal of Biological Chemistry* **284**: 20275-20284.

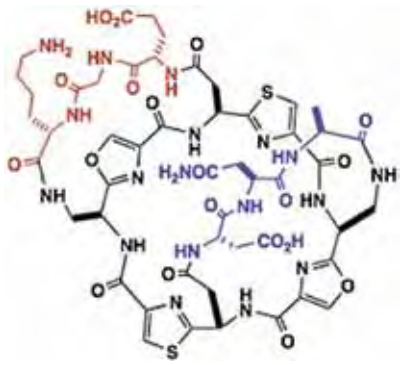
Huang, Y.H., Colgrave, M.L., Daly, N.L., Keleshian, A., Martinac, B., and Craik, D.J. (2009). The biological activity of the cyclotides is modulated by the formation of a multimeric pore. *Journal of Biological Chemistry* **284**: 20699-20707.

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

Chemistry and human therapeutics

DAVID FAIRLIE





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 chemical reactions/mechanisms/compounds/structures, 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 enzymology, biochemistry, pharmacology, immunology, virology, oncology or neurobiology.

RESEARCH PROJECTS

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

- Drug design (for inflammatory disorders, cancers, viral/parasite infections, neurodegenerative, metabolic syndrome)
- Organic and medicinal chemistry
- Structures by 2D NMR spectroscopy
- Enzymology & protein-protein interactions
- Mimicry of protein surfaces
- Pharmacology: molecular (cellular) and experimental (animal models)

KEY PUBLICATIONS

Stoermer, M.J., *et al.* (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.

Blakeney, J.S., *et al.* (2007). Nonpeptidic Ligands For Peptide-Activated GPCRs. *Chemical Reviews* **107**: 2960-3041.

Kahnberg, P., *et al.* (2006). Design, Synthesis, Potency and Cytoselectivity Of Anticancer Agents Derived By Parallel Synthesis From Alpha-Aminosuberic Acid. *Journal of Medicinal Chemistry* **49**: 7611-7622.

Levick, S., *et al.* (2006). Antifibrotic Activity of an Inhibitor of Group IIa Secretory Phospholipase A_2 in Young Spontaneously Hypertensive Rats. *Journal of Immunology* **176**: 7000-7007.

Shepherd, N.E., *et al.* (2006). Modular Alpha Helical Mimetics With Antiviral Activity Against Respiratory Syncitial Virus. *Journal of the American Chemical Society* **128**: 13284-13289.

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March, D.R., *et al.* (2004). Potent Cyclic Antagonists Of The Complement C5a Receptor On Human Polymorphonuclear Leukocytes. Relationships Between Structures and Activity. *Molecular Pharmacology* **65**: 868-879.

LAB MEMBERS

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

Research Officers: Dr Renee Beyer, Dr Jade Blakeney, Dr Frederik Diness, Dr Dhiraj Hans, Dr Tim Hill, Dr Huy Hoang, Dr Fredrik Lindahl, Dr Rink-Jan Lohman, Dr Andrew Lucke, Dr Praveen Madala, Dr Gloria Ruiz-Gómez, Dr Conor Scully, Dr Jacky Suen

PhD Students: Russell Driver, Praveer Gupta, Maria Halili, Rose Harrison, Junxian Lim, Ranee Singh

Masters Students: Anh Do, Annika Yau

Research Assistant: Adam Cotterell

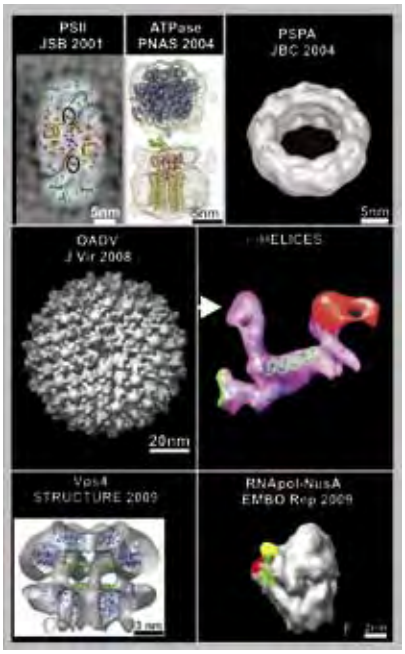
Honours Students: Sheila Barbero, Shaio Chow, Matt Lovell, Tony Reed

Undergraduate Students: Johan Hamidon, Nor Hana Hamzah, Annette Spierings

Office Manager: Barbara Feenstra

Structural biology of membrane proteins, macromolecular assemblies and viruses

BEN HANKAMER



Determining the structures of membrane proteins, macromolecular assemblies and viruses is one of the great challenges of cell and structural biology. Using advanced high-resolution cryo-electron microscopes it is now possible to capture atomic-resolution information of biological macromolecules. However, as the captured images are inherently 'noisy', this information must be recovered by aligning many copies of the protein (~10^5-10^6 individual molecules) either computationally (by single particle analysis), or biochemically (via crystallography).

As part of the IMB's *Visible Cell® project* 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 merging large numbers of 2D projection images of randomly-oriented molecules to calculate 3D reconstructions. Our current benchmark resolution is ~10 Å at which individual α-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) and icosahedral viruses. These structures provide fundamental new insights into many fascinating molecular machines and feed into the Visible Cell® project. These technologies are also being used to develop new bio-fuel production systems within the Solar Bio-fuels consortium.

The Solar Bio-fuels consortium (www.solarbiofuels.org), co-directed by Ben Hankamer, has brought together an international team of specialists to develop high-efficiency 2nd-generation bio-fuel production systems using microalgae. This represents a rapidly expanding area of biotechnology of global significance. Our specialisation is the structural biology and biochemistry of the photosynthetic machinery, which drives the first step of converting solar energy into chemical energy (fuels). Consequently its optimisation offers significant downstream benefits for all bio-fuel production systems (bio-ethanol, bio-diesel, BTL diesel, bio-H_2 and bio-methane). With colleagues, we are now taking the 'Visible Cell' approach to develop a 3D atlas of the photosynthetic machinery within the cellular context. This 3D atlas will assist in the fine-tuning of the light capture and conversion processes of photosynthesis, just as a manual is required to tune the engine of a car.

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
- 2nd-generation micro-algal biofuel 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

Landsberg, M.J., Vajjhala, P.R., Rothnagel, R., Munn, A.L., and Hankamer, B. (2009). 3D structure of the AAA ATPase Vps4: Advancing structural insights into the mechanisms of endosomal sorting and enveloped virus budding. *Structure* **17**: 427-437.

Yang, X., Molimau, S., Doherty, G.P., Marles-Wright, J., Rothnagel, R., Hankamer, B., Lewis, R.J., and Lewis, P.J. (2009). The structure of bacterial RNA polymerase in complex with the essential transcription elongation factor NusA. *EMBO Reports* **10**: 997-1002.

Pantelic, R.S., Lockett, L.J., Rothnagel, R., Hankamer, B., and Both, G. (2008). Cryo-electron microscopy map of *Atadenovirus* reveals cross-genus structural differences from human adenovirus. *Journal of Virology* **82**: 7346-7356.

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.

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

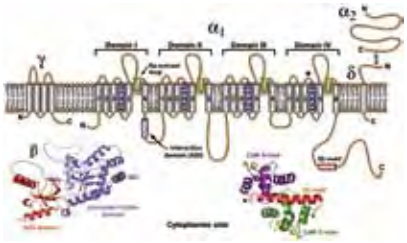
Honours Students: Hong Wai Tham, Anne Sawyer

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

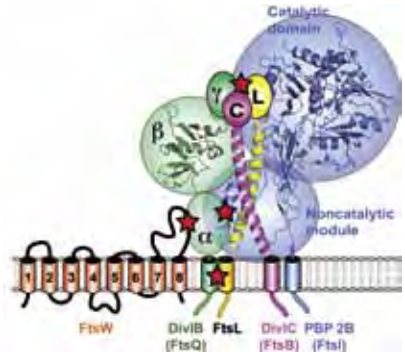
Bugs and drugs: rational development of novel antibiotics, analgesics, and environmentally-friendly insecticides

GLENN KING

Mexican red-kneed tarantula (Brachypelma smithii).



Schematic of a voltage-gated calcium channel.



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

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

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.

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.

Gorbatyuk, V.Y., Nosworthy, N.J., Robson, S.A., Bains, N.P.S., Maciejewski, M.W., dos Remedios, C.G., and King, G.F. (2006). Mapping the phosphoinositide-binding site on chick cofilin explains how PIP_2 regulates the cofilin-actin interaction. *Molecular Cell* **24**: 511-522.

Robson, S.A., and King, G.F. (2006). Domain architecture and structure of the bacterial cell division protein DivIB. *Proceedings of the National Academy of Sciences USA* **103**: 6700-6705.

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Rowland, S.L., Burkholder, W.F., Cunningham, K.A., Maciejewski, M.W., Grossman, A.D., and King, G.F. (2004). Structure and mechanism of Sda, an inhibitor of the histidine kinases that regulate initiation of sporulation in *Bacillus subtilis*. *Molecular Cell* **13**: 689-701.

LAB MEMBERS

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

Research Officers: Dr Raveendra Anangi, Dr Kathryn Greenwood, Dr Volker Herzig, Dr Rikki Hvorup, Dr Brit Winnen

Research Assistant: Radha Seshadri

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MSc Students: Sing Yan Er, Lena Grimm, Madeleine Kuenz, Xiao Zhen Lin, Chek-Fong Low, Ramya Ramachandran, Sebastian Senff

Honours Students: Carus Lau, Tomas Miljenovic, Darshani Rapasinghe

Molecular pharmacology of venom peptides

RICHARD LEWIS

A major focus of my group is the discovery and development of peptides as research tools and leads to new therapeutics, especially in the area of pain management. This research involves the assay-guided isolation of venom peptides, peptide synthesis, tissue pharmacology, high-content imaging, radioligand binding, 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 Xenome's Xen2174 for chronic neuropathic, postsurgical and cancer pain that was developed from χ-MrIA, originally discovered in my group.

RESEARCH PROJECTS

- Discovering conopeptides that modify pain pathways (NHMRC Program Grant)
- Determining sites and mode of conotoxin binding to the α1-adrenoceptor, noradrenaline transporter or nicotinic acetylcholine receptor
- Discovering conotoxins that modulate calcium and sodium channels
- Discovering and characterising novel bioactives using high-content screens
- Developing mass spectrometric approaches to unravel the peptide diversity of cone snail venoms (venomics)

KEY PUBLICATIONS

Davis, J., Jones, A., and Lewis, R.J. (2009). Remarkable inter- and intra-species complexity of conotoxins revealed by LC/MS. *Peptides* **30**: 1222–1227.

Vetter, I., and Lewis, R.J. (2009). Characterization of endogenous calcium responses in neuronal cell lines. *Biochemical Pharmacology* **79**: 908-920.

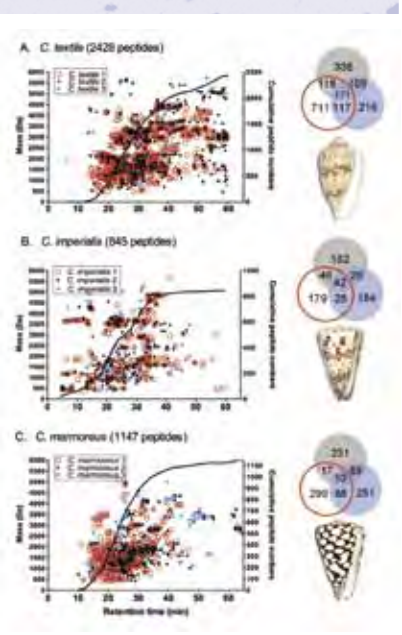
Wang, C.I., and Lewis, R.J. (2009). Emerging structure-function relationships defining monoamine NSS transporter substrate and ligand affinity. *Biochemical Pharmacology* **79**: 1083-1091.

Schroeder, C.I., Ekberg, J., Nielsen, K.J., Adams, D., Loughnan, M., Thomas, L., Adams, D.J., Alewood, P.F., and Lewis, R.J. (2008). Neuronally selective μ-conotoxins from *Conus striatus* utlise an a-helical motif to target mammalian sodium channels. *Journal of Biological Chemistry* **283**: 21621-21628.

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.

Ekberg, J., Jayamanne, A., Vaughan, C.W., Aslan, S., Thomas, L., Mould, J., Drinkwater, R., Baker, M.D., Abrahamsen, B., Wood, J.N., Adams, D.J., Christie, M.J., and Lewis, R.J. (2006). μO-conotoxin MrVIB selectively blocks Nav1.8 sensory neuron specific sodium channels and chronic pain without motor deficits. *Proceedings of the National Academy of Sciences USA* **103**: 17030-17035.

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



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

LAB MEMBERS

Research Officers: Dr Irina Vetter, Dr Anderson Wang, Dr Lotten Ragnarsson-McGrath

Research Assistants: the late Dianne Alewood, Asa Anderson, Nausad Shaikh, Hareshwar Goswarmi, Anand Mistry

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

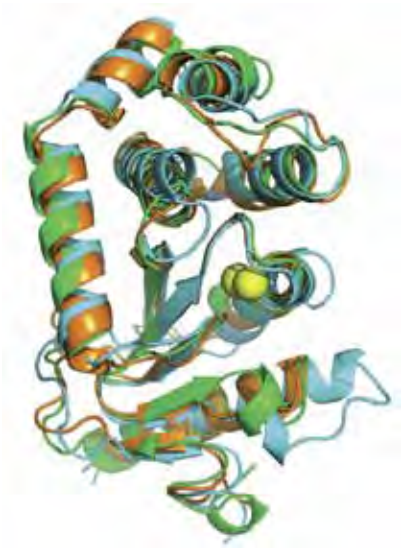
MSc Students: Ramu Soumya, Woo Ram Jung, Anand Mistry

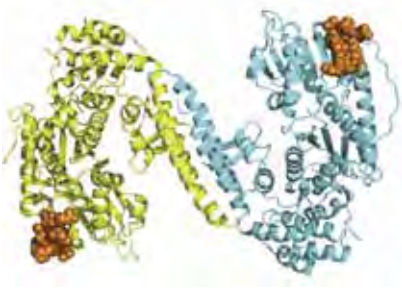
Honours Student: Christian Reichhold

DIVISION OF CHEMISTRY AND STRUCTURAL BIOLOGY

Protein structure and drug design

JENNY MARTIN





Our work aims to better understand the role of proteins in disease and to develop novel drugs targeting these 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 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. Our recent results, in collaboration with Professor David James (Garvan Institute), show that the Munc18c protein binds to a short N-terminal peptide of the SNARE syntaxin4 protein, and that this interaction stimulates SNARE ternary complex formation thereby promoting vesicle fusion. We determined the structure of the Munc18c:Sx4 peptide complex showing that the N-peptide interaction is evolutionarily conserved in almost all SNARE systems (Hu *et al. PNAS* 2007). This work led directly to the award of a 2009 NHMRC program grant with James and four other diabetes researchers at the Garvan Institute.

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* using data measured at the Australian Synchrotron (Shouldice *et al., AntiOx Redox Signal* 2009). We are now focusing our attention on developing inhibitors of DsbA as potential antibacterial agents (Heras *et al. Nature Rev Microbiol* 2009), using fragment-based screening. We have already successfully applied this approach to PNMT, using the automated UQ ROCX diffraction facility. 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 be inhibitors of 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

Heras, B., Shouldice, S.R., Tokrina, M., Scanlon, M.J., Schembri, M., and Martin, J.L. (2009). Dsb proteins and bacterial pathogenicity. *Nature Reviews Microbiology* **7**: 215-225.

Shouldice, S.R., Heras, B., Jarrott, R., Sharma, P., Scanlon, M.J., and Martin, J.L. (2009). Characterisation of the DsbA oxidative folding catalyst from *Pseudomonas aeruginosa* reveals a highly oxidizing protein that binds small molecules. *Antioxidants and Redox Signaling* **12**: 921-931. (front cover)

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.

Latham, C.F., Lopez, J.A., Gee, C.L., Hu, S.-H., Westbury, E., Blair, D., Armishaw, C., Alewood, P.F., Bryant, N.J., James, D.E., and Martin, J.L. (2006). Molecular dissection of the Munc18c/Syntaxin4 interaction: Implications for regulation of membrane trafficking. *Traffic* **7**: 1408-1419.

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

UQ ROCX X-ray Lab Manager: Karl Byriel

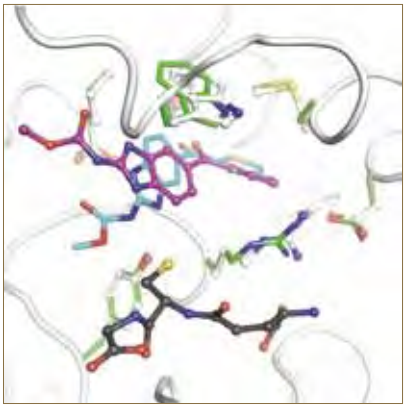
Research Assistant: Russell Jarrott

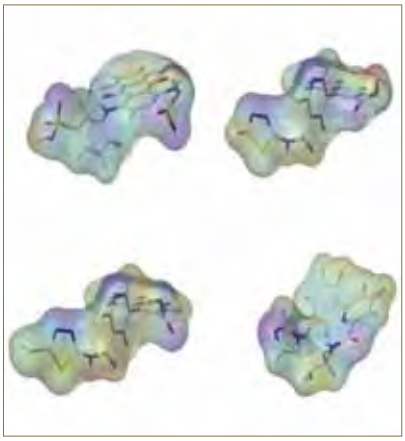
PhD Students: Nyssa Drinkwater, Michelle Christie, Kevin Chen, Nurliyana Ahmad Zawawi, Asma Rehman, Patricia Walden

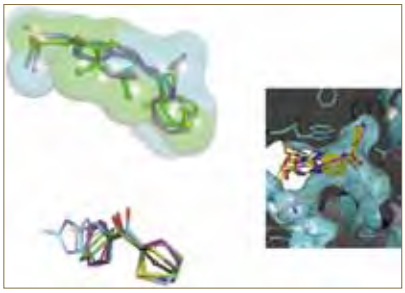
Visiting Students: Pooja Sharma (Monash University), Fabian Kurth (Ludwig-Maximillian University, Germany)

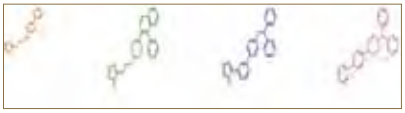
Combinatorial chemistry and molecular design

MARK SMYTHE









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 D2 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

Research Assistants: Jill Turner, Jaimee Duncan, Angelika Christ, Christie Bentley, Aleisha Griffin, Ryan Nugent, Phillip Walsh

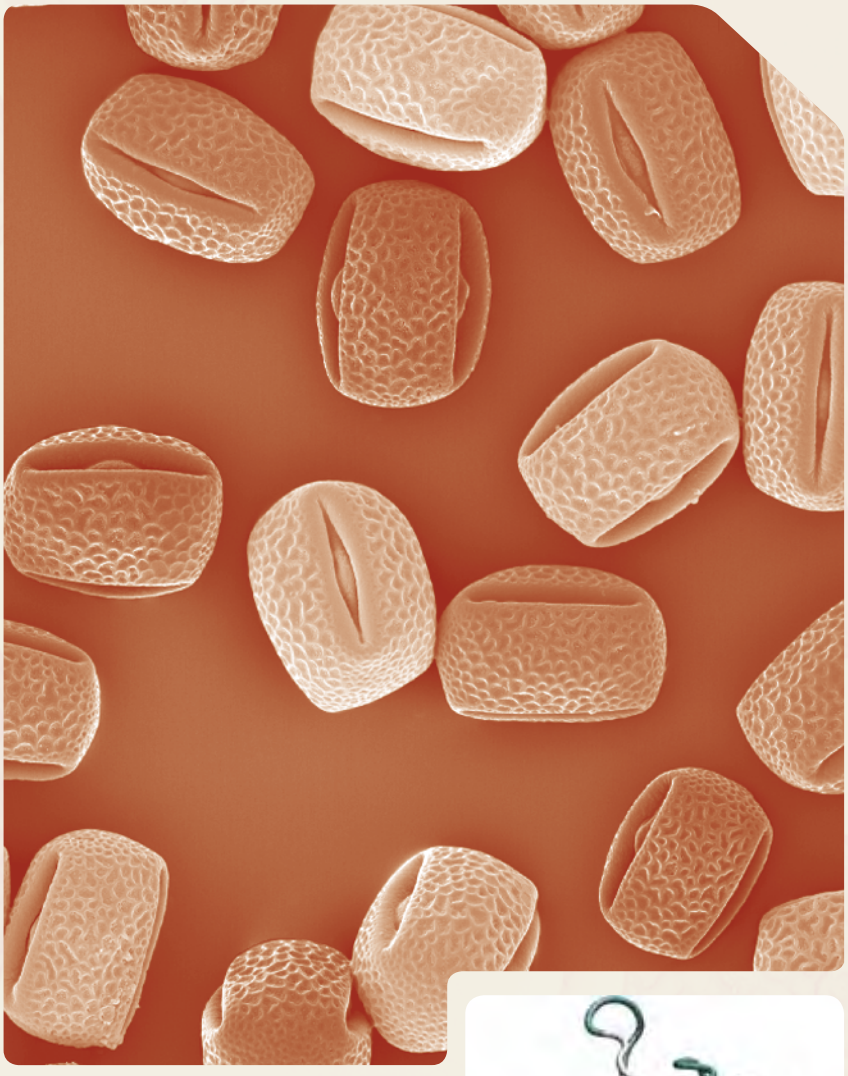
PhD Student: Christina Kulis

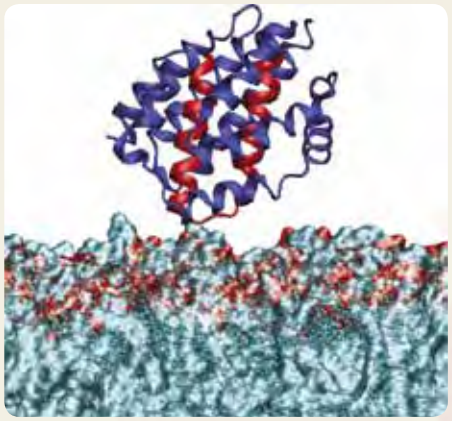
IMB RESEARCHERS

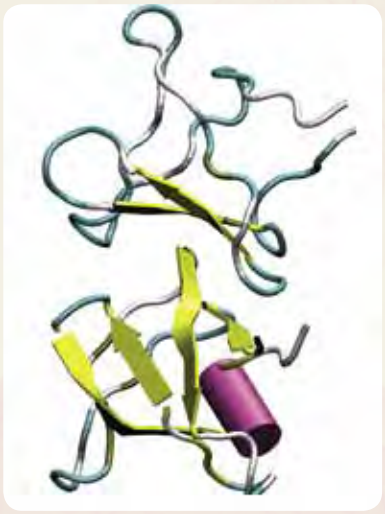
The IMB is a highly collaborative environment where researchers from different fields combine to contribute to strategic research programs investigating the basis of growth and development at the genetic, molecular, cellular and organ levels.

Only by understanding the complex molecular and cellular events that occur throughout a normal human life can scientists understand abnormalities responsible for many common human diseases and to find treatments for them.

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 Appointments in 2009 were Professor Alan Mark and Professor Geoff McLachlan.

Molecular dynamics of biomolecular systems

ALAN E. MARK

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. Currently, it is not possible to directly simulate the folding of proteins in atomic detail. Dramatic progress has, however, been 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. For example, we are investigating the mechanism by which low pH triggers the activation of the Dengue E protein, which plays a critical role in the entry of the virus into cells. We are also investigating the structural changes associated with the binding of human growth hormone to the growth hormone receptor.

Third, how do membrane proteins assemble? Cell membranes are the archetypal self-organised supramolecular structure. Membrane protein complexes also represent a new frontier in structural biology. Using simulations, we are able to directly investigate how bilayers and vesicles form. We are also investigating the assembly of functional structures such as the assembly of anti-microbial peptides into transmembrane pores. This in turn is being used to understand the mechanism by which larger complexes form in heterogeneous environments.

RESEARCH PROJECTS

- Simulating peptide folding and assembly
- Pore-forming peptides as models for protein assembly
- The nucleation and growth of amyloid fibrils
- Mechanism of activation of the human growth hormone receptor
- New methods in drug design

KEY PUBLICATIONS

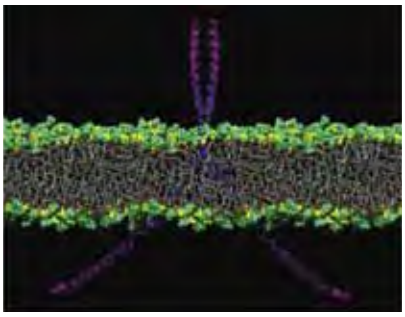
Periole, X., Rampioni, A., Vendruscolo, M., and Mark, A.E. (2009). Factors that affect the degree of twist in b-sheet structures: A molecular dynamics simulation study of a cross-ß filament of the GNNQQNY peptide. *Journal of Physical Chemistry B* **113**: 1728-1737.

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.

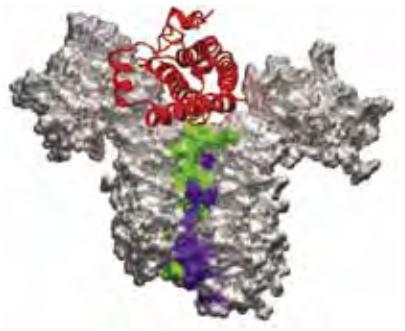
Periole, X., and Mark, A.E. (2007). Convergence and sampling efficiency in replica exchange simulations of peptide folding in explicit solvent. *Journal of Chemical Physics* **126**: 014903.

Leontiadou, H., Mark, A.E., and Marrink, S.J. (2006). Antimicrobial peptides in action. *Journal of the American Chemical Society* **128**: 1256-12161.

Fan, H., Mark, A.E., Zhu, J., and Honig, B. (2005). Comparative study of generalised Born models: Protein dynamics. *Proceedings of the National Academy of Sciences USA* **102**: 6760-6764.



A model of the transmembrane domains of the growth hormone receptor.



The interaction of human growth hormone (red) with the extracellular domain of the growth hormone receptor showing the contact area predicted by atomistic molecular dynamics simulations.

LAB MEMBERS

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

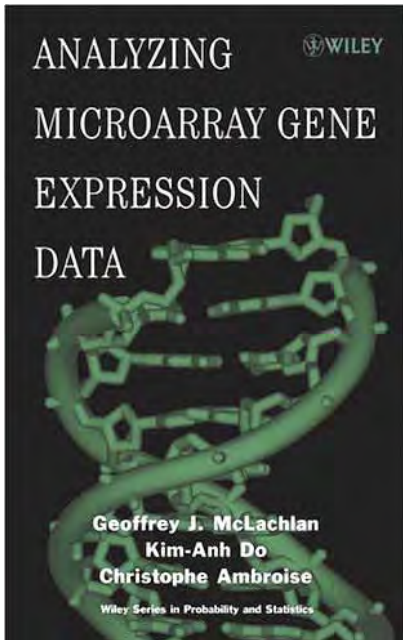
Administration: Helene Hooper

Research Assistant: Matthew Breeze

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

Applied statistics and bioinformatics

GEOFFREY McLACHLAN



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. I also wish to utilise high-throughput genomic data to understand biological regulatory networks.

Concerning statistical methodology being developed for the aforementioned problems, I am working on very fast methods for factorising data matrices for 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.

RESEARCH PROJECTS

- Ongoing research into the modelling of gene profiles for use in the detection of differentially expressed genes and in time-course studies
- Development of diagnostic methods for cancer, using multiple indices in conjunction with clinical factors
- Development of fast methods for the factorisation 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
- 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

Flack, L.K., and McLachlan, G.J. (2009). Clustering methods for gene-expression data.In *Handbook of Research on Systems Biology Applications in Medicine*, A. Daskalaki (Ed.). Hershey, Pennsylvania: Idea Group Publishing, pp. 209-220.

McLachlan, G.J., and Ng, S.K. (2009). The EM Algorithm. In *The Top-Ten Algorithms in Data Mining,* X. Wu and V. Kumar (Eds.). Boca Raton, Florida: Chapman & all/CRC, pp. 93-115.

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

McLachlan, G.J., *et al*. (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., *et al*. (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.

Baek, J., Son, Y.S., and McLachlan, G.J. (2007). Segmentation and intensity estimation of microarray images using a gamma-t mixture model. *Bioinformatics* **23**: 458-465.

McLachlan, G.J., *et al*. (2006). A simple implementation of a normal mixture approach to differential gene expression in multiclass microarrays. *Bioinformatics* **22**: 1608-1615.

LAB MEMBERS:

Research Officer: Dr Kim-Anh Le Cao, Dr Emmanuelle Meugnier

PhD Student: Leesa Wockner

AFFILIATE APPOINTMENTS


Professor Matt Brown


Dr Dave Edwards


Professor Nicholas Fisk


Professor Ian Frazer


Professor Tom Gonda


Professor Jane Hunter


Assoc. Prof. Stuart Kellie


Assoc. Prof. Bostjan Kobe


Assoc. Prof. Fred Meunier


Assoc. Prof. Joe Rothnagel


Professor Ranjeny Thomas


Professor Istvan Toth


Dr Jon Whitehead


Assoc. Prof. Paul Young

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

Dr Dave Edwards
Australian Centre for Plant Functional Genomics

Professor Nicholas Fisk
UQ Centre for Clinical Research

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

Professor Tom Gonda
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

Associate Professor Fred Meunier
Queensland Brain Institute

Associate Professor Joe Rothnagel
School of Molecular and Microbial Sciences

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

Professor Istvan Toth
School of Chemistry and Molecular Biosciences

Dr Jon Whitehead
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

Associate Professor Paul Young
School of Chemistry and Molecular Biosciences

IMB OCCUPATIONAL HEALTH AND SAFETY REPORT

THE IMB HAS a well-established health and safety infrastructure based on a combination of local Floor Managers, an effective training and induction process, and an integrated database built specifically for research support. This model is closely aligned with the overall OH&S policies and goals of The University of Queensland, and provides great flexibility as developments in regulatory requirements or University policies occur.

In 2009, 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 Radiation Safety and Protection Plan,
- revised induction process,
- risk assessment database review and modification,
- implementation of periodic online safety audits,
- development of a tasks database to systematically monitor compliance with various regulatory bodies and legislation,
- cytotoxic handling audit and risk assessment review,
- implementation of an external contractor safety induction system, and
- certification of all laboratory areas for use as Quarantine-approved premises.

In 2009, all audits by federal and state bodies such as OGTR, AQIS, ANSTO and QFRS have shown excellent compliance. Informal internal audits for the upcoming Self-Insurance Audit due in 2010, and for the UQ Environmental Management System, have also indicated that the IMB has a strong OH&S and regulatory compliance system in place.

The IMB safety structure is therefore in good shape to meet the current safety, regulatory and occupational requirements of its staff and students, but there is still room for improvement. Injuries involving eyes remain a significant proportion of incidents at the IMB, closely followed by chemical splashes and minor cuts. Correct use of equipment, PPE and chemical handling have been identified as areas for improvement and further training, and we look forward to fewer incidents with respect to these factors in 2010.

Challenges for the IMB's safety infrastructure in 2010 include:

- preparing IMB systems for the implementation of the new Federal OH&S legislation,
- preparing IMB systems for the upcoming changes to biosecurity requirements,
- preparing for the Self-Insurance Audit in late 2010, and
- implementing a chemical inventory system for quarterly reports.

While we believe the safety and compliance systems at the IMB are of world standard, we depend upon the assistance of all staff and students at the Institute to help make our workplace a safe one.

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, IMBcom has a skilled, independent Board of Directors and operates 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.

IMBcom uses a model of cooperative integration with the discovery activities of the research labs. IMBcom staff members are involved from the earliest disclosure stages with the planning and delivery of ways to add value to the 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 11 new biotechnology startup companies, two in conjunction with UniQuest. These companies have raised more than $50 million through private sector investment, $16 million in federal and state government commercial grants and currently employ or contract over 30 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 exited 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 the "proof-of-concept" funds for future IP and product development.

In 2009, IMBcom brokered three major deals resulting from IMB research:

- a non-exclusive technology licence with PROLOR Biotech to a human growth hormone receptor cell line,
- an exclusive technology licence with Sequenom to UQ's Foetal Cell Isolation and Enrichment Technology, which potentially improves the safety margin when testing foetuses for disease, and
- licence agreements with Wyeth and Cyclogenix for rights to a novel drug discovery platform used for generating therapeutic peptides.

The IMB has a commitment to the training of high-quality graduate students in the molecular biosciences and aspires to provide a more holistic training that includes commercial dimensions. IMBcom delivers this objective through the provision of workshops. These "bootcamps", or BioBusiness Retreats, incorporate elements of career preparation, understanding and working in a commercial environment, and working in teams to produce 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 330 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 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 State/ Towards Q2 agenda. IMBcom showcases not only the IMB and the University to industry and investment, but also Queensland as an industry destination.

POSTGRADUATE RESEARCH

As predicted in last year's report, it has been a time of change for the IMB's postgraduate program, with UQ's introduction of Candidature Milestones and the full implementation of the continuous assessment of scholarship applications for both domestic and international students. Since the formal start of Semester 1 2009 (01-Dec 2008), we have had 31 students commence and three other students transfer to the institute from other programs. Of these 34 students, 27 were international, from countries as diverse as Italy, Spain, Germany, Russia, the Ukraine, China, Vietnam, India, Pakistan, Malaysia and Singapore. This continues last year's trend of increased international enrolments, with overseas students now comprising 50 percent of our cohort. Our total number of active RHD students has stabilised at around 130 students, an amazing 28 candidates of which completed their PhD degree in 2009 (for a full list see page 72). While some of our graduates have remained within IMB throughout the year to complete research projects, many have taken up positions both locally and overseas (for details see page 72).

As in past years, a number of our students received accolades throughout the year. These included Maggie Gentz from the King group, who was Founder and inaugural Coordinator of the IMB Science Ambassador Program (see page 81). She was also an invited speaker at the World Congress of Science and Factual Producers where she presented her research to media outlets from around the world in a session called "Skinning your Cat: A Workshop for Scientists". Throughout the year Maggie also served as one of the Queensland Government's Talking Scientists (visiting Toowoomba, Townsville and Mitchell), presented at the Queensland Science in Parliament event in a talk focused on science communication, and in December 2009 was elected as first Secretary of the newly-founded International Branch of the Entomological Society of America (the largest society of entomologists in the world). Marga Gual Soler (Stow group) won the Spanish "Sa Nostra" Foundation Award for continuing postgraduate studies overseas, Tom Whitington (Bailey group) received an internal grant from the Computational Biology Research Centre (CBRC) in Tokyo to pursue three months of collaborative research in Japan in early 2009, and Muharrem Akan (Craik group) won a 2009 Trans-Pacific Fellowship worth over $11,000 to undertake research in a collaborator's lab in Seattle, which he shall take up in 2010. Paulo Amaral (Mattick group) was awarded a fellowship to attend the 74th Cold Spring Harbor Symposium on Quantitative Biology and present a talk entitled "Evolution: The Molecular Landscape". Reena Halai (Craik group) received an American Peptide Society travel bursury to attend the American Peptide Symposium held in the US in June, winning a Young Scientific Investigator poster award at the meeting. She and Russell Driver (Fairlie group) also won a HOPE meeting travel award from the Australian Academy of Science to attend the 2nd Hope meeting in Japan in September 2009, with Reena again winning the Best Poster Presenter Award at that meeting. Zakir Tnimov (Alexandrov group) won second prize in the Poster division at the East Coast Protein Meeting in Coffs Harbour in August 2009 and Markus Muttenthaler was awarded the Protein Science Young Investigator Travel Award to attend the VIII European Symposium of the Protein Society in Zurich. Markus was also awarded the prestigious "Best Thesis Award" for 2008 and 2009 from the Royal Australian Chemistry Institute. We also had three students appearing on the UQ Dean's List for 2008: congratulations to Dr Natalie Butterfield (Wicking group), Dr Rebecca Pelekanos (Waters group) and Dr Cas Simon (Mattick group).

Our honours cohort was small but continued to excel. We had 13 students commencing in Feb 2009, seven students who carried over from July 2008 and two others who commenced July 2009. As in previous years, 80 percent of those students completing their year in 2009 obtained a grade of First Class honours. The Amgen Award for the most outstanding honours student at the IMB was won by Elanor Wainwright from the Koopman group. Elanor, whose honours project explored "The role of Mir-202 in gonad development", has been working as a research assistant in the Wilhelm group and is intending to commence a PhD in the same group in 2010. Amgen Australia has been presenting our honours students with this award for over a decade and we are thrilled by their continued support of our young researchers. The IMB also continued the Undergraduate Research Scholarship Scheme (URSS) in 2009, placing 23 second- and third-year students within laboratories in one of our divisions for eight hours per week during semester. Additionally, a number of third-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 17 students in summer projects of six to 10 weeks duration as part of UQ Summer Vacation program, which this year included four high-calibre students from New Zealand and one from the University of Melbourne. 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 and 11 students from schools

Postgraduate research

throughout Queensland to undertake a brief period of work experience within research laboratories.

Our IMB Student Association, SIMBA, organised a range of social events throughout the year and on several occasions pitched both the brains and brawn of the IMB student body against those from the other research institutes on campus. The events conducted throughout 2009 included the IMB/AIBN inter-institute Trivia Evening, the first annual IMB vs AIBN paintball competition and the highly successful Inter-Institute Ball (coordinated in conjunction with QBI and AIBN). There were also several IMB-based BBQs to meet and greet new students, and the AGM, held in August 2009 to usher in the new SIMBA Executive for 09/10. This year we welcomed to the posts Robert McLeay (President), Nilesh Bokil (Vice President), Selene Fernandez Valverde (Secretary), Peter Yee (Treasurer), Erin Ahern (SIMBAlize editor-in-chief) and Marga Gaul Soler (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 a mentoring afternoon tea in May, and successfully hosting the second IMB ECR Symposium in September, they organised a series of events discussing the presentation of scientific data in oral and written format. These included a seminar by Professor Koopman entitled "How to give a talk like Barack Obama", which provided valuable insights into the dos and don'ts of scientific presentation; a presentation entitled "Research in view to publication" delivered by Professor Jenny Martin and Associate Professor Alpha Yap, who were joined by Professor Kirill Alexandrov and Dr Dagmar Wilhelm for a panel discussion on the topic after the lecture; a seminar by visiting speaker Professor David Vaux, entitled "Ten rules for the presentation and interpretation of data in publication"; and a live web seminar by Dr Mike Rossner (Executive Director, Rockefeller University Press and former managing editor of the *Journal of Cell Biology*) entitled "What editors want – an insight". In addition, the ECR committee continued to coordinate the institute-wide Monday Midday Meetings and arranged for ECRs to lunch with speakers after the Friday Seminar Series, produced an ECR website and newsletter, and maintained an active and very positive presence throughout the IMB. During 2009, the members of the ECR committee included Dr Andrew Brooks (President), Dr Daniel Abankwa (Vice-President), Dr Simon Wilkins (completed PhD in 2009), Dr James Palmer, Dr Adi Haji Idris (completed PhD in 2009), Dr Michael Hanzal-Bayer, Dr Rehan Villani, Dr Karin Kassahn, Dr Andrea Bugarcic, Dr Eva Kovacs, Dr Alex Combes (completed PhD in 2009), Dr Johanna Barclay, Dr Mathias François, Dr Rikki Hvorup, Dr Richa Dave, and Natalie Eriksson and Evan Stephens (PhD students).

The Postgraduate Program continued to run a set of workshops designed to assist students in overall career development, which complemented those run by the ECR committee. These included IMBcom's three-day BioBusiness Retreat for the third-years, which was held this year from 1st to 3rd April at Noosa Springs Resort, Noosa Heads. Once again, feedback from the retreat was extremely positive, with students really enjoying the information and interactive sessions. We also offered our students the opportunity to attend the workshop "Introducing R" (a freeware statistics package) run by Dr Simon Bloomberg in conjunction with the School of Biomedical Science. Our Grants Officer, Michelle Foley, provided an information session covering fellowship applications, and Bronwyn Adams, our Communications Officer, organised several training sessions for students chosen to be IMB Science Ambassadors. We also conducted the IMB three-minute thesis challenge in which our second-year PhD students gave presentations as part of their Candidature Milestone. A panel of judges then selected two students to represent the IMB in the inter-Institute final, which was part of the university-wide three-minute thesis competition run by the UQ Graduate School. Both Rhonda Kan (Wainwright group) and Lindsey McFarlane (Wilhelm group) made us proud, with Lindsey receiving the People's Choice award in the inter-institute semi-final of the competition.

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 throughout the year. His commitment to the Postgraduate program (and in fact all student matters) is amazing, as illustrated by his IMB Postgraduate Roadmap document which was released this year as a blueprint for describing the way in which the IMB will manage the new candidature milestones. He was chosen as one of four PGCs to present their school's implementation of milestones at a UQ-wide forum run by the Graduate School earlier in the year and at the meeting presented both the Roadmap and the IMB PG Database, both of which were met with much enthusiasm from the UQ RHD community. In fact, the IMB postgraduate database (created by Oz Data Solutions) has been adopted by several other schools at UQ as a means of best managing student candidature and the involvement of its academics in postgraduate activities. Professor Capon also initiated and hosted the inaugural Biosciences Institutes Research Higher Degree (BIRHD) Roundtable in November 2009, as a means of sharing RHD knowledge, experiences, concerns and ideas across the biologically inclined research institutes of UQ (IMB, Queensland Brain Institute, Australian Institute of Bioengineering and Nanotechnology, and Diamantina Institute for Cancer, Immunology and Metabolic Medicine). These are but three examples of how Rob is directing the program to ensure IMB delivers on providing our students the best possible research experience. His commitment and vision have been welcome throughout the year.

PhD CONFERRALS FOR 2009

LAST NAME	FIRST NAME	GROUP	DEGREE	THESIS TITLE	WHERE ARE THEY NOW?
Beaumont	Kimberley	Sturm	PhD	The molecular mechanism of MC1R association with skin cancer risk phenotypes	Sturm group, IMB
Chang	Ming Kang	Hume/ Sweet	PhD	Role of macrophages, residing on the bone surface, in bone remodelling and repair	Institute for Biomechanics, Zürich, Switzerland
Cho	Kwang-Jin	Hancock	PhD	Hypervariable regions of Ras isoforms dictate distinct functionality by targeting to specific protein complexes at microdomains	University of Texas Medical School at Houston, USA
Combes	Alexander	Koopman	PhD	The morphogenesis of testis cords	Queensland Institute of Medical Research, Herston, Brisbane
Dave	Keyur	Gorman	PhD	Analysis of post-translational modification sites in the aryl hydrocarbon receptor	Queensland Institute of Medical Research, Herston, Brisbane
El-Naggar	Mohamed	Capon		Cytotoxic alkaloids from Australian sponges	Egypt
Farkas Ross	Diana	Koopman	PhD	Sex determination and sex ratio manipulation in beef cattle	UQ School of Pharmacy PACE Institute, Princess Alexandra Hospital, Woolloongabba
Faulkner	Geoffrey	Grimmond	PhD	Short Sequence Tags Reveal Global Transcription Of Repetitive Elements In Mammalian Genomes	The Roslin Institute and R(D)SVS, University of Edinburgh, Midlothian, Scotland, UK
Greenwood	Kathryn	Craik	PhD	The development of the cyclotide MCoTI-II as a molecular engineering framework in drug design	King group, IMB
Gunasekera	Sunithi	Craik	PhD	Bioactivity grafting of cyclic peptides: structure activity studies of grafted cyclotides and SFTI-1	Division of Pharmacognosy, Department of Medicinal Chemistry, Uppsala University, Sweden
Haji Idris	Adi	Sweet/ Stacey	PhD	Cellular activation and death in response to cytoplasmic DNA	School of Chemistry and Molecular Biosciences, UQ
Hans	Dhiraj	Fairlie	PhD	Constraining short B cell epitopes as alpha helices	International Centre for Genetic Engineering and Biotechnology, New Dehli, India
Kinna	Genevieve	Little	PhD	Charactersising crim1 in vertebrate developmentsbA	Australian Institute for Bioengineering & Nanotechnology, UQ
Lattin	Jane	Sweet	PhD	Beta-Arrestin Expression and Function in Macrophages	Sweet group, IMB
Mercer	Timothy	Mattck	PhD	The expression of long noncoding RNAs during mouse development	Mattick group, IMB
Muttenthaler	Markus	Alewood	PhD	Peptide Engineering--Controlling the folding of disulfide-rich peptides	Alewood group, IMB
Sangermani	Daniel	Stow	PhD	Exocytosis and Endocytosis in LPS-activated macrophages: pathways and regulators	Queensland Brain Institute, UQ
Spiller	Cassy	Koopman	PhD	Investigating Sex Specific Cell Cycle Regulation in Fetal Germ Cells	Koopman group, IMB
Suen	Yung Jacky	Fairlie	PhD	Regulating Protease Activated Receptor 2	Fairlie group, IMB
Taft	Ryan	Mattick	PhD	Adding gears to the RNA machine: discovery and characterisation of new classes of small RNAs in eukaryotesy	Mattick group, IMB
Tallack	Michael	Perkins	PhD	Etythoid Kruppel-Like Factor Regulates the Cell Cycle in Erythroid Cells	Perkins group, IMB
Town	Liam	Wicking	PhD	Novel genes regulated by the hedgehog pathway, and their contribution to limb and craniofacial development	Wicking group, IMB
van Zuijlen	Wendy	Sweet	PhD	Regulation and Function of Schlafen in Macrophage Biology	University of Montreal, Quebec, Canada
Villani	Rehan	Wainwright	PhD	The Role of Patched1 in Epidermal Homeostasis	Wainwright group, IMB
Wadsworth	Kimberly	King	PhD	Unraveling the role of the bacterial cell division protein DivIB	University of Minnesota, Minneapolis, USA
Wang	Conan	Craik	PhD	Structural and functional studies of cyclotides	Department of Biochemistry, University of Science and Technology, Hong Kong
Wilkins	Simon	Perkins	PhD	Global analysis of transcriptional control driving zebrafish gastrulation	Melbourne Ventures, University of Melbourne, Victoria
Wood	Stephanie	Stow	PhD	Endosomal membrane fusion in macrophages and NK cells	Center for Infectious Medicine, Karolinska University Hospital, Sweden

VISITING SPEAKERS

DR THOMAS D. ALBRIGHT
Salk Institute for Biological Studies, La Jolla, California, USA
Associate learning and visual imagery

DR SASSAN ASGARI
School of Biological Sciences, UQ
Role of viral and cellular microRNAs in insect host-virus interactions

PROFESSOR COLIN BARROW
Deakin University, Victoria
Omega-3 biotechnology: functional foods and pharmaceuticals

PROFESSOR JOHN BATEMAN
Murdoch Children's Research Institute, Melbourne, Victoria
Cellular protein and mRNA quality control systems in inherited disorders

ASSISTANT PROFESSOR JAMES BEAR
Carolina Cardiovascular Biology Center, Chapel Hill, North Carolina, USA
Coronins: conserved regulators of the actin cytoskeleton

THE HON. PETER BEATTIE
Queensland Trade and Investment Commissioner for the Americas and former Premier of Queensland
Los Angeles, California, USA
Local to global: the big challenges

DR TIM BERGBREDE
Max Planck Institute for Molecular Physiology, Dortmund, Germany
Enabling protein research by automation and parallelisation

DR EWAN BIRNEY
European Bioinformatics Institute
European Molecular Biology Laboratories, Cambridge, United Kingdom
Applications of de Bruijn graphs in biology, including short-read sequence assembly and metagenomics

GLEN BORLACE
Sansom Institute
University of Adelaide, South Australia
Helicobacter pylori *killing and phagosome mutation*

PROFESSOR DOUG BROOKS
University of South Australia, Adelaide
Therapeutic strategies for genetic diseases

DR JANUSZ BUJNICKI
International Institute of Molecular and Cell Biology, and Institute of Molecular Biology and Biotechnology
Adam Mickiewicz University, Pozna, Poland
New methods for template-based and template-free modelling of RNA 3D structure

DR BLANCHE CAPEL
Duke University, Durham, North Carolina, USA
Beneath the battle of the sexes: defining the transcriptional architecture underlying mammalian sex determination

DR ALISTAIR CHALK
Eskitis Institute for Cell and Molecular Therapies
Griffith University, Brisbane
Transcriptome analysis of patient olfactory derived cell lines

DR BENNY CHOR
School of Computer Science
Tel Aviv University, Israel
Genomic DNA k-mers Distributions: models and modalities

PROFESSOR JOHN CHRISTODOULOU
The Children's Hospital, Sydney, New South Wales
New frontiers in Rett Syndrome research: the Sydney experience

TUNG-LIANG CHUNG
Australian Institute of Bioengineering and Nanotechnology, UQ
Discovery of a novel epigenetic effect of vitamin C on human embryonic stem cells

MATTHEW COOK
Mater Medical Research Institute, Brisbane
Expansion of functional HSC on a mesenchymal derived stromal layer

ASSOCIATE PROFESSOR HELEN M. COOPER
Queensland Brain Institute, UQ
Neogenin establishes polarity during neural tube formation

DR GARY COWIN
Centre for Magnetic Resonance, UQ
Magnetic resonance microimaging at 16.4T

DR KEYUR DAVE
Queensland Institute of Medical Research, Brisbane
Analysis of post-translational modification sites in the Dioxin receptor

CHRIS DURAN
Australian Centre for Plant Functional Genomics, UQ
SNP discovery in cereals using autoSNPdb

PROFESSOR NICHOLAS FISK
Director
Centre for Clinical Research, UQ
Foetal mesenchymal stem cells in endogeneous and therapeutic tissue repair

PROFESSOR DAVID GALAS
Institute for Systems Biology (Seattle, Washington) and Battelle Memorial Institute (Columbus, Ohio), USA
Systems biology of complex human diseases

DR CHRISTINE GEE
Department of Molecular and Cell Biology
University of California at Berkeley, USA
Regulation of the essential M. tuberculosis *peptidoglycan-precursor flippase*

DR EVGENY GLAZOV
Diamantina Institute, UQ
Small regulatory RNA in vertebrates: exceptions rule!

PROFESSOR TOM GONDA
Diamantina Institute, UQ
The ARVEC initiative: development and establishment of high-throughput functional screening technologies

DR PAUL GREGOREVIC
Baker IDI Heart and Diabetes Institute, Melbourne, Victoria
Exploring muscle biology and pathology with the help of viral vectors

DR BRETT HAMILTON
Queensland Institute of Medical Research, Brisbane
Interfacing imaging mass spectrometry and proteomics with histopathology

DR KIERAN HARVEY
Peter Mac Cancer Centre, Melbourne, Victoria
Growth control by the hippo pathway

DR WOLFGANG HOFMEISTER
School of Biomedical Sciences, UQ
The role of Syndecans as potential axon guidance molecules in zebrafish

MIKE IMELFORT
Australian Centre for Plant Functional Genomics, UQ
Short read assembly for dummies

PROFESSOR KENNETH JACOBSON
University of North Carolina, Chapel Hill, USA
Functional nano- and microdomains: revisiting the raft hypothesis

PROFESSOR DAVID JAMES
Garvan Institute, Sydney, New South Wales
Protein trafficking, insulin secretion and diabetes

PROFESSOR MIKE JAMES
University of Alberta, Edmonton, Canada
The structural biology of lysine biosynthesis in bacteria and plants

PROFESSOR NANCY JENKINS
Co-Director
Institute of Molecular and Cell Biology, Singapore
Harnessing transposons for cancer gene discovery

DR KARYN JOHNSON
School of Biological Sciences, UQ
Interaction between microbes within a host: a bacteria that mediates antiviral protection

KATE KOLLAR
Mater Medical Research Institute, Brisbane
Teaching an old dog new tricks - enhanced MSC Migration

PROFESSOR ROBB KRUMLAUF
Director
Stowers Institute for Medical Research, Kansas City, Missouri, USA
Tinkering with teeth: regulating size and number

ASSOCIATE PROFESSOR PAIGE LACY
University of Alberta, Edmonton, Canada
Signalling pathways in innate immune cells

DR CATHY LEAMEY
Bosch Institute
University of Sydney, New South Wales
Role for multiple teneurins in the generation of binocular circuits

DR SANG HYUN LEE
Institute for Advanced Medical Research, School of Medicine
Keio University, Tokyo, Japan
The mitotic spindle assembly checkpoint (SAC) and its anti-cancer therapeutic potential

ASSOCIATE PROFESSOR PETER LEWIS
University of Newcastle, New South Wales
The interaction of an essential transcription factor with RNA polymerase - a new antibiotic target?

ASSOCIATE PROFESSOR JIUYONG LI
University of South Australia, Adelaide
Exploring microRNA and mRNA interactions and their roles in human diseases with computational methods

PROFESSOR LEENDERT LOOIJENGA
Erasmus Medical Centre, Rotterdam, The Netherlands
Human germ cell tumours: news and views

RODRIGO LOPEZ
European Bioinformatics Institute, Cambridgeshire, UK
Bioinformatic services from the EMBL-EBI: past, present and future

DR GORAN MALOJCIC
Institute of Molecular Biology and Biophysics
Eidgenössische Technische Hochschule, Zürich, Switzerland
Structure and mechanisms of a PAPS-independent aryl sulfotransferase

DR ASHLEY MANSELL
Monash Institute for Medical Research, Melbourne, Victoria
Mal-functioning pathogen recognition responses

PROFESSOR MARK MARSH
MRC Laboratory for Molecular Cell Biology
University College London, United Kingdom
HIV replication in macrophages - insight to pathogenesis?

DR MARIA MARTIN
European Bioinformatics Institute, Cambridgeshire, UK
Bioinformatic services from the EMBL-EBI: past, present and future

PROFESSOR MALCOLM MCCONVILLE
Melbourne University, Victoria
The use of metabolomics to investigate host-parasite interactions

PROFESSOR GEOFF MCFADDEN
ARC Federation Fellow
University of Melbourne, Victoria
The relict chloroplast of malaria parasites: origin, function and therapeutic potential

PROFESSOR ANDREW MCMAHON
Harvard University, Boston, Massachusetts, USA
Sonic hedgehog morphogen signalling and the regulation of neural diversity
and
Developmental programs and stem cells in regenerative medicine

Visiting speakers

ASSOCIATE PROFESSOR NIGEL MCMILLAN
Deputy Director
Diamantina Institute, UQ
RNAi for cancer therapy

PROFESSOR JILL MESIROV
Broad Institute of MIT and Harvard, Cambridge, Massachusetts, USA
Knowledge-based approaches for computational genomics

RUTH MIRAMS
School of Chemistry and Molecular Biosciences, UQ
The mechanism of DISC assembly: the structure and mode of interaction of a FADD- vFLIP complex

ASSISTANT PROFESSOR KEVIN MORRIS
The Scripps Research Institute, La Jolla, California, USA
Long non-coding antisense RNAs epigenetically regulate transcription in human cells

DR JASON MULVENNA
Queensland Institute of Medical Research, Brisbane
Using biotin and shotgun proteomics to characterise the host-parasite interface in Schistosoma japonicum

DR SHIVASHANKAR NAGARAJ
CSIRO
Improved in silico approaches to analyse expressed sequence tags (ESTs): validation and application to parasitic nematodes

PROFESSOR LARS NIELSEN
Australian Institute for Bioengineering and Nanotechnology, UQ
Properties of the reconstructed Mus musculus *genome-scale metabolic network*

PROFESSOR RAY NORTON
Walter and Eliza Hall Institute, Melbourne, Victoria
Toxins, immunosuppressants and human enzymes: the versatile protein domain ShK

ASIAH OSMAN
Eskitis Institute for Cell and Molecular Therapies
Griffith University, Brisbane
Membrane and glycosaminoglycan binding of parasite annexins

DR PETER PAPATHANASIOU
Australian National University, Canberra, Australian Capital Territory
ENU stem cell mutants

DR BLESSY PAUL
Eskitis Institute for Cell and Molecular Therapies
Griffith University, Brisbane
Structure-based drug design of novel inhibitors of carbonic anhydrase for treatment of glaucoma and cancer

DR RICHARD PAYNE
University of Sydney, New South Wales
New strategies for the production of glycopeptides and glycoproteins

SIEW PING
School of Chemistry and Molecular Biosciences, UQ
Evolution of the hnRNP A/B genes

DR RICK REISDORPH
National Jewish Health Mass Spectrometry Core Facility, Denver, Colorado, USA
Quantitative proteomics workflows: evaluation and application

DR MIKE ROSSNER
Executive Director
Rockefeller University Press, New York, New York, USA
What's in a picture? The temptation of image manipulation

DR MARTIN J. SCANLON
Monash Institute of Pharmaceutical Sciences
Monash University, Melbourne, Victoria
Fragment-based drug design. Small is beautiful

STACY SCOTT
Institute for Glycomics
Griffith University, Gold Coast, Queensland
An investigation into the transition from a reduced to an oxidized form of human galectin-1

PROFESSOR DIETER SEEBACH
Eidgenössische Technische Hochschule, Zürich, Switzerland
Beta-peptidic peptidomimetics

DR TETYANA SHANDALA
Sansom Institute
University of Adelaide, South Australia
Drosophila 14-3-3e plays a critical role in innate immunity by regulating the secretion of anti-microbial peptide

DR ANNETTE SHEWAN
University of California San Francisco, USA
Molecular regulation of epithelial polarity by lethal giant larvae

DR CAMERON SIMMONS
Hospital for Tropical Diseases
Oxford Clinical Research Unit, Ho Chi Minh City, Vietnam
Dengue-viral epidemiology, pathogenesis and treatment options

PROFESSOR STEVE SIMPSON
University of Sydney, New South Wales
Integrative behaviour: from neurons to societies (a tale of swarms, cannibals, obesity and ageing)

DR LILA SOLNICA-KREZEL
Vanderbilt University, Nashville, Tennessee, USA
Genetic regulation of gastrulation movements in zebrafish

MITCHELL STANTON-COOK
School of Chemistry and Molecular Biosciences, UQ
Computing protein dynamics with paramagnetic NMR

DR VIKTOR STEIN
University of Cambridge, United Kingdom
A covalent DNA display system based on O6-alkyltransferase (AGT) and in vitro compartmentalisation

AMBER STEPHENS
CSIRO
Identification and functional characterisation of F. graminearum *virulence genes during crown rot of wheat*

NANA SUNN
Micro-Ultrasound Core Facility Manager Queensland Brain Institute, UQ
Research applications of micro-ultrasound imaging in mice

DR ALEX SYKES
Queensland Brain Institute, UQ
Evidence for a high-affinity 2:4 TrkA:p75 neurotrophin receptor NGF complex

ELAINE THOMAS
Diamantina Institute, UQ
IMPDH, a sensor of intracellular energy?

ASSOCIATE PROFESSOR PETER THORN
School of Biomedical Sciences, UQ
Complex vesicle dynamics during secretion

PROFESSOR LEANN TILLEY
Monash University, Melbourne, Victoria
Multi-mode high-resolution imaging of malaria parasite-infected erythrocytes

DR JOE TIRALONGO
Institute for Glycomics Griffith University, Gold Coast, Queensland
CMP-sialic acid transporter: elucidation of structure-function relationship

PROFESSOR DAVID TREMETHICK
John Curtin School of Medical Research Australian National University, Canberra, Australian Capital Territory
Understanding the dynamic link between chromatin structure and function during development

PROFESSOR PETER VISSCHER
Queensland Institute of Medical Research, Brisbane
From genome-wide association studies to individual risk prediction for disease in humans: prospects and limitations

DR JANE VISVADER
Walter and Eliza Hall Institute of Medical Research, Melbourne, Victoria
Getting abreast of mammary development and cancer subtypes

PROFESSOR CLAES WAHLESTEDT
The Scripps Research Institute, Florida, USA
Regulatory RNAs in CNS disorders

PROFESSOR HERBERT WALDMANN
Max Planck Institute of Molecular Physiology, Dortmund, Germany
Chemical biology of Ras lipidation: are there new cancer targets in the Ras signalling pathway?

DR TRISTAN WALLIS
Queensland Institute of Medical Research, Brisbane
Optimising LC-MALDI

DR NATHAN WATSON-HAIGH
CSIRO Livestock Industries
Weighted co-expression networks shed light on the molecular mechanism of action of Metyrapone on wool follicle development

DR ROLAND WEDLICH-SÖLDNER
Max-Planck Institute of Biochemistry, Munich, Germany
Cell cortex organisation in yeast and mammals - new roles for myosins

DR CHRISTINE WELLS
Eskitis Institute for Cell and Molecular Therapies Griffith University, Brisbane
Networking through the nose

PROFESSOR JAMES WELLS
University of California San Francisco, USA
Engineering cells to death

PROFESSOR WOLFGANG WENINGER
Centenary Institute of Cancer Medicine and Cell Biology University of Sydney, New South Wales
Visualising immune responses in tumours and infections

PROFESSOR EMMA WHITELAW
Queensland Institute of Medical Research, Brisbane
Epigenetic reprogramming within and across generations

DR STEPHEN WOOD
Eskitis Institute for Cell and Molecular Therapies Griffith University, Brisbane
Neural progenitors: in development and disease

DR SHERRY WU
Diamantina Institute, UQ
RNAi therapy for cancer: It's all about delivery!

PROFESSOR BAUKE YLSTRA
VU University Medical Centre, Amsterdam, Netherlands
Chromosomal copy numbers aberrations for diagnosis and patient treatment

PROFESSOR PAUL YOUNG
School of Chemistry and Molecular Biosciences, UQ
How much can a koala bare: retroviral invasion of the koala genome

EMMA ZHENG
University of British Columbia, Vancouver, Canada, and Diamantina, UQ
Quantitative proteomics analysis of membrane microdomains using SILAC

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.

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").

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 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.

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.

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. Professor Koopman's laboratory is also expanding this program, under the auspices of the CRC, to develop a similar management strategy for the cane toad, currently ecological public enemy number one in Queensland. John Abramyan, a PhD student in the Koopman group, was part of the first cohort of postgraduates of the CRC and is working on the daughterless cane toad project. Lindsey McFarlane 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 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. The facility, which includes a 300kV Technai microscope, 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 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 funds excellence in stem cell research across Australia. The IMB has very close links with the ASCC. In 2009, Professor Brandon Wainwright was appointed to the Board of Directors. Professor Melissa Little spent a period as Chief Scientific Officer, responsible for developing strategy, scientific review and management. She also developed a Queensland division of the ASCC based at UQ, and is a member of the Centre's Senior Scientific Faculty.
In 2009, the ASCC restructured its research portfolio. Instead of funding individual projects, the Centre now 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 Sean Grimmond is also funded by the ASCC. He is leader of a module in Stream 1. This stream focuses on understanding reprogramming of cells and the induction 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 & Eliza Hall Institute, is developing a database containing multiple datasets of genetic information across stem cell lines.

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, and the Waite Campus of the University of Adelaide.

ACRF DYNAMIC IMAGING FACILITY FOR CANCER BIOLOGY

This facility was launched in August 2005 with the aid of a grant from the Australian Cancer Research Foundation (ACRF). It is the only one of its kind in Australia and the laboratory at the IMB houses two technologically-advanced microscope systems that will enable cutting-edge research into cancer biology. IMB researchers are now able to make live movies and track the movements and behaviour of breast cancer cells with a higher resolution, greater capability and more quickly than ever before. The facility also allows researchers to optically dissect cancerous and non-cancerous cells and reconstruct them in 3D, revealing much greater detail about their inner workings. Researchers can now examine a vast range of proteins at the same time and examine their dynamics in live cells over time. In 2009, IMB received a further grant from the ACRF to expand the Facility, which will be opened anew in early 2010.

RIKEN

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 transcriptomes, resulting in a series of papers. In 2009, FANTOM4 published a series of papers in *Nature Genetics* on gene control in mammals. Professors John Mattick and Sean Grimmond were senior authors on a paper each, while PhD students Ryan Taft and Geoff Faulkner were first authors on those respective papers.

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. It is rapidly becoming a leader in supporting the bioinformatics requirements of research-intensive universities, institutions and companies, beyond the capability of any single organisation in Australia or the Asia-Pacific region. It provides the bioinformatics, ICT, research biology and clinical community with secure access to data and the tools to efficiently deliver relevant solutions. Its projects cover: programmatic access to large data sets and tools, data integration and workflow technology for biological and health data, mirror site for genome browsers, annotation pipelines and workflows for biological and health data, genotype/phenotype linkages, analysis and visualisation of biological data and building and using web-based tools. In 2009, QFAB launched the Arachnoserver, a database of spider toxins that can be accessed by researchers worldwide.

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. The only Australian node is at the IMB in the laboratory of Dr Brad Marsh, who in addition to his research also chairs the Communications & Awareness Subcommittee. 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.

COMMUNITY ENGAGEMENT

THE IMB WEBSITE (www.imb.uq.edu.au) is the main source of information about the Institute. In 2009, the website underwent a redesign in order to fit with the new UQ corporate look. In addition to rebranding the site, staff took the opportunity to redesign sections of the site, especially the home page, in order to make them more attractive and user-friendly. The website received over 230,000 hits in 2009. Although this is slightly down on 2008, the number of pages these visitors viewed increased to nearly 1.4 million. The website remains in the number one position when 'molecular bioscience' is searched in Google. IMB continued to produce the quarterly 'Output' newsletter, which can be viewed on the IMB website and details the research and activities of the institute. To receive Output either by email or post, please click the green subscribe button on the IMB homepage.

The main community outreach initiative in 2009 was the creation of the IMB Science Ambassador Program. Early career researchers were invited to apply for the program. Successful applicants received extra training in communication in order to represent the institute at events and create content to disseminate to the wider community. The rationale behind the program was to take researchers who are passionate about science communication and give them training to enable them to effectively represent the institute. The program was also a way of recognising those who volunteered for events and activities on a regular basis. It was the brainchild of PhD student Maggie Gentz, who has been involved in applied science research, education and outreach programs for the public for a number of years.

21 researchers were part of the pilot year. They were: Melanie Andrews (Sweet group), Dr Johanna Barclay (Waters group), Denis Bauer (Bailey group), Dr Andrew Brooks (Waters group), Alex Combes (Koopman group), Dr Richa Dave (Wainwright group), Marianne Diaz (Muscat/Leong group), Dr Marcel Dinger (Mattick group), Maggie Gentz (King group), Dr Sonia Henriques (Craik group), Dr Markus Kerr (Teasdale group), Emily Knauth (Hankamer group), Darren Korbie (Mattick group), Jane Lattin (Sweet group), Tim Mercer (Mattick group) Samantha Murphy (Parton group), Elizabeth Skippington (Ragan group), Phillippa Smith (Craik group), Evan Stephens (Hankamer group), Dr Rehan Villani (Wainwright group) and Simon Wilkins (Perkins group). The ambassadors were required to complete 15 hours of outreach during the year. Although some subsequently left the IMB and thus were unable to complete their full commitment of hours, the group as a whole contributed well over 300 hours of community outreach in 2009, and many have applied to the program again for 2010.

Researchers in the program assisted with events including: Brisbane's Royal Show, ABC's Scientists on the Loose, Kenmore State High School Careers Night, UQ School of Journalism mock press conference, Talking Scientists (an initiative of the Queensland Government), Biofutures, Frontiers in Science, Experience Science, UQ Open Day, Kids's STEM Convention, Science in Parliament, Ironside Primary School Science Day, and the National Science Contest.

The ambassadors also hosted tours of the institute. There were over 3000 visitors to the IMB in 2009, and while not all of these visitors were hosted by the ambassadors, they did an exemplary job in showing off the institute and its facilities to those they did guide. Visitors ranged from school students to government ministers, both Australian and international, and represented 26 countries. IMB welcomes enquiries from groups or individuals wishing to tour the Institute. Please email imb@imb.uq.edu.au in the first instance.

Other researchers chose to perform community outreach independent of the Science Ambassador program. Dr Melissa Davis (Ragan group) participated in both Scientists in Schools and the Queensland Government's Talking Scientists program, where she travelled to Bundaberg and Toowoomba to give presentations and workshops. Dr Davis was partnered with Ironside State School for the CSIRO Scientists in Schools program, in which a scientist is partnered with a particular class of students. The program is flexible, and allows the scientist and teacher to devise a partnership that suits the scientist's area of expertise while engaging the students with science and making them aware of careers available in the field. Dr Davis was one of four IMB researchers to be a Scientist in Schools. Dr Dagmar Wilhelm partnered with Wellers Hill State School, Dr Brad Marsh continued his partnership with Graceville State School, and Adi Idris (Sweet group) was a scientist at Wooloowin State School until he finished his PhD in mid-2009.

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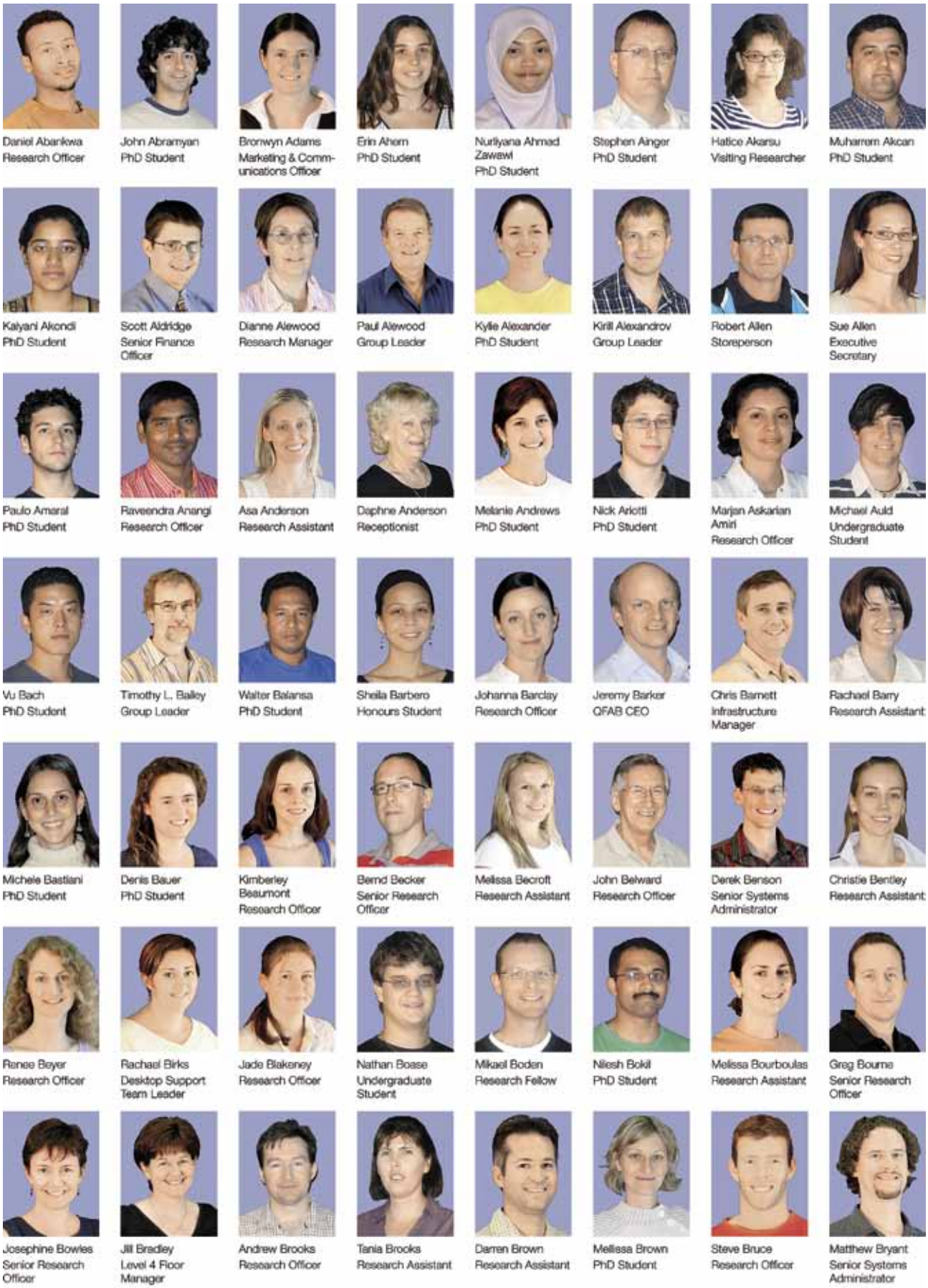

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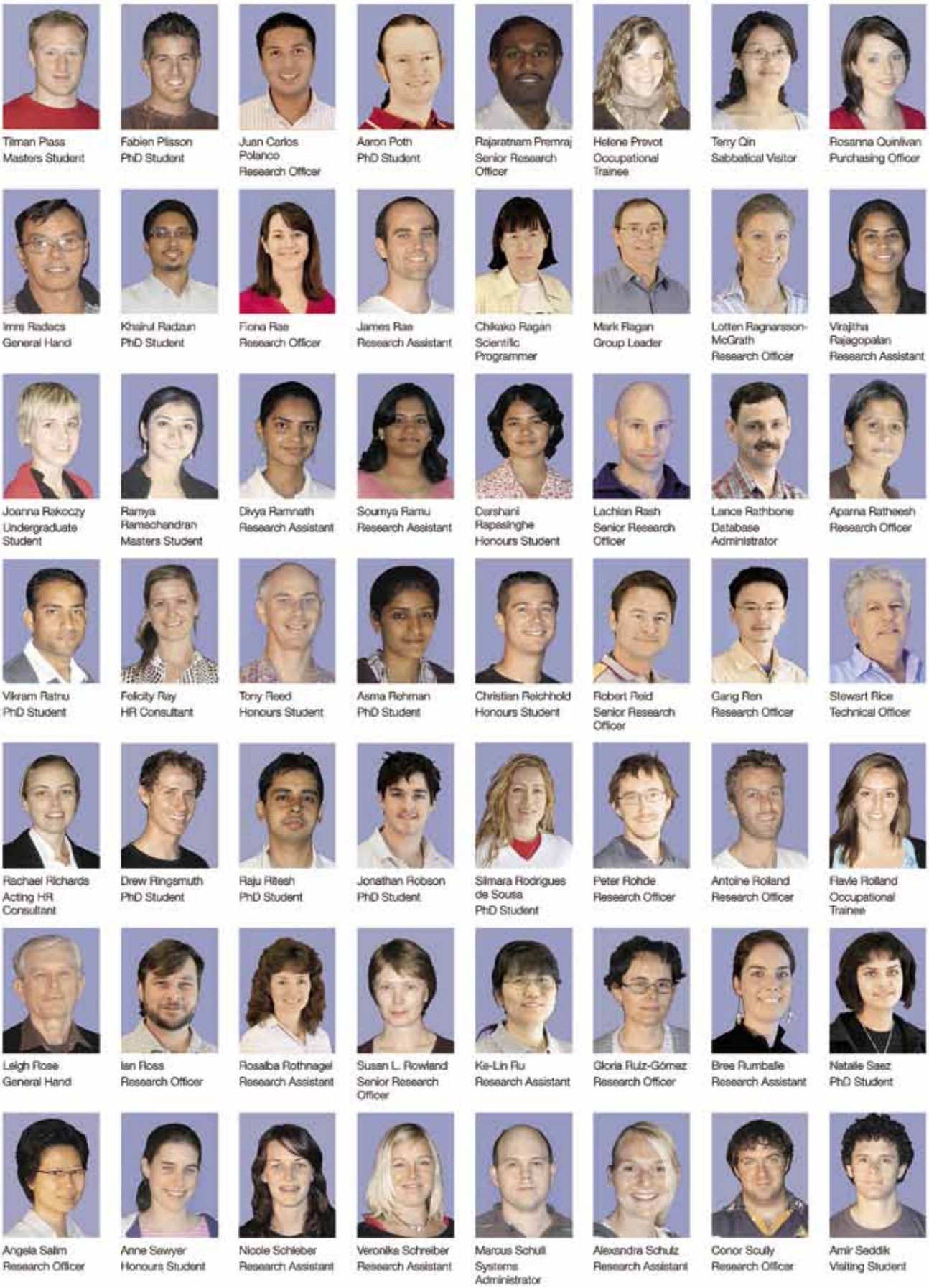

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PhD Student


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Jack Wang
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Shivangi Wani
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Jane Weber
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Tom Whittington
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Andrew Whitten
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Mark Ziza
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Leah Creed
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Manager, IP & Development

Karen Soxsmith
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Desktop Support Analyst

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FINANCIAL STATEMENT

Statement of Operating Income and Expenditure
Year Ended 31 December 2009

INCOME	NOTES	2005	2006	2007	2008	2009
University of Queensland (Operating Grant)	1	7,225,765	10,767,311	11,087,942	11,062,918	13,383,853
University of Queensland Research Grants		334,500	252,252	300,436	190,291	311,370
State Government		10,425,000	10,175,000	11,127,168	10,857,620	14,867,120
SRC Grant (Australian Research Council)		1,137,436	1,159,047	1,182,516	1,206,166	0
Australian Research Council	2	4,744,519	5,218,279	6,010,239	5,977,542	7,637,369
Arthritis Foundation of Australia		14,950	0	0	0	0
Australian Cancer Research Foundation		600,000	0	0	0	1,250,000
Australian Nuclear Science & Technology Organisation		85,355	78,757	230,492	61,326	8,540
Australian Stem Cell Centre		161,691	159,780	467,335	770,065	1,342,609
Baker IDI Heart & Diabetes Institute		0	0	0	0	76,237
Cancer Council Queensland (previously QCF)		215,100	148,700	312,000	554,000	402,000
Clive and Vera Ramaciotti Foundation		0	0	60,000	30,000	0
Community Health + Tuberculosis Australia		0	49,000	0	0	0
CRC for Chronic Inflammatory Diseases		1,367,457	1,326,058	1,462,776	1,214,510	0
CRC for Pest Animal Control		0	122,210	0	47,952	0
Dairy Australia		203,765	167,644	700,321	333,084	0
Dept Industry Science and Technology (Commonwealth) was DISR		0	0	200,000	135,000	37,245
Department of Primary Industries		0	0	50,000	0	0
Diabetes Australia Research Trust		0	45,000	0	50,008	60,000
Human Frontiers Science Program		0	0	81,783	58,180	279,530
Japanese Science & Technology Agency		0	0	0	106,462	142,331
The John Trivett Foundation		0	0	267,817	0	0
Juvenile Diabetes Foundation International		177,814	178,634	147,708	110,723	167,904
The Mazda Foundation		0	0	0	150,000	0
The Murdoch Childrens Research Institute		0	0	347,527	235,515	379,122
National Breast Cancer Foundation		0	0	0	0	413,490
National Institute of Health (US)		1,132,358	1,176,642	969,415	561,829	503,882
National Health and Medical Research Council	2	9,819,880	7,888,967	11,054,142	12,445,955	15,622,119
National Heart Foundation		50,000	0	0	65,800	0
New Zealand Dept Science & Technology		0	0	81,392	40,738	0
Oncology Children's Foundation		0	0	0	0	100,000
Post Graduate Scholarships		140,237	261,263	305,255	234,520	142,619
Wellcome Trust		150,311	0	0	0	0
Commercial Income		1,856,012	2,018,054	4,880,234	4,585,955	2,521,961
Cross-Institutional contributions to LIEF or Facilities		60,000	509,472	188,000	50,000	0
University of Newcastle (re ARC Centre)		47,727	252,562	128,218	153,218	150,000
QBP recoveries		316,211	386,092	371,257	363,065	346,442
Shared Grants		262,062	234,685	4,000	40,772	0
Conference Income		73,032	66,615	184,340	70,558	91,656
QBP Store		247,890	276,819	314,057	326,215	357,613
Wesley Research Institute		0	20,000	93,645	98,423	101,628
Miscellaneous Income		416,707	399,887	357,293	391,776	186,154
TOTAL INCOME:		**41,265,779**	**43,338,729**	**52,967,307**	**52,580,186**	**60,882,794**
Funds brought forward from previous year	3	**6,557,150**	**9,050,612**	**11,441,270**	**15,641,004**	**18,495,763**
TOTAL FUNDS AVAILABLE		**47,822,929**	**52,389,341**	**64,408,577**	**68,221,190**	**79,378,557**

EXPENDITURE		2005	2006	2007	2008	2009
Salaries – Research		18,430,158	20,110,376	22,878,237	24,750,517	24,717,110
– Administration		1,343,782	1,205,466	1,349,056	1,345,709	1,548,200
– Infrastructure		2,383,622	2,673,620	2,368,795	2,862,623	3,090,792
Research Services		9,976,365	10,995,871	13,099,865	13,092,074	14,696,645
Education Programs	4	375,177	358,445	332,919	380,733	458,699
Administration	5	379,317	529,612	521,743	496,666	370,541
Corporate Services (UQ)	1	0	0	0	0	0
Infrastructure	6	1,287,442	1,295,139	1,862,212	2,160,052	1,693,759
Capital Equipment	7	3,389,715	2,569,801	5,156,825	3,438,525	6,847,087
IMBcom		1,206,738	1,209,741	1,197,920	1,198,528	1,200,000
TOTAL EXPENDITURE		**38,772,317**	**40,948,071**	**48,767,573**	**49,725,426**	**54,622,833**
Funds carried forward	8	**9,050,612**	**11,441,270**	**15,641,004**	**18,495,763**	**24,755,724**

Explanatory Notes to Statement of Income and Expenditure

1(a) In-kind Contributions

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

	Location	Percentage
K. Burrage	University of Oxford	50
G. McLachlan	UQ Mathematics	90
A. Mark	UQ SMMS	80
P. Leo	UQ Diamantina Inst.	75
M. Smythe	Protagonist	80
G. Leong	Mater Children's Hospital	50

1(b) Gross Income & Corporate Services Charge

University of Queensland Operating Grant Income shown is the nett amount and includes a Corporate Services charge. Although the treatment in 2006 showed this separately under expenditure, in this report the 2006 figures have been adjusted and now show the nett for better direct comparison.

2 Fellowship/Projects from Government Agencies

Australian Research Council	
Projects	6,199,982
Fellowships	1,437,387
	7,637,369
National Health and Medical Research Council	
Projects	11,876,056
Fellowships	3,746,063
	15,622,119

3 Funds carried forward to 2009

University of Queensland Operating Grant	10,508,870
University of Queensland Research Grants	27,742
Post Graduate Scholarships	53,427
State Government	1,972,027
SRC Grant	-49,706
Fellowships (as approved by funding bodies)	41,002
Overseas Grants funded mid year	608,423
Contract Research	1,815,335
Project Grants (as approved by funding bodies)	3,518,644
	18,495,764

4 Education Programs

Postgraduate scholarships	363,614
Postgraduate recruitment & training	95,085
Total Education Services	**458,699**

5 Administration

Annual Report	16,799
Marketing	36,985
Personnel Recruitment and Training	46,631
Visiting Scientists/Seminars	27,210
Fees	27,203
Quinquennial Review	0
Entertaining	4879
Photocopying	29,488
Postage and Freight	4330
Printing & stationery	65,147
Telephone	59,790
Travel Expenses	52,079
Board Fees	0
Total Administration	**370,541**

6 Infrastructure

Building Maintenance	63,543
Rental - Storage	10,810
Safety Equipment	49,286
Laundry	5749
Minor Equipment & Furniture	25,079
Equipment Maintenance	261,486
Animals	293,389
Computer Services	674,959
Glass washing and replacement	61,124
Reticulated gases, RO water & dry ice	78,070
Cost Recovery	-146,843
Stores	317,107
Total Infrastructure	**1,693,759**

7 Capital Equipment

Scientific Equipment	4,988,475
Minor Equipment	1,858,612
Total Capital Equipment	**6,847,087**

8 Funds carried forward to 2010

University of Queensland Operating Grant	11,316,716[#]
University of Queensland Research Grants	835,049
Post Graduate 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

[#] Of this, $1.58M is the carry forward on IMB Group Leader core accounts & $2.64M relates to oustanding 2009 equipment commitments.
* Of this, $5.85M is late received income ($1.25M Int. Cancer Genome Consortium, $3.35M NIRAP Pancreatic Cancer & $1.25M ACRF Cancer Biology Imaging Facility)

GLOSSARY OF TERMS

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

Adiposity Composed of, or related to, fat or fatty tissue.

Adrenergic Signalling that uses the same paths as adrenaline and thus has the same effects.

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

Allele One of a number of possible versions of a gene. Each person inherits two alleles per gene, one from each parent.

Alpha-helices Coiled formations that occur frequently in proteins and peptides and often present an interaction site for other proteins.

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

Antinociceptive Counters the effect of anything caused by, or in response to, pain.

Apoptosis Programmed cell death.

ARC Australian Research Council.

Aromatase An enzyme that causes testosterone to transform into estrogen.

Array An ordering of samples on a slide.

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

ATPase An enzyme that causes an energy-releasing chemical reaction.

BAC A piece of genetic material used to clone DNA.

Bilayer Two layers of molecules.

Bioactive Has an effect on a living organism.

Biodiscovery The exploration of biodiversity to identify molecules that have useful applications.

Biodiversity The diversity of organisms within a specified area.

Biogenesis The production of material from living organisms.

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

Biophysical The intersection between physics and biology.

Biopolymer A polymer (large molecule) produced by a living organism.

Bioscience Any of the branches of science dealing with the structure and behaviour of living organisms.

Biosynthesis The production of material from living organisms.

Biotechnology Any technology that uses biological systems or living organisms to make or modify products or processes.

BRET Bioluminescence resonance energy transfer. A cell-based assay allowing the direct study of complex protein-protein interactions in living cells.

BSE Bovine spongiform encephalopathy. Commonly known as mad cow disease.

Cadherin A class of transmembrane protein that ensures cells adhere to one another within a tissue.

Cerebellum The part of the brain that co-ordinates voluntary movement.

Chelate The process where an organic molecule bonds to a metal.

Chondrogenesis The development of cartilage.

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

Chromatography A method of separating chemical compounds into their base constituents by transporting the compound in liquid form through a porous substance. The different rates of absorbency of the constituents mean that as they pass through the substance they will separate.

CNS Central nervous system.

Co-factor A chemical that must be present in order for another molecule to function.

Combinatorial Chemistry Methods used to synthesise numerous, related chemical compounds.

Cryo-election microscopy A type of microscopy in which an electronically-magnified image is produced from a sample at very low temperatures.

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.

Cytokinesis The point in somatic cell division where the cytoplasm splits, as opposed to the splitting of the nucleus, which occurs first.

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

Cytoskeleton The protein framework of a cell.

Cytosol The fluid component of cytoplasm, in which all other structures are suspended.

De novo Not previously present.

Deterministic Something that is predictable, not random, given known initial conditions. The opposite of stochastic.

Dimer An organic molecule formed by combining two smaller molecules.

Discrete Separate and independent.

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

EGFR Epidermal growth factor receptor.

Embryogenesis The development of an embryo.

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

Endocytic Pertaining to endocytosis.

Endocytosis Uptake of material into a cell.

Endogenous Within the body.

Endosome An organelle involved in protein trafficking.

Enzyme 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.

Epithelium Membranous cellular tissue that covers the internal and external surfaces of the body.

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

ERK A messenger kinase belonging to the MAPK family.

Erythrocytes Red blood cells.

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.

Exocytosis The discharge of material from the cell.

Ex vivo Taking place outside an organism.

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

Factor A sequence of DNA involved in producing a polypeptide chain.

Ferritin A protein that stores iron.

Flaviviruses A family of small RNA viruses that are often transmitted by mosquitoes and ticks.

FRET Fluorescence Resonance Energy Transfer. A method of quantifying molecular dynamics such as protein-protein interactions.

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.

Genomics The study of genes and their function.

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

Glycolytic Relating to the process through which carbohydrates and sugars are broken down.

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

Growth factors Proteins that stimulate the growth of cells.

Haemotopoietic Relating to the formation of blood cells.

Histidine A type of amino acid that binds to form proteins. Histidine is found in proteins involved in the repair and growth of tissue.

Homeostasis A condition where the body uses negative feedback processes to maintain its systems at a constant equilibrium.

Homology Similarity due to common ancestry.

Hypercholesterolemia High blood cholesterol.

Icosahedron A structure with twenty equal faces.

Immunoprecipitation The process whereby an antigen is formed in a solution using a specific antibody.

Inducible Pluripotent Cells A stem cell artificially derived from a non-stem cell.

Innate immunity Natural immunity that fights off infection in a non-specific manner.

In vitro A process occurring in an artificial environment that would normally occur in an organism.

In vivo A process occurring within an organism.

Isoprenoids Naturally occurring organic molecules.

Isothermal calorimetry A technique of measuring the heat and heat capacity of chemical reactions; often used to characterise potential drug candidates.

Keratinocyte 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.

Knockout A technique in which specific genes are made inactive, so scientists can determine their effect.

Ligand 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.

Lipogenesis The production of fat.

Lymphatic Pertaining to 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, large heterogeneous, dynamic vesicles.

MAPK Mitogen-activated protein kinase.

Meiosis The process by which cells divide to produce eggs and sperm.

Melanin Skin and hair pigment.

Melanocortin A group of hormones.

Melanocytes Cells that produce melanin, the pigment that gives skin, hair and eyes their colour.

Melanosome The structure within skin cells that contains melanin.

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.

Metabolites A chemical involved in or produced during metabolism.

Metagene A pattern of gene expression.

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.

MicroRNA MiRNA, RNA molecules around 20 nucleotides long that regulate gene expression.

Morphogenesis The process where cells differentiate into different structures.

MRSA Metacillin-resistant *Staphylococcus aureus.*

Murine Relating to mice or rats.

Mutagenesis The process of intentionally creating mutations in an organism's DNA.

Myosin A protein, along with actin, responsible for muscle contraction.

Glossary of terms

NBCF National Breast Cancer Foundation.

Nephron Tubes within the kidney that act as filters.

Neuropathic Pain from nerves themselves, as opposed to injured or diseased body parts.

NHMRC National Health and Medical Research Council.

NMR Nuclear Magnetic Resonance. A spectroscopic technique that analyses the disruptions to a high magnetic field to elucidate the chemical structure and molecular dynamics of a sample.

NS1 Non-structural protein 1, involved in virus replication.

Nucleators Something that either forms into a nucleus or aids in this formation.

Nucleosomes The repeating subunit of chromatin.

Nucleotides The subunits of DNA and RNA.

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.

Oncogenesis The formation and growth of tumours.

Organelle A discrete subcellular structure with a specialised function.

Organic Containing carbon.

Organogenesis The formation of organs.

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.

Pathogen A disease-causing organism.

Pathogenicity The capacity to cause disease.

Pathophysiology A change in function caused by a disease or condition.

Peptide A compound of two or more amino acids.

Phage A virus that infects bacteria.

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.

Pharmacophore A framework with the properties necessary for a drug's activity.

Pharming Farming genetically-modified animals and plants to produce drugs.

Phenotype The characteristics of an organism resulting from the interaction between its genotype and its environment.

Photosynthesis The process through which plants convert energy from sunlight into chemical energy that acts as their fuel.

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.

Prostaglandin Any of a group of compounds derived from fatty acids with a variety of actions and effects on cells.

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.

Proteinase Enzymes that break down proteins.

Radioligand A radioactive substance injected into tissue that binds to receptors and allows researchers to study its behaviour.

Recombineering A process through which mutations are artificially introduced into a bacterial chromosome and used to produce transgenic mice.

Redox A reduction/oxidation reaction, where the oxidation number of an atom changes.

Retromer complex A protein complex that is involved in the transport of proteins to the Golgi.

Retrotransposons Segments of DNA that can move around the genome and amplify themselves.

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.

RNAi RNA interference. A process where small RNAs are used to control gene expression.

Scission Splitting.

Secretory Relating to secretion.

Sequencing Determining the order of nucleotides in a DNA or RNA strand.

SNP Single nucleotide polymorphism. A single base of DNA which can differ in a population.

Somatic Refers to any of the non-reproductive parts of the body, also used to mean a condition that is non-inherited.

Spectroscopy The study of the interaction between matter and radiation (eg. light).

Stat5 A protein that regulates gene expression.

Steatotic Has an accumulation of fat in the liver.

Stochastic A process that is governed by random chance.

Synthase An enzyme that catalyses the synthesis of a biological compound.

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.

Transgenic An organism that has a transferred gene (transgene) incorporated into the chromosome of all its cells.

Translation The production of proteins from messenger RNA.

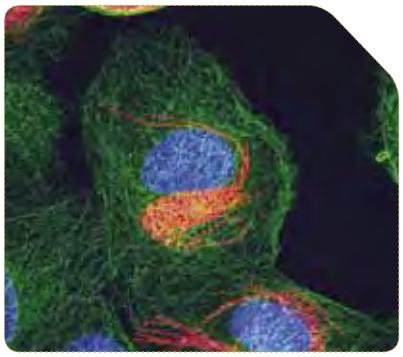
Transmembrane Passes through or occurs on the membrane.

Triplex Consisting of three parts.

Vascular Pertaining to anything related to or containing conductive vessels, eg. blood vessels.

Vesicle A closed membrane shell.

2009 PUBLICATIONS



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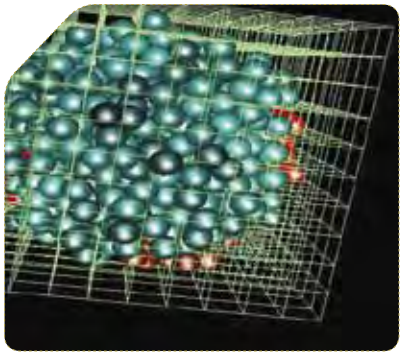

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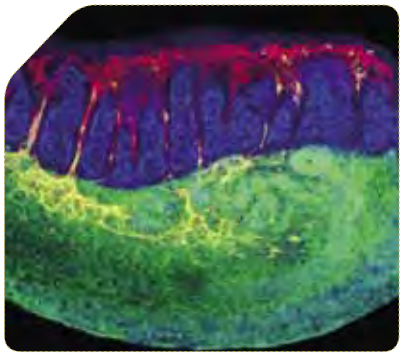

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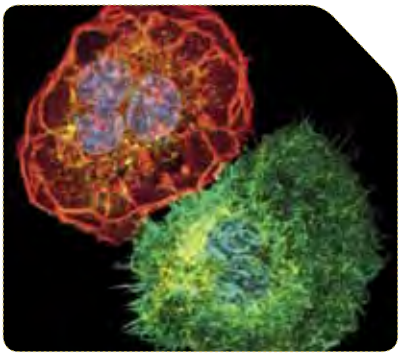

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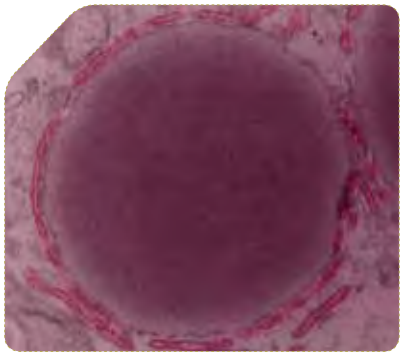

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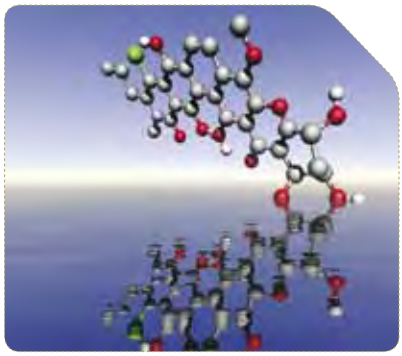

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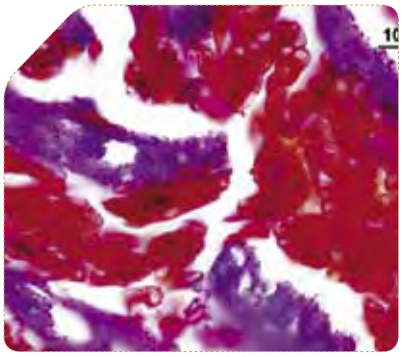

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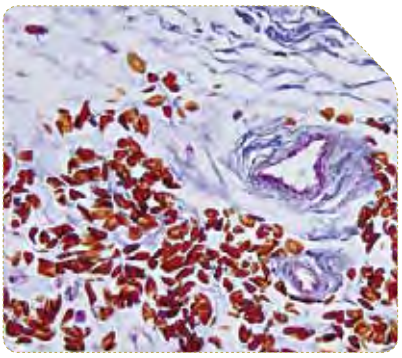

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