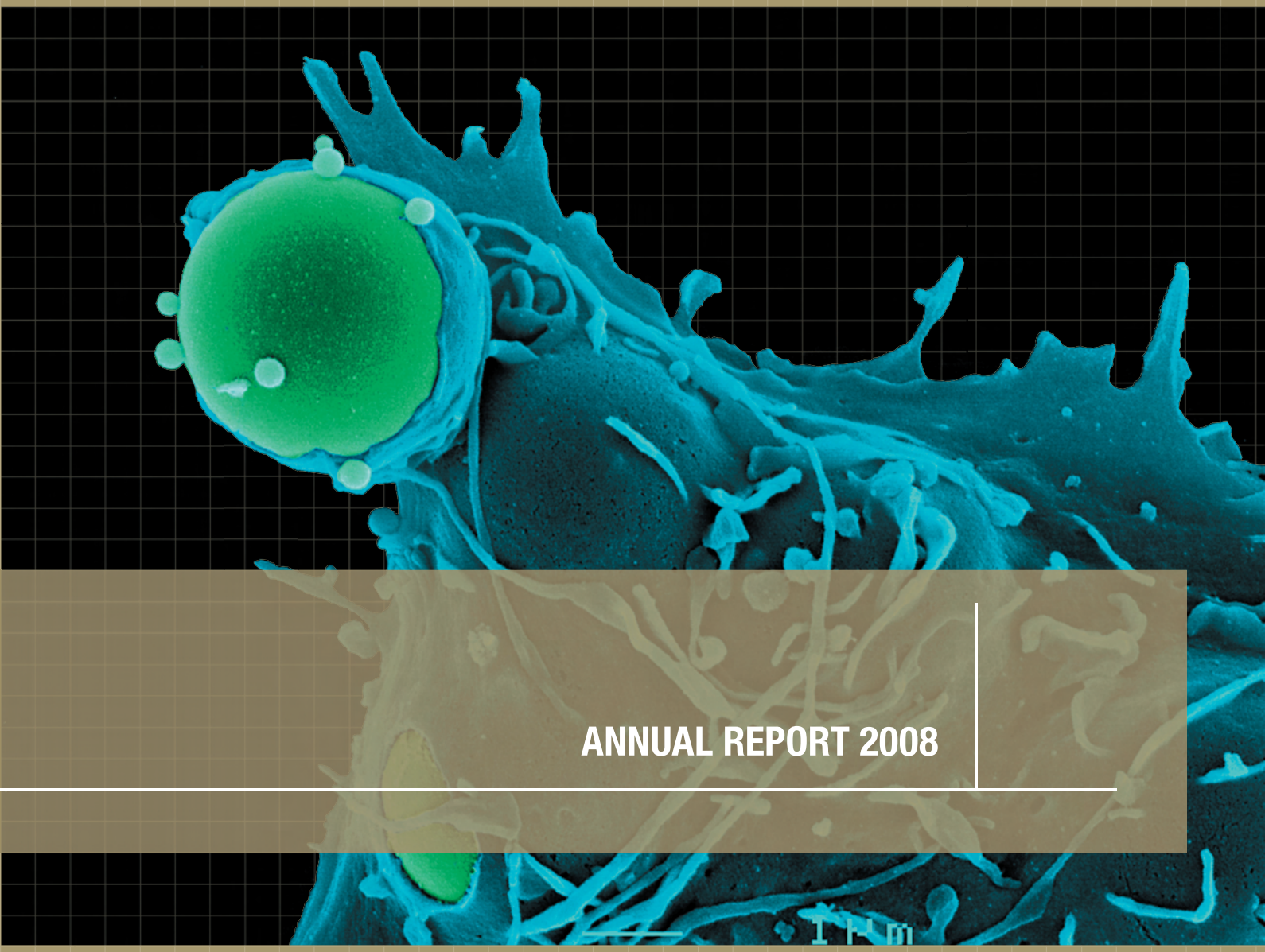
THE UNIVERSITY OF QUEENSLAND
AUSTRALIA

IMB Institute for Molecular Bioscience



ANNUAL REPORT 2008

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.

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CHAIR'S MESSAGE

2008 has been a year of progress and consolidation for the Institute for Molecular Bioscience in the vital areas of human capital, material infrastructure, national and international reputation, and returns to the community.

The freeing up of laboratory space previously rented by a government department gave the IMB an opportunity to expand its discovery workforce by adding four research groups. A successful recruitment campaign showed that three senior employees had the ability to step up as group leaders, and the appointments of Dr Brett Collins, Dr Nick Hamilton and Dr Dagmar Wilhelm reflect well on training and mentorship in the Institute.

The fourth new group leader is Professor Kirill Alexandrov, who came to us from the prestigious Max Planck Institute in Germany. Arriving in September, he quickly succeeded in the 2008 Australian Research Council (ARC) and National Health and Medical Research Council grant rounds, in much the same way as Brett Collins succeeded in the ARC grant round.

The recruitment focus will now turn to early career researchers, who will make significant immediate and short-term contributions and gain the expertise to augment the next generation of group leaders.

Throughout 2008 the IMB continued to justify the significant investments in cutting-edge equipment made in previous years by The Atlantic Philanthropies, the Queensland and Federal Governments, the University, and industry partners such as Applied Biosystems.

The latter company has supplied new generation SOLiD™ sequencers which have enabled IMB experts to pioneer globally significant territory in genomics and transcriptomics – specialisations that will influence the worldwide direction of healthcare. It speaks volumes for the reputation of IMB researchers that the institute was only the third venue, and the first outside of the United States of America, to host these sequencers through an early-access program to develop applications for the technology.

In late 2007 IMB received two of these machines and in 2008 Associate Professor Sean Grimmond and his team developed a new method for sequencing an entire biological sample in a single experiment, published in the high-impact journal *Nature Methods*. Such progress is typical of an institute that is resolutely focused on high-quality research which has strong potential to translate into tangible human benefits, particularly in relation to health.

I congratulate IMB Director Professor Brandon Wainwright, Deputy Directors Dr Ian Taylor and Professor Jenny Stow, all IMB staff and students, and the team at IMBcom, on achievements made throughout 2008.

I thank board directors for their contributions to the IMB's success, and for the advice and support they have provided me since I became chair on January 1. Their experience and sagacity will prove invaluable as the interlocked circles of research and business face up to deepening challenges linked to the global economic slowdown.

Professor Paul Greenfield, AO

The University of Queensland
Vice-Chancellor

2008 has been another busy year for the Institute with some changes at the senior management level, the appointment of four new Group Leaders to the IMB, success in national competitive grant funding schemes and the graduation of 18 PhD students. In our report to the Queensland State Government in November of 2008 we continued to exceed all of our Key Performance Indicators for the State Government – a testament to the ability and hard work of our academic and support staff and our commercialisation company, IMBcom.

In April of 2008 Professor Jenny Stow was appointed as the new Deputy Director (Research) for the IMB, following the departure of Professor John Hancock to the USA on leave of absence. Since this appointment was made Jenny has instigated reviews of a number of our policies and procedures, including the introduction of a publication incentive bonus scheme, has been closely involved in the appointment of new Group Leaders, and has provided valuable advice and mentoring to a number of our junior Group Leaders and senior postdocs. Jenny and Associate Professor Alpha Yap also led the successful bid to Australian Cancer Research Foundation (ACRF) for the establishment of the ACRF Cancer Biology Imaging Facility at IMB, a facility that will come on line early in 2009 and will provide sophisticated imaging equipment and technologies to cancer researchers across Queensland.

The IMB was established in 2000 and many of the senior academic staff at the Institute have been with us since establishment and, indeed, came to the IMB from the CMCB and 3D Centre – the forerunners of the IMB. This year we set out to achieve some generational change and devoted considerable time and resources to the recruitment of new Group Leaders to the IMB, with an emphasis on scientists who would 'value add' to the current research strengths of the IMB or who would bring a new and complementary specialisation to our existing research profile. We have already made four new appointments and expect to make at least two more appointments in 2009.

Dr Brett Collins joined IMB as a senior postdoctoral fellow 3 years ago and has consolidated his research profile since arriving. Brett's research focuses on cell trafficking and his work utilises structural biology to answer important questions in cell biology. He holds an R. Douglas Wright Fellowship from the NHMRC as well as being the recipient of an Early Career Researcher Grant from The University of Queensland. His contributions have been excellent and this year was appointed to Group Leader.

At a more senior level, we appointed Professor Kirill Alexandrov to a Group Leader position held jointly between the IMB and AIBN. Kirill was previously a Group Head at the Max Planck Institute in Dortmund. He arrived to take up his position in early September 2008 and had success in both the recent ARC Discovery Grant and NHMRC Project Grant round. Kirill is a cross-Divisional appointee, with research interests that lie in structural biology, chemistry and cell biology. His major research interest is the control of the process of protein prenylation – a key regulatory step in many biochemical processes of medical relevance. He has developed novel chemistry to probe the "prenylome" and, aligned with his expertise in structural biology/cell biology and his collaborative nature, we expect that he will have a significant impact on the research profile of the Institute.

Other internal recruits who have been achieving well in their respective areas for a number of years were appointed to junior Group Leader roles in 2008. Dr Dagmar Wilhelm, a developmental biologist, has been working at the IMB since 2002 and has achieved success as a Chief Investigator in both the NIH and the ARC schemes in the last two years. In the last year or so, Dagmar's research interests have widened to encompass the role on non-coding RNA in embryonic development and her appointment as a Group Leader will give her the opportunity to explore these cross-Divisional collaborations more closely.

Dr Nick Hamilton has a PhD in Pure Mathematics from the University of Western Australia and works in bioinformatics. In 2004 he began collaborating with researchers in the ARC Centre of Excellence in Bioinformatics and he quickly established himself within the cell imaging community at the IMB, collaborating with Dr Rohan Teasdale, Professor Jenny Stow and Professor Mark Ragan in the building of mathematical models to assist with cell imaging work at the Institute. Nick has a growing publication record and has received a number of awards and prizes during his relatively short career. Appointment as a Group Leader gives him the opportunity to build on current collaborations and to work towards a self-funding research group through success in competitive grant schemes.

Congratulations and welcome to all of the new Group Leaders and I look forward to the exciting times ahead.

Other activities for 2008 include the hosting of visits from four of our Scientific Advisory Committee members with the Divisions of Molecular Cell Biology, and Chemical and Structural Biology, being reviewed by two-member Scientific Advisory Committee panels. The visitors spent two days with the relevant Divisions and then provided feedback to the Executive Committee on the scientific performance of the relevant Division. Recommendations from the visitors have been taken on board by the relevant Division Heads and will inform future strategic research directions. We very much appreciate the efforts of the SAC members in helping to shape our science.

A highlight for the Institute is when staff members receive peer recognition for their achievements at the highest level and this year I am pleased to report that Professors Peter Koopman and John Mattick were elected Fellows of the Australian Academy of Science in May of 2008. My congratulations to them both and, indeed, to all the staff at the IMB whose hard work and dedication every year ensures that we continue to be ranked as a leading national and international bioscience research institute.

Professor Brandon Wainwright
IMB Director

DIRECTOR'S MESSAGE

DEPUTY DIRECTOR (RESEARCH) REPORT

This report marks my first as Deputy Director of Research at the IMB. I took up this position in mid-2008 after Professor John Hancock departed the Institute for a year's sabbatical in Houston. The year at IMB has gone quickly amidst many changes and new opportunities.

In his Director's report, Professor Brandon Wainwright has already detailed the exciting research brought to IMB by our four new group leaders. I would like to add my enthusiastic support for our new colleagues and express my confidence that their research will be the source of important new collaborations and new discoveries.

It is encouraging that three of the four recent group leader appointments were of internal candidates. IMB is now turning out young scientists of the highest calibre who are doing research at the cutting edge of their fields and who can compete successfully in an international arena for these highly sought-after positions. As a counterpoint, we are also pleased that IMB is attracting scientists from major research institutions overseas. Brisbane is now very definitely on the map as a destination for research, a hub of scientific revolution – and, of course, as a great place to live. Like all major institutions, IMB both collaborates and competes in science on a world stage and so enhancing our reputation nationally and internationally is always a priority.

The four scientific Divisions of IMB are each growing in reputation and size. With new incentives and initiatives at the Division level we aim to create strength and unity in these teams and in so doing to further enhance cross-disciplinary research. The same is true for collaborations with other UQ Institutes. Joint appointments for some of our new group leaders and shared technologies will increasingly drive research that blurs the boundaries of traditional scientific disciplines. Increasing ties within the University, with other Institutes and with industry in our locale will be an important factor in shaping the future and in ensuring that outcomes flow from our discoveries to the public.

While change pervaded IMB in 2008, our mission of producing the highest quality research remained rock-solid. In publishing, IMB's record is highly competitive and continues to climb. IMB scientists published a total of 194 papers in 2008, in journals such as *Nature, Science* and *Cell*. A full list of publications can be viewed at the back of this report, and more details on some of the IMB's research findings can be seen in our Highlights section, beginning on page 9.

The IMB continued to exceed national success rates in both the ARC Discovery and NHMRC Project grant rounds, receiving more than $10 million. Professor David Craik received the single largest grant from this round - $1.28 million from the ARC, which included an Australian Professorial Fellowship. Our researchers were also successful in winning funds from other sources, including a US$1.3 million grant from the Human Frontier Science Program to an international team including Associate Professor Alpha Yap.

Associate Professor Yap was, along with myself, also one of the major drivers behind a $2.5 million grant from the Australian Cancer Research Foundation, awarded late in the year. This grant will establish the 'ACRF Cancer Biology Imaging Facility', which will represent an expansion of the current ACRF Dynamic Imaging Facility for Cancer Biology. The current facility has been enormously successful in underpinning cancer biology research at IMB for the past five years, and has allowed IMB researchers to generate some of the highest-quality and innovative imaging to date. However, fluorescence imaging is being widely hailed as the fastest-growing area of cancer research. While the imaging capabilities and findings generated through the IMB facilities have had (and will continue to have) a wide-reaching impact on research nationally, the new facility will empower and enable this high-level research into the future and ensure increasingly insightful discoveries. Most importantly our enhanced imaging capacity will increasingly underpin the translation of basic science discoveries into real outcomes for the public in cancer prevention and treatment.

Translation of research is a serious mission at IMB. During 2008, our scientists continued to work closely with IMBcom to ensure their research was examined for commercial possibility and taken further if necessary. An example of success in 2008 was research into RNA by Professor John Mattick and Dr Marcel Dinger, which was licensed by Invitrogen and developed into a high-density microarray chip that was launched in the U.S. market.

It is both a great privilege and a very great challenge to serve as Deputy Director (Research) at IMB and I look forward to the coming year and the new opportunities it brings. As the Institute grows and evolves – in the way of all good things scientific- it will be important to keep pace with the ideas and technologies that will take our research into the future. The dedication and serious talent of all those who work at IMB, our researchers and our support staff, not only sustain the Institute but make anything seem possible in the year ahead. While the world experiences hard times in many quarters, IMB is assigned the task of producing good news stories to offset the bad. Creative technologies and new medicines are the good news we work hard to produce and I look forward to my role in making sure we have much to offer in this regard.

Professor Jenny Stow
IMB Deputy Director

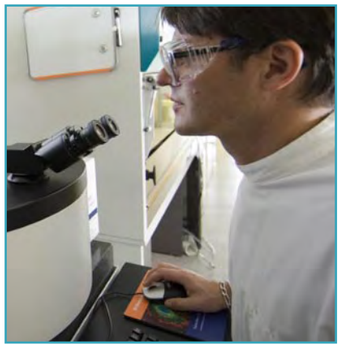
DEPUTY DIRECTOR (SYSTEMS & ADMINISTRATION) REPORT

IMB researchers are supported by staff in a number of areas, including: laboratory and infrastructure management, student co-ordination, administration, reception, HR, information technology, finance, central sterilisation, mail, stores, technical services, building maintenance, animal house, grant administration, and marketing and communications. These staff do an excellent job of providing the essential services that allow the institute to function.

There was some movement of senior staff over the year. The opening of new laboratory space on Level 6 necessitated the appointment of a Floor Manager for that level; Jane Weber, previously a Research Assistant with the Sweet group, was successful. Another change in floor managers occurred when Level 2 Floor Manager Dr Michelle Newman returned to live in the USA. She was replaced by Mikiko Miyagi. Barb Clyde, IMB's HR Consultant, moved on to new challenges after 12 years with the IMB. She was replaced by Felicity Ray from the Diamantina Institute. Finally, Store Manager Stratios Manolis left to live in Townsville. He had been co-managing the Store with Barry Pitt, who then took over as sole Manager.

Postgraduate Administrative Officer Dr Amanda Carozzi was recognised during the year with a UQ Miracle Workers award. The awards acknowledge staff who continually go above and beyond expectations, inspire, deliver and are generally outstanding. This certainly describes Dr Carozzi, as any who have come into contact with her will attest. She was nominated for the award by IMB student association president Jonathan Robson, who lauded her enthusiasm, positive outlook and sound advice.

Funding for the ARC Special Research Centre for Functional and Applied Genomics finished at the end of the year. The Centre was founded to provide specialist technical infrastructure support to the Institute's research programs, but the end of the Centre will not mean the end of this goal, as several of the facilities established under its auspices will continue to operate.

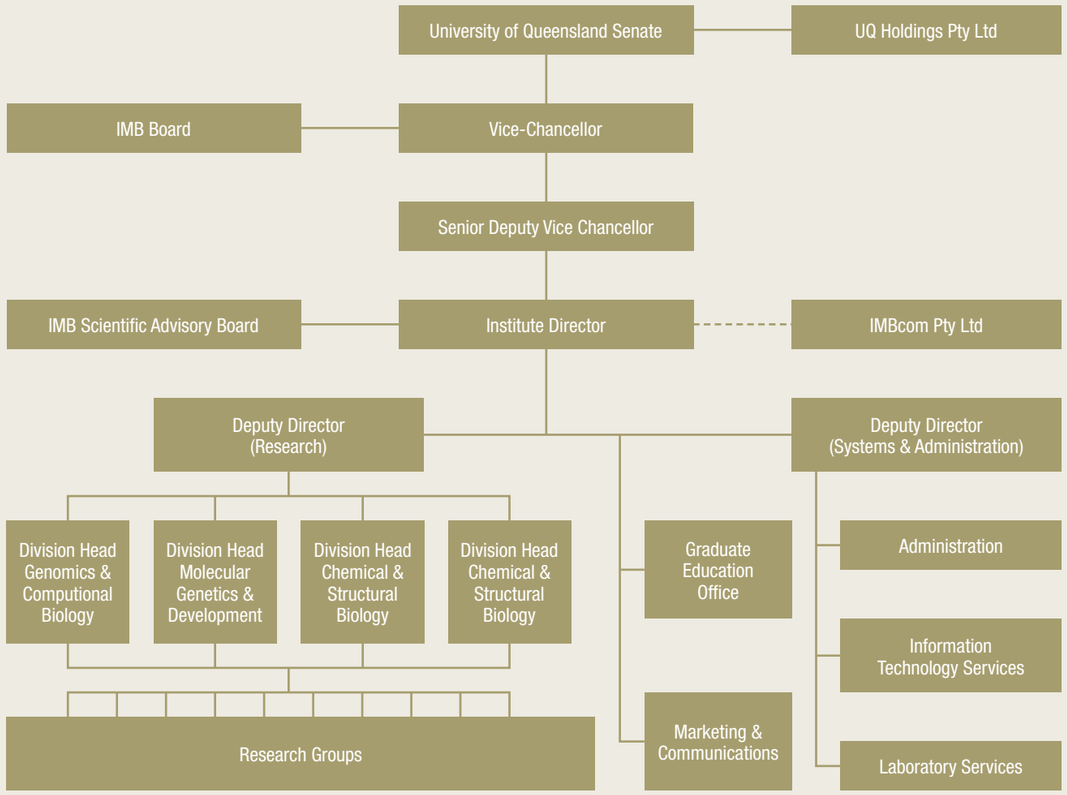


There were several grants won during 2008 that will enable us to upgrade our facilities in 2009, the most significant being $2.5 million from the ACRF, as outlined in Professor Stow's report on the opposite page. The funding will be used to purchase new microscopes and computing equipment and expand the current ACRF Dynamic Imaging Facility for Cancer Biology. Computing equipment will receive a further boost thanks to a $400,000 ARC LEIF grant received by a group of researchers led by Professor Mark Ragan. The funding will be used to establish an advanced computational platform to study biological processes at a systems level. This equipment will allow us capabilities that are not currently present in Australia, helping our researchers remain internationally competitive.

The Queensland Bioscience Precinct, which houses the IMB, is still considered to be a leading example in laboratory design, even five years after its construction. People come from around the world to view it and discuss collaborations; in 2008, we hosted over 300 international delegates from countries including China, New Zealand, Germany, Denmark, Vanuatu, USA, India, Japan, Italy, Vietnam, Chile, Malaysia, Peru, Spain, France, Singapore, Norway, Scotland, the Netherlands, England, Switzerland, Pakistan, Greece, Fiji, Zimbabwe and Zambia.

Dr Ian Taylor
IMB Deputy Director

2008 IMB ORGANISATIONAL CHART



IMB 2008 HIGHLIGHTS

Highlights

NEW DEPUTY DIRECTOR FOR IMB

Professor Jenny Stow was appointed Deputy Director (Research) of the IMB, after the previous Deputy Director, Professor John Hancock, went to the U.S. on sabbatical. Professor Stow studied at Monash University, and worked at Harvard and Yale before moving to UQ in 1994. She took up the Deputy Director's position in April.

"I am looking forward to being able to contribute to research on a big scale, and I believe IMB has all the raw material to do that," Professor Stow said. "We have an incredible opportunity to harness our talent and to really make an impression on research in key areas of human health and wellbeing."

NEW GROUP LEADERS FOR IMB

Dr Brett Collins joined the IMB in 2006 after a stint as a Senior Research Associate at the Cambridge Institute for Medical Research in the United Kingdom. Originally part of Dr Rohan Teasdale's group, Dr Collins was promoted to running his own laboratory in 2008. His lab focuses on defining the structure of the retromer complex, a protein coat found on the endosome, an intracellular structure that transports proteins into cells.

Dr Kirill Alexandrov joins the IMB from the Max-Planck Institute of Molecular Physiology in Dortmund, Germany. He will conduct research and share his expertise in protein engineering and production.

Dr Dagmar Wilhelm focuses on understanding how gene expression is controlled, particularly in embryonic development and its related diseases. Dr Wilhelm received her PhD from the German Cancer Research Centre in Heidelberg. She worked at the Institute for Genetics at the Research Centre, Karlsruhe, and at the Biocentre at the University of Wulzburg, both in Germany, before joining the IMB in 2002.

Dr Nick Hamilton will develop new methods of analysing cellular data, made necessary by the growing amount of imaging information that researchers create in the course of their work. Dr Hamilton has a PhD in Pure Mathematics from the University of Western Australia. He held several positions at The University of Queensland and one at the University of Gent in Belgium before joining the IMB in 2004.

Dr Michelle Hill and Professor Rob Parton.

KNOCKING THE SOX OFF CANCER AND LYMPHATIC DISORDERS

Researchers have identified a gene critical for the development of the lymphatic system in a discovery that will have implications for the treatment of cancer and lymphatic disorders and other diseases. The team, led by Professor Peter Koopman and Dr Mat François from the IMB, found that a single gene – Sox18 – triggers the development of the lymphatic vessels.

"The rate at which new lymphatic vessels can form is thought to be one of the key factors in determining how quickly a tumour can spread and thus how severely a patient will be affected by cancer," Professor Koopman said. "The lymphatic vessels also play a central role in maintaining fluid balance in the body and carrying infection-fighting white blood cells, so greater knowledge about the lymphatic system can offer insights and suggest therapies for a range of diseases."

BRAIN TUMOUR ORIGIN IDENTIFIED

IMB scientists were part of a team that identified the origins of the most malignant type of brain tumour in a discovery that could lead to better therapies and improve our understanding of how tumours initiate. The team, led by Professor Brandon Wainwright of IMB and Dr Robert Wechsler-Reya from Duke University in the US, studied medulloblastomas. They found that these tumours can originate from two types of cell: multipotent neural stem cells and granule neuron precursors.

The discovery provides a target for treatments, and could have wider implications for treating other types of cancer, as the team found that cancer doesn't always originate in the same way.

PROTEIN DISCOVERY OFFERS HOPE FOR PROSTATE CANCER

IMB scientists are studying a possible way of making aggressive prostate cancer cells less invasive after their discovery of a protein essential for the normal functioning of cells.

Professor Rob Parton and Dr Michelle Hill led a team of researchers from the IMB who discovered that the protein PTRF-cavin is required for caveolae formation. Caveolae, pits on the cell surface, are essential for many functions, including tumour suppression. Scientists had already identified one protein involved in caveolae formation, caveolin. In most cancers, the cells stop expressing caveolin, and caveolae don't form.

But some aggressive prostate cancer cells show much higher levels of caveolin than normal. The IMB team found this was because although caveolin levels were high, caveolae still weren't forming, and this was because PTRF-cavin was missing. The team is studying if this change could alter the invasive properties of the cancer cells.

MEDICAL RESEARCH TO BE QUICKER AND CHEAPER WITH NEW GENE SEQUENCER

A research team led by Associate Professor Sean Grimmond from the IMB has pioneered a new approach to studying gene content and activity that stands to revolutionise the future of genetics. The international team showed that it is now possible to sequence the DNA code of every gene in a biological sample in a single experiment.

"The completion of the Human Genome Project took worldwide effort, an estimated US$2.7 billion and 13 years to complete. In testing this new approach, we were able to sequence four times the sequence content of the entire human genome in our laboratory at only a fraction of the cost," Dr Grimmond said.

GENETIC BLUEPRINT REVEALED FOR KIDNEY DESIGN AND FORMATION

IMB researchers were among a team that generated the first comprehensive genetic blueprint of a developing mammalian organ, shedding light on the genetic and molecular dynamics of kidney formation. The detailed genome-based atlas will serve as a resource for understanding healthy and abnormal kidney development and disease.

SCIENTISTS IDENTIFY HIDDEN LAYER IN BRAIN FUNCTION

Hundreds of new molecules that are likely to be important for brain function, and ultimately human development, have been identified by scientists from the IMB. The molecules, known as long non-coding RNAs, are derived from parts of the genome that do not encode proteins and until recently have been largely regarded as non-functional or 'junk' DNA.

The researchers, including Dr Marcel Dinger and Mr Tim Mercer and led by Professor John Mattick, discovered that many of these molecules are turned on, or expressed, in parts of the brain responsible for important functions, including memory formation, behaviour and sensory perception. The discovery provides a new understanding of how the brain works and in the future may provide additional avenues for the development of drugs to treat neurological conditions such as Alzheimer's Disease and dementia.

IMB GENE TECHNOLOGY LAUNCHED IN US

A new gene expression analysis platform developed in collaboration between Australian scientists and Invitrogen Corporation to help other researchers understand fundamental aspects of human development has been launched in the US market. Professor John Mattick and Dr Marcel Dinger from the IMB developed content that was exclusively licensed to Invitrogen for the first commercially available high-density microarray chip, the NCode™ Human and Mouse non-coding RNA microarray, which can be used by researchers to profile both messenger and non-coding RNAs.

FEAR AND BACTERIA: POSSIBLE WAYS OF CONTROLLING THE CANE TOAD

Scaring cane toads and targeting their bacteria are two control strategies that were suggested by an IMB scientist at the Australian Vertebrate Pest Conference in Darwin. Professor Rob Capon led a two-year study into the chemical ecology of the Australian cane toad.

They found a range of potential control strategies that could selectively target and reduce the survival of cane toad eggs, tadpoles and adults. These include exposing them to an alarm chemical which causes tadpoles to turn into toads prematurely, resulting in underweight toadlets with lower chances of survival, and targeting the bacteria that expand the range of toad toxins and influence the toads' behaviour.

CHILDHOOD OBESITY STUDY LAUNCHED

The KOALA Childhood Obesity study was officially launched on Saturday January 12, 2008, with an activity day for kids at Brisbane's Riverlife Adventure Centre. The study is a one-year pilot being conducted by UQ and Mater Children's Hospital researchers and will investigate the social, behavioural and genetic reasons behind childhood obesity. Dr Gary Leong, who works at both the IMB and the Mater Children's Hospital, is leading the study.

PROFESSOR MARTIN IN SYNC WITH REMOTE ACCESS

Professor Jenny Martin, who was the first Queensland researcher to use the Australian synchrotron, became the first user to access the facility remotely. Professor Martin sent her samples to Melbourne via courier, but instead of following them down, she loaded a special program on her computer and ran the experiment from a meeting room at the IMB.

Remote access has saved time for Professor Martin's group and is much more efficient, as they no longer have to send people to Melbourne every time they have beamtime allocated at the synchrotron. "It's changed the way we do science, and many other researchers are wanting to learn how to run their experiments in this way…" Professor Martin said.

GENE PIONEER GIVES MEMORIAL LECTURE

Associate Professor Jozef Gecz, from the Women's and Children's Hospital and University of Adelaide, presented the Dr Toshiya Yamada Memorial Lecture on Thursday, March 13. His seminar was titled, "The genetic landscape of learning and memory: what do we learn from naturally occurring mutations?" It was the fourth Dr Toshiya Yamada Memorial Lecture, established to commemorate an IMB researcher who passed away suddenly in 2001, and co-hosted by the IMB and the Queensland Brain Institute.

Grants

$2.5 MILLION TO EXPAND CANCER RESEARCH FACILITY

IMB researchers will have access to even more cutting-edge cancer research equipment after being awarded a $2.5 million grant from the Australian Cancer Research Foundation (ACRF). The grant, whose application was led by Professor Jenny Stow and Associate Professor Alpha Yap, will allow the expansion of the ACRF Dynamic Imaging Facility for Cancer Biology currently in place at IMB.

CONE SNAILS AND PLANTS USED TO DEVELOP ORAL DRUG FOR PAIN

Molecules from cone snail venom and plants are being used by Queensland researchers as a blueprint to develop an oral drug to treat chronic pain. Professor David Craik and Dr Richard Clark received $218,275 from the National Health and Medical Research Council to aid in translating their research into a product available for Australians to use. Studies on the molecule they have developed have shown that it is effective in relieving neuropathic pain in animals.

Peptides (small proteins) from cone snail venom have attracted recent attention from scientists, as they can target receptors with a high degree of accuracy, thus eliminating severe side effects. But peptides have the drawback of degrading rapidly in the body. Professor Craik and Dr Clark have overcome this problem by engineering a circular peptide, using a circular protein backbone discovered by Professor Craik and found in plants such as violets.

INDUSTRY AND RESEARCHERS JOIN FORCES TO DEVELOP BETTER BIOFUELS

Associate Professor Ben Hankamer will lead a collaboration between researchers and industry that aims to develop carbon-neutral biofuels that don't compete with food production and that can use saline water sources.

The collaboration, between UQ and German researchers and the companies Pacific Seeds and Advanta India, has received $674,344 from the Australian Research Council. Algae naturally capture sunlight and use its energy to yield feedstocks for the production of biofuel. The group is developing ways of enhancing the efficiency of the algae's hydrogen production, as well as oil for biodiesel synthesis.

FELLOWSHIP FOR SMART IMB RESEARCHER

IMB researchers will be developing new anti-cancer drugs thanks to funding from the Queensland State Government. Dr Norelle Daly was awarded a $300,000 Smart State Fellowship to develop a new generation of cancer therapeutics. Dr Daly and her team will investigate using peptides, the building blocks of proteins, to form the basis of a new type of stable therapeutics.

"My project will focus on fusing unstable peptides to a circular protein framework that will overcome their stability problems, and result in a drug with far fewer side effects than existing anti-cancer drugs," Dr Daly said.

HIGH-PERFORMANCE COMPUTING TO POWER SYSTEMS BIOLOGY INVESTIGATION

A consortium of eight researchers, seven of whom are from the IMB, won a $400,000 Australian Research Council Linkage Infrastructure, Equipment and Facilities grant, which they will use to establish an advanced computational platform to study biological processes at a systems level. Systems biology is the study of the organism as a whole and provides a deeper understanding of biological processes than is possible by studying components separately.

"The platform's hardware and specialised software will allow Australian researchers to examine complex pathways involved in animal and human health and disease, as well as in biotechnology and environmental processes," Professor Mark Ragan said. "It will provide unique capabilities not currently available in Australia, and help us to remain internationally competitive."

US $1.3M INTERNATIONAL GRANT SHARED BY IMB CELL BIOLOGIST

Associate Professor Alpha Yap and three international collaborators have been awarded a grant from the Human Frontier Science Program worth US$450,000 per annum for three years.

Dr Yap will join his collaborators, Dr Anna Akhmanova from the Netherlands, Dr Nicholas Brown from the United Kingdom and Assistant Professor Ivan Maly from the USA, in a project investigating cell-cell interactions.

"Interactions between cells determine how our bodies grown and develop," Dr Yap said. "If these interactions go wrong, diseases such as cancer and inflammation can occur."

STATE GOVERNMENT BOOST FOR PHD RESEARCH

Four IMB PhD students tackling the problems of disease and obesity have received Queensland State Government scholarships to support them while studying, out of a total of eighteen scholarships awarded across the state. Each researcher will receive up to $21,000 to provide them with the financial support they need to focus on their research efforts. In addition, researchers will receive a bonus payment of $15000 if they complete their thesis within 3.5 years.

The IMB recipients were Robert McLeay (Bailey group), Elizabeth Skippington (Ragan group), Carol Kistler (Parton group) and Marianne Diaz (Muscat group).

Left: Cone snail.

Below left: Associate Professor Ben Hankamer with microalgae.

Awards

IMB SCIENTISTS ELECTED TO TOP NATIONAL BODY

Two IMB researchers have been acknowledged as being among the country's top scientists after being elected Fellows of the Australian Academy of Science. Professor Peter Koopman and Professor John Mattick, AO, were recognised by the Academy for significantly advancing, and continuing to advance, the world's scientific knowledge.

Professor Koopman was elected for his work on mammalian embryonic development, while Professor Mattick was elected for his research into the structure of genetic systems in higher organisms.

EXCELLENT RESEARCH BY GROUP LEADER

Dr Brett Collins won a UQ Foundation Research Excellence Award, receiving $85,000 to investigate how material coming into and out of cells is sorted, thus providing information that will improve understanding of diseases such as cancer. Dr Collins is the fifth IMB researcher to receive one of these awards.

TRAVEL FUNDING FOR YOUNG ACHIEVER

Dr Johanna Barclay from the Waters group won the Merck UQ Young Achiever Award, receiving $3500 to contribute to the cost of attending a conference in the Northern Hemisphere. Dr Barclay's research, published in *Molecular Endocrinology*, examined how growth hormone signalling is regulated, which has implications for the development of cancer.

PHD PRIZES

PhD student Jane Lattin from the Sweet lab took out 2nd prize for her oral presentation at the Australian Society for Medical Research Queensland Postgraduate Student conference. Mrs Lattin is studying beta-arrestins, proteins involved in the regulation of the body's immune response.

Eight IMB students were named on the UQ 2007 Dean's Commendation List, recognising the outstanding quality and exceptionally innovative nature of the research performed for their PhD thesis. Fewer than 10 percent of PhD graduates are recognised in this way each year. The eight commended students were: Marion Loughnan (Lewis group), Jason Kay (Stow group), Julita Imperial (Alewood group), Christian Gruber (Craik group), Melissa Davis (Teasdale group), David Woolford (Hankamer group), Ranjala Ratnayake (Capon group), and David Ireland (Craik group). Dr Ireland completed the first PhD in Queensland that combines science and business.

AMGEN AWARD

Pei Ching (Regine) Low from the Stow lab won the Amgen Award for being the best overall honours student at the IMB in 2007. The award was presented during 2008, when Ms Low was in the first year of a PhD, also in the Stow lab. Ms Low's honours project involved establishing and optimising a high-content screening assay for TNF trafficking and secretion in macrophages. It has already been used to screen molecules including natural product libraries and drugs.

VALEDICTORIAN FROM IMB

A honours student at the IMB was named 2008 Valedictorian of the UQ Bachelor of Science. Elanor Wainwright, who completed her honours thesis under the supervision of Dr Dagmar Wilhelm, was ranked first out of over 300 graduating students. Ms Wainwright is now employed as a research assistant in the Wilhelm group.

SPECIAL AWARD FOR YOUNG RESEARCHER

Andrew Noske, a PhD student from the Marsh group, presented a talk titled, "3D reconstruction and analysis of whole mammalian cells by new tomographic and computational approaches" at the Queenstown Molecular Biology meeting. The organisers were so impressed with his presentation, deeming it one of the best of the meeting, that they created a special Young Investigator Award in recognition.

AWARD FOR MIRACLE WORKER

Dr Amanda Carozzi, IMB's Postgraduate Administrative Officer, was awarded a UQ Miracle Workers Award. The awards acknowledge staff who continually go above and beyond expectations, inspire, deliver and are generally outstanding. In nominating Dr Carozzi, PhD student Jonathan Robson said, "Her enthusiastic attitude towards aiding students of the IMB as well as her positive outlook on all IMB students make her an ideal recipient for this prestigious reward." Mr Robson, who is President of the IMB student association, also lauded Dr Carozzi for being "a source of sound advice on matters relating to PhD management and financial support".

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 worked at 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 of Maxygen and one of the company's founders. Since the creation of Maxygen in 1997, its core technologies have been used to create several independent businesses. Today, Maxygen is 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.







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

Bob McCarthy is the Director-General of the Queensland Department of Tourism, Regional Development and Industry. He leads a staff totaling more than 800 people, and is 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 chairs or co-chairs 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 is 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

Professor Siddle is the Deputy Vice-Chancellor (Research) of The University of Queensland. He is responsible for enhancement of the University's research and research training profile, and development of research collaborations. Areas under his direct management include the six research Institutes (including IMB), the Research and Research Training Division, the Graduate School and UQ Biological Resources. He became DVC (Research) in 2002 following his September 2001 appointment 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 is 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.

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 Chairman 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.

IMB SCIENTIFIC ADVISORY COMMITTEE

PROFESSOR NICOS NICOLA (CHAIR)
Professor of Molecular Haemotology
Assistant Director
Walter and Eliza Hall Institute of Medical Research, Melbourne

PROFESSOR CHRIS ABELL
Professor in Biological Chemistry
Department of Chemistry
University of Cambridge, Cambridge, UK

PROFESSOR DAVID GALAS
Vice-President
Chief Academic Officer & Norris Professor of Applied Life Sciences
Keck Graduate Institute of Applied Life Sciences, USA

PROFESSOR NANCY JENKINS
Institute of Molecular and Cell Biology
Singapore

PROFESSOR ROB KRUMLAUF
Stowers Institute
Kansas City, 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, MA, USA

PROFESSOR GREG PETSKO
Gyula and Katica Tauber Professor of Biochemistry and Chemistry
Director, Rosenstiel Basic Medical Sciences Research Center
Brandeis University, 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

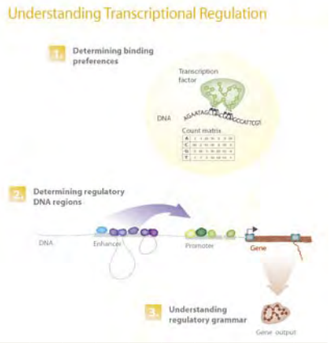
RESEARCH FOCUS

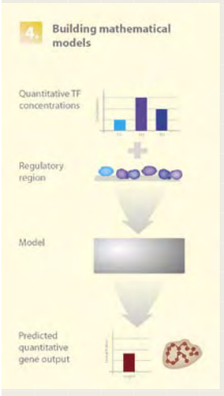
This program includes the ARC Centre of Excellence in Bioinformatics and the Queensland Facility for Advanced Bioinformatics. It intersects with the Department of Mathematics and the School of Information Technology and Electrical Engineering. It focuses on understanding the genetic programming of humans, specifically, comparative mammalian and vertebrate functional genomics; rnomics; and computational modelling of genetic and cellular regulatory networks (i.e. the Visible Cell® project).

Research Group Leaders

Tim Bailey
Kevin Burrage
Sean Grimmond
Nick Hamilton
John Mattick
Mark Ragan
Rohan Teasdale

TIM BAILEY





Pattern Recognition and Modelling in Computational Biology

My research develops and applies 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.

This year my group studied combining multiple types of high-throughput data for predicting the places in the genome where transcription factor proteins bind to DNA to control gene transcription. We extended our "evolutionary motif model" of binding sites to allow for the loss of sites during evolution, and conducted a survey of the relative power of various conservation-based binding site prediction methods. We also published the first study showing that using another type of data—epigenetic modification—can greatly improve prediction accuracy. We extended our work on *ab initio* binding motif discovery to include the use of non-sequence data such as "binding intensity" data from chromatin immunoprecipitation experiments. This year we also refined our computational model of the regulation of gene transcription, showed that it can predict gene expression in novel species, and studied algorithms for "training" models of expression. We also created several new algorithms that use binding site motifs to predict biological functions such as the role of transcription factors. We have integrated these algorithms into the popular MEME Suite of motif-based sequence analysis tools, of which I am a principal author.

In the coming year, we will apply the tools we developed this year to the study of the regulation of gene expression in developing blood and neural cells. We will also continue to develop novel algorithms for pattern discovery and modelling, especially algorithms that combine additional types of non-sequence data for discovering the targets of transcription factors and for identifying interactions among factors. We will also initiate a project to analyse the role of DNA-RNA triplex formation in gene expression.

KEY PUBLICATIONS

Bauer, D.C., and Bailey, T.L. (2008). Studying the functional conservation of cis-regulatory modules and their transcriptional output. *BMC Bioinformatics* **9**: 220.

Bodén, M., and Bailey, T.L. (2008). Associating transcription factor binding site motifs with target GO terms and target genes. *Nucleic Acids Research* **36**: 4108-4117.

Frith, M.C., Saunders, N.F.W., Kobe, B., and Bailey, T.L. (2008). Discovering sequence motifs with arbitrary insertions and deletions. *PLoS Computational Biology* **4**: e1000071.

John Hawkins and Timothy L. Bailey, "The statistical power of phylogenetic motif models", Twelfth Annual International Conference on Computational Biology, (RECOMB 2008), pp. 112-126, Springer-Verlag, Berlin, March, 2008.

Whitington, T., Perkins, A.C., and Bailey, T.L. (2008). High-throughput chromatin information enables accurate tissue-specific prediction of transcription factor binding sites. *Nucleic Acids Research* **37**: 14-25.

Gupta, S., Stamatoyannopolous, J.A., Bailey, T.L., and Noble, W.S. (2007). Quantifying similarity between motifs. *Genome Biology* **8**: R24.

LAB MEMBERS

Research Fellow: Dr Mikael Bodén

Research Officers: Dr John Hawkins, Dr Philip Machanick

PhD Students: Denis Bauer, Tom Whitington, Robert Mcleay

Modelling and visualising cellular processes

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 the group of John Hancock 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

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* **10**: 1007/s11075-008-9239-y.

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.

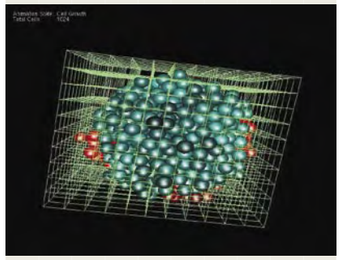
MacNamara, S., Burrage, K., and Sidje, R.B. (2008). Multiscale modeling of chemical kinetics via the master equation. *SIAM Journal: Multiscale Modelling and Simulation* **6**: 1146.

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.

Tian, T., and Burrage, K. (2008). An effective stepsize selection procedure for discrete simulation of biochemical reaction. *ANZIAM Journal* **48**: 1022-1040.

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.

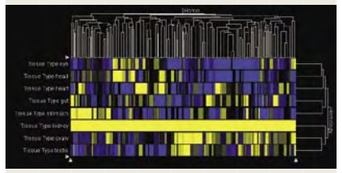
LAB MEMBERS

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

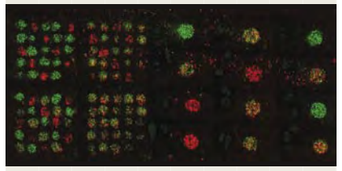
PhD Students: Shev MacNamara, Alhadi Bustamam, Duncan Mortimer

Expression Genomics

SEAN GRIMMOND



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



Photomicrograph of HEK cells transfected using a robotically generated cell microarray.

The central focus of the IMB's expression genomics lab is to globally survey genomic, transcriptomic and epigenomic information and then use these data to define the underlying molecular networks controlling key biological processes (such as cell division and differentiation) and pathological states (breast and pancreatic cancer). These systems-wide studies give us the opportunity to identify both the key genes driving specific phenotypes and also the chance to recognise the different layers of control guiding biological states. It also provides a strong foundation from which to study novel genome biology (such as the role of miRNAs, non-coding RNAs, retrotransposons, RNA editing etc). As the capturing of "omic" data is a key component of our research, we are actively pursuing the use of microarray-based profiling, automated in situ hybridisation screening and next-generation sequencing technologies for these studies.

For more information on our research and details of the research projects listed below, please see our webpage at: www.imb.uq.edu.au/index.html?id=11679

RECENT PROJECTS

- Studying mammalian transcriptomes at single nuclear resolution
- Predicting the function of miRNA-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

RECENT PUBLICATIONS

Cloonan, N., Forrest, A.R., Kolle, G., Gardiner, B.B., Faulkner, G.J., Brown, M.K., Taylor, D.F., Steptoe, A.L., Wani, S., Bethel, G., Robertson, A.J., Perkins, A.C., Bruce, S.J., Lee, C.C., Ranade, S.S., Peckham, H.E., Manning, J.M., McKernan, K.J., and Grimmond, S.M. (2008). Stem cell transcriptome profiling via massive-scale mRNA sequencing. *Nature Methods* **5**: 613-619.

Brunskill, E.W., Aronow, B.J., Georgas, K., Rumballe, B., Valerius, M.T., Aronow, J., Grimmond, S.M., McMahon, A.P., Patterson, L., Little, M.H., and Potter, S.S. (2008). Atlas of Gene Expression in the Developing Kidney. *Developmental Cell* **15**: 781-791.

Cloonan, N., Brown, M.K., Steptoe, A.L., Wani, S., Chang, W.L., Forrest, A.R.R., Kolle, G., Gabrielli, B., and Grimmond, S.M. (2008). The miR-17-5p microRNA is a key regulator of the G1/S phase cell cycle transition. *Genome Biology* **9**: R127.

LAB MEMBERS

Senior Research Officer: Dr Paul Leo

Research Officers: Dr Brooke Gardiner, Dr Nicole Cloonan, Dr Gabriel Kolle, Dr Nicola Waddell, Dr Logan Walker, Dr Ehsan Nourbkash

Senior Research Assistants: Graeme Bethel, Anita Steptoe

Research Assistants: Milena Gongora, Shivangi Wani

PhD Students: Geoff Faulkner, Melissa Brown

Masters Students: Rathi Thiagarjan, Ajay Panwar

Honours Student: Alan Robertson

Modelling, visualisation and classification of live cell imaging

NICK HAMILTON

High throughput bio-image visualisation.

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. The approach will enable whole-proteome imaging to be analysed in days rather than months. 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 and their true diversity to be seen for the first time. 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 and solute concentration. Other areas of interest include modelling of recruitment and expulsion of proteins from membrane surfaces.

The group is strongly multidisciplinary and collaborative, with a focus on delivering methodologies and tools to be used by researchers. This year has seen the public release of iCluster and OBCoL, both available under open-source license via Institute-hosted websites.

RESEARCH PROJECTS

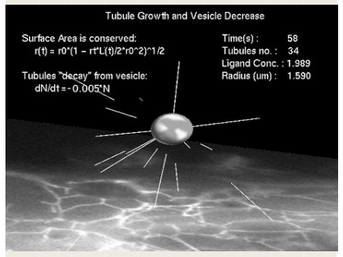
- Automated classification of bio-imaging via machine learning
- Clustering and information visualisation methodologies for high throughput bio-data sets
- Statistical testing and content-based searching of bio-imaging
- Modelling endosomal systems from live cell video microscopy imaging
- Segmentation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

KEY PUBLICATIONS

Hamilton, N.A., 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. The dynamics and geometry of vesicles and tubules in endocytosis. In: Current Protocols in Cell Biology Suppl. **35**, June 2007. 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.



Automated classification of subcellular imaging.

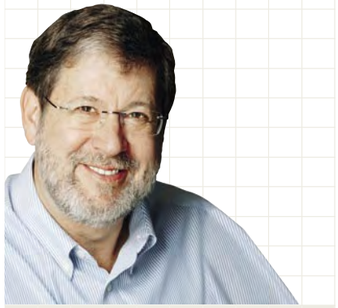
LAB MEMBERS

Research Officers: Dr John Belward, Dr Fawang Liu

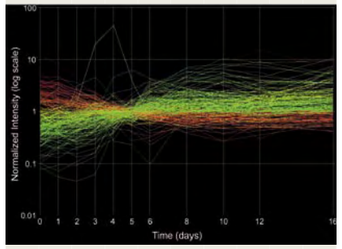
PhD Student: Ahmed Arefin

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

Rnomics: RNA in mammalian evolution and development



JOHN MATTICK



Dynamic expression of non-coding RNAs during embryonal stem cell differentiation.

Validation of bioinformatically-predicted small RNAs from mice using high-density arrays.

LAB MEMBERS

Research Officers: Dr Marjan Askarian-Amiri, Dr Larry Croft, Dr Marcel Dinger, Dr Martin Hansen, Dr Igor Makunin, Dr Lorenzo Malquori, Dr Harald Oey, Dr Michael Pheasant

Senior Research Assistant: Kelin Ru

PhD Students: Paulo Amaral, Pierre Cattenoz, Michael Clark, Chol Hee Jung, Darren Korbie, Tim Mercer, Satu Nakhuri, Cas Simons, Stuart Stephen, Martin Smith, Ryan Taft, Selene Ferdandez Valverde

We are exploring the thesis that the genetic programming of higher organisms has been fundamentally misunderstood for the past 50 years, because of the assumption that most genetic information is transacted by proteins. It is now clear, despite the fact that only a small fraction encodes proteins, that the majority of the genomes of mammals and other complex organisms is transcribed in a developmentally-regulated manner, and that most complex genetic phenomena are RNA-directed. Working in conjunction with collaborators in the United States, Europe and Japan, we are working to characterise and understand the functions of the mammalian transcriptome, and to validate the prediction that most genetic information in mammals is conveyed by RNAs that control differentiation and development. This includes the identification of small RNAs that regulate gene expression at various levels, including transcription, and to determine the expression patterns and function of the tens of thousands of longer noncoding RNAs that are dynamically expressed during differentiation in mammalian cells, including embryonal stem cells. Among our recent findings we have shown that it is possible, if not likely, that most of the mammalian genome is under evolutionary selection, and demonstrated that the majority of long noncoding RNAs are expressed in the brain, many in precise cellular and subcellular locations, some of which are novel. We use advanced computational, visual and experimental methods, integrating in silico, in vitro and in vivo approaches. The outcomes of our research will be to expand our understanding of human evolution, genetics and development, with important practical implications in medicine, genetic engineering and programming of self-assembling systems.

RESEARCH PROJECTS

- Bioinformatic prediction and experimental validation of new classes of small RNAs in animals
- Analysis of the dynamic expression of long noncoding RNAs during the differentiation of embryonal stem cells, neural stem cells, muscle, macrophages, T-cells and developing tissues such as the male and female genital ridge, as well as the alteration of noncoding RNA expression in pathological states such as cancer
- Analysis of the subcellular location of noncoding RNAs to expand knowledge of existing cellular compartments and discover new ones
- Targeted functional analysing of selected non-coding RNAs involved in developmental processes and neurogenesis
- Analysis of the conservation patterns of noncoding regions in the mammalian genome and alignment on the basis of RNA structural rules
- Deep sequencing of the small and large RNA transcriptome in embryonal stem cells, and various tissues in mouse and human, as well as of RNAs associated with chromatin modification complexes, transcription factors, RNA editing enzymes and DNA:RNA triplex structures in chromatin

KEY PUBLICATIONS

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.

Dinger, M.E., Amaral, P.P., Mercer, T.R., Pang, K.C., Bruce, S.J., Gardiner, B.B., Askarian-Amiri, M.E., Ru, K., Soldà, G., Simons, C., Sunkin, S.M., Crowe, M.L., Grimmond, S.M., Perkins, A.C., and Mattick, J.S. (2008). Long noncoding RNAs in mouse embryonic stem cell pluripotency and differentiation. *Genome Research* **18**: 1433–1445.

Mercer, T.R., Dinger, M.E., Sunkin, S.M., Mehler, M.F., and Mattick, J.S. (2008). Specific expression of non-coding RNAs in mouse brain. *Proceedings of the National Academy of Sciences USA* **105**: 716-721.

Mattick, J.S., and Mehler, M.F. (2008). RNA editing, DNA recoding and the evolution of human cognition. *Trends in Neuroscience* **31**: 227-233.

Computational genomics

MARK RAGAN

LAB MEMBERS

Research Officers: Dr Aaron Darling, Dr Melissa Davis, Dr Karin Kassahn, Dr Krzysztof Kurowski, Dr Muhammad Shoaib Sehgal

Visible Cell® team: Oliver Cairncross (Project Leader), Dr Tim McComb, Tim Sullivan, David Wood

Data Grid Developer / Administrator: Mhairi Marshall (ARC Centre of Excellence / QFAB)

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

Manager, ARC Centre of Excellence in Bioinformatics: Lanna Wong

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Scientific Programmer: Chikako Ragan

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Honours Students: Vinh Dang, Andrés Esteban-Marcos, James Johnson

Interns: Zoran Boskovic (The University of Queensland), Pierre-Alain Chaumeil (Université Bordeaux), Sana Hakim (Université Bordeaux), Nikhil Lilaria (Indian Institute of Technology, Bombay), Anton Lord (The University of Queensland), Michal Lorenc (Universität Hamburg), Eleanor McDonald (The University of Queensland), James Sokolich (The University of Queensland)

Research Trainee: Cindy Yan (Queensland University of Technology)

We use advanced computational and data management methods to investigate similarities and differences among genomes and the gene products 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. We are particularly interested in scalable approaches, including those based on Semantic Web technologies, approaches that let us interrogate diverse data types including molecular sequences and structures, signalling pathways, regulatory and molecular interaction networks, gene expression patterns, subcellular localisation and cellular function.

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) in bacterial pathogens, teleosts and mammals. Within the Nuclear Receptors in Breast Cancer consortium we are responsible for expression informatics and network inference. We also collaborate in the Visible Cell® e-research project.

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

RESEARCH PROJECTS

- Automatic inference of vertical and lateral gene transmission, genetic recombination breakpoints, and molecular interaction networks in pathogenic bacteria
- Genome dynamics and the evolution of new protein functions in teleosts
- Fine-scale mapping of orthologous and paralogous regions of mammalian genomes
- Vertebrate protein-protein interaction networks in cellular context
- Computation discovery of novel miRNA targets in mammalian genomes
- Integration and querying of molecular network and cellular structure information, and querying-over these data, using Semantic Web technologies
- Software and data infrastructure for the Visible Cell®

KEY PUBLICATIONS

Dang, V.T., Kassahn, K.S., Marcos, A.E., and Ragan, M.A. (2008). Identification of human haploinsufficient genes and their genomic proximity to segmental duplications. *European Journal of Human Genetics* **16**: 1350-1357.

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.

Höhl, M., and Ragan, M.A. (2007). Is multiple-sequence alignment required for accurate inference of phylogeny? *Systematic Biology* **56**: 206-221.

Beiko, R.G., Harlow, T.J., and Ragan, M.A. (2006). Searching for convergence in phylogenetic Markov chain Monte Carlo. *Systematic Biology* **55**: 553-565.

Chan, C.X., Beiko, R.G., and Ragan, M.A. (2006). Detecting recombination in evolving nucleotide sequences. *BMC Bioinformatics* **7**: 412.

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.

ROHAN TEASDALE

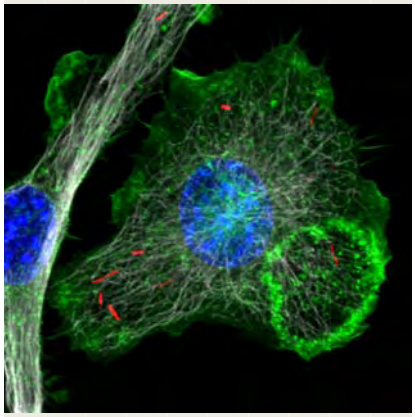
Endosomal dynamics: regulated endocytosis, host-pathogen interactions and protein trafficking

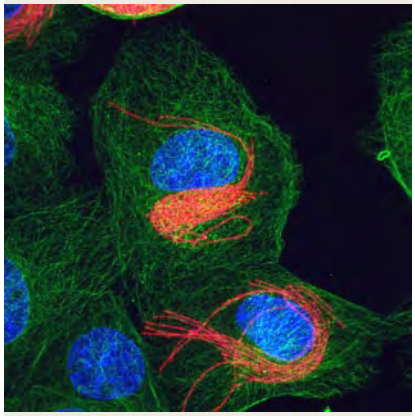
The endosomal/lysosomal system of mammalian cells is a highly dynamic organelle, and the trafficking pathways within the endosomal system are fundamental for a wide variety of key cellular processes. My group is developing cellular and computational approaches to identify novel mammalian proteins associated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

The regulated movement of membrane receptors and ligands between the cell surface and intracellular compartments is vital to many cellular operations, including communication between cells and their environment. A major current focus of the group is the characterisation of the mammalian retromer complex. 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.





LAB MEMBERS

Senior Research Officer: Dr Zheng Yuan

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

Research Assistant: Seetha Karunaratne

PhD Students: Rajith Aturaliya, Josefine Sprenger, Jack Wang

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

KEY PUBLICATIONS

Fink, J.L., *et al.* (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., *et al.* (2007). LOCATE: A Mammalian Protein Subcellular Localization Database. *Nucleic Acids Research* **36**: 230-233.

Aturaliya, R.N., *et al.* (2006). Subcellular Localisation of Mammalian Type II Membrane Proteins. *Traffic* **7**: 613-625.

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.

Division of Molecular Genetics & Development

RESEARCH FOCUS

This program includes IMB's participation in the Cooperative Research Centre for Chronic Inflammatory Diseases; the ARC Centre of Excellence in Biotechnology and Development; and the NIH-funded project Nephrogenix, an initiative designed to develop new therapies for renal regeneration. It focuses on urogenital development, inflammation, cell signalling and cancer, molecular genetics and molecular biology of human diseases.

Research Group Leaders

Peter Koopman
Melissa Little
George E.O. Muscat
Andrew Perkins
Rick Sturm
Matt Sweet
Brandon Wainwright
Carol Wicking
Dagmar Wilhelm

PETER KOOPMAN

How genes regulate embryo development

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 the identification and characterisation of sex development genes using techniques such as microarray screening and transgenic mouse models. Further projects are focusing on identifying the timing and mechanism of sex differentiation in cattle and cane toads, in an effort to manipulate sex ratios and population numbers respectively.

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 gives us profound insight into mechanisms of disease and cancer. In particular, a detailed knowledge of sex determination will have vast biomedical significance, with up to 80% of human sex reversal cases currently unexplained. The use of new technologies and the availability of genome sequences of many species may allow us to better understand these cases, and aid in new therapies for patients. Our research also has the potential to assist the industrial sector through pest management and livestock sex-ratio manipulation.

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).

RESEARCH PROJECTS

- Sex Determination and Gonadal Development
- Development of Male Germ Cells
- Sox Gene Function and Evolution
- Molecular Genetics of Lymphatic Development
- Sexual Development in Cane Toads
- Pilot Study for Male-Only Offspring Production in Beef Cattle

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 initiates lymphatic development in mice by direct activation of Prox1 expression. *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 Officers: Dr Josephine Bowles, Dr Catherine Browne, Dr Dagmar Wilhelm

Research Officers: Dr Annemiek Beverdam, Dr Mathias François, Dr Terje Svingen, Dr Brett Hosking, Dr Kallayanee Chawengsaksophak, Dr Ken-Ichi Kashimada, Dr Juan Carlos Polanco, Dr Nira Gamage

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Admin Assistants: Rebekka van Kampen / Mei Goh

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Honours Student: Elanor Wainwright

MELISSA LITTLE

Kidney development, damage, repair and regeneration

Each of us has a pair of kidneys that play 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 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, and as 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 urogenital development
- Characterising the molecular basis of nephron formation
- Looking for stem cells in the adult kidney
- Investigating the link between the processes of development and the normal repair in the kidney
- Reinitiating kidney development to repair an adult kidney
- Characterising the process of vascular development in kidney

KEY PUBLICATIONS

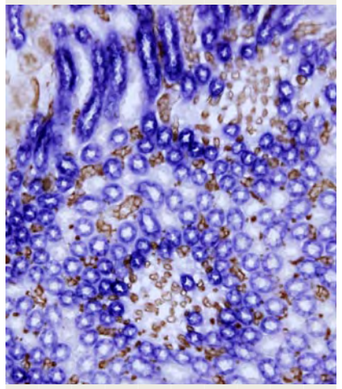
Little, M., *et al.* (2007). A high-resolution anatomical ontology of the developing murine genitourinary tract. *Gene Expression Patterns* **7**: 680-699.

Pennisi, D.J., Wilkinson, L., Kolle, G., Sohaskey, M.L., Gillinder, K., Piper, M.J., McAvoy, J., Lovicu, F., and Little, M.H. (2007). *Crim1*$^{KST264/KST264}$ mice display a disruption of the Crim1 gene resulting in perinatal lethality with defects in multiple organ systems. *Developmental Dynamics* **236**: 502-511.

Rae, F., Woods, K., Sasmono, T., Campanale, N., Taylor, D., Ovchinnikov, D., Grimmond, S., Hume, D.A., Ricardo, S., and Little, M.H. (2007). Characterisation and trophic functions of murine embryonic macrophages based upon the use of a CSF-1R-EGFP transgene reporter. *Developmental Biology* **308**: 232-246.

Wilkinson, L., Gilbert, T., Pennisi, D., Challen, G., Ruta, L.-A., Kett, M., Cummings, M., and Little, M.H. (2007). *Crim1*$^{KST264/KST264}$ mice implicate Crim1 in the regulation of VEGF–A activity during glomerular vasculature development. *Journal of the American Society of Nephrology* **18**: 1697-1708.

Little, M.H. (2008). Tracing the life of the kidney tubule – re-establishing dogma and redirecting the options. *Cell Stem Cell* **2**: 191-192.



Section of renal medulla from an adult murine kidney showing gene and protein expression in the nephron tubules. Uromodulin gene expression in distal straight tubules (blue) is detected by RNA in situ hybridization, with dual immunohistochemistry to detect Aquaporin 1 protein expression in thin descending limb tubules of the Loop of Henle.

LAB MEMBERS

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

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PhD Student: Caroline Hopkins

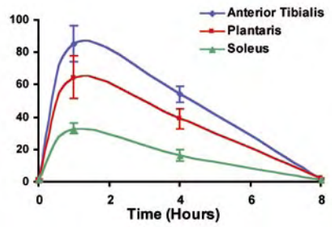
Masters Student: Divya Ramnath

Honours Student: Yu Leng Phua

Undergraduate Student: Brittney Harrington

GEORGE E.O. MUSCAT

Nuclear receptors, skeletal muscle and metabolic disease



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

Nuclear Hormone Receptors (NRs) control lipid, glucose and energy homeostasis in metabolic, cardiovascular and endocrine organs. The importance of NRs in human health is underscored by the therapeutic utility of medicinals that target dysfunctional hormone signalling in the context of inflammation, cancer, endocrine and metabolic diseases. NRs function as agonist-dependent DNA-binding factors that translate metabolic and pathophysiological signals into gene regulation.

Proteins have been identified that belong to the NR superfamily on the basis of homology, but the molecules that regulate their activity have not yet been identified and are denoted as 'orphan' NRs. The orphans provide a platform for the unearthing of new signalling cascades that may have potential therapeutic utility. Many 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. Thus, the tissue has a significant role in the development of metabolic disease. Not surprisingly, NRs are emerging as targets against obesity and type II diabetes.

Surprisingly, the function of these 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 skeletal muscle in the regulation of metabolism. Secondly, we have utilised mouse models to demonstrate that dysfunctional NR1F (RORalpha) expression leads to reduced adiposity, dyslipidemia and resistance to diet-induced obesity. Muscle-specific perturbation of RORalpha signalling leads to aberrant insulin signalling in this lean tissue. In the context of understanding crosstalk between NRs and other signalling pathways in obesity, we have utilised the Ski transgenic mouse model to investigate the role of ski and NR crosstalk in mediating reduced adiposity, and increased fatty acid oxidation.

Collaboratively, we have shown regulatory crosstalk between melanocortin 1 receptor (MC1R) and NR4A signalling in melanocytic cells. We have identified that NR4A is an important step in MC1R-mediated DNA repair in melanocytes. Furthermore, impaired NR4A induction in melanocytes harbouring homozygous red hair colour variant MC1R alleles may underlie an increase in melanoma susceptibility. In the context of cancer, we are also involved in an NBCF program to completely profile NR and cofactor expression in normal, estrogen receptor (ER) positive, and ER negative breast cancers.

RESEARCH PROJECTS

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

KEY PUBLICATIONS

Lau, P., Fitzsimmons, R.L., Raichur, S., Wang, S.C., Lechtken, A., and Muscat, G.E.O. (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.

Pearen, M.A., Myers, S.A., Raichur, S., Ryall, J.G., Lynch, G.S., and Muscat, G.E.O. (2008). The orphan NR, NOR-1, regulates gene expression that controls oxidative metabolism in skeletal muscle. *Endocrinology* **149**: 2853-2865.

LAB MEMBERS

Research Officers: Dr Patrick Lau, Dr Stephen Myers, Dr Mary Wang

Research Assistant: Rebecca Fitzsimmons, Natalie Eriksson, Rachel Burow (Jan- Sept 2008)

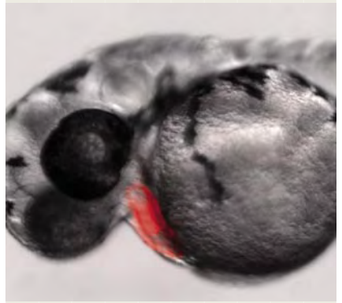
PhD Students: Michael Pearen, Sathiya Ramakrishnan, Suryaprakash Raichur, Lisa Crowther

Gary Leong (Joint appointment Senior Research Officer, IMB, and Staff Specialist, Mater Childrens Hospital, NHMRC Clinical CDA)

Research Assistant: Nick Martel

ANDREW PERKINS

Blood development



Our group is interested in the transcriptional regulation mesoderm specification. 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. Our group uses mouse and zebrafish model systems to examine gene function in vivo, and a wide variety of biochemical assays to examine gene function in vitro.

We have four primary focus areas:

1. Transcriptional hierarchies which are active during embryonic stem (ES) cell differentiation into mesoderm-derived tissues such as the kidney and blood. 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. Zebrafish are used as a vertebrate model for dissection of some of the earliest transcriptional events which underpin morphogenetic movements which lead to the generation and 'education' of stem cells within the mesoderm germ layer. Once again we are concerned primarily with the activities of key 'master regulator' transcription factors of zinc finger and homeodomain classes. We have established expression profiling in zebrafish and have established assays and systems for study of morphogenesis.

4. The role played by the Kruppel-like factor (KLF) family of zinc finger genes in normal differentiation and human skin, colon and blood cancers.

RESEARCH PROJECTS

- Studying transcriptional hierarchies active during ES cell differentiation into mesoderm-derived tissues
- Investigating the transcriptional regulation of erythropoiesis
- Studying morphogenesis using zebrafish models
- Researching role of KLF in differentiation and cancer

KEY PUBLICATIONS

Cloonan, N., *et al.* (2008). Stem cell transcriptome profiling via massive scale shotgun short tag sequencing. *Nature Methods* **5**: 613-619.

Dinger, M.E., *et al.* (2008). Non-coding RNA in Mouse ES cell pluripotency and differentiation. *Genome Research* **18**: 1433-1445.

Whitington, T., *et al.* (2008). Using epigenetic chromatin information to improve in vivo transcription factor binding predictions. *Nucleic Acids Research* **37**: 14-25. Nov 6 [Epub]

Bruce, S.J., *et al.* (2007). Dynamic transcription programs during ES cell differentiation towards mesoderm in serum versus serum-free (BMP4) culture. *BMC Genomics* **8**: 365.

Wilkins, S.J., Yoong, S., Verkade, H., Mizoguchi, T., Plowman, S.J., Hancock, J.F., Kikuchi, Y., Heath, J.K., and Perkins, A.C. (2007). Mtx2 directs zebrafish morphogenetic movements during epiboly by regulating microfilament formation. *Developmental Biology* **314**: 12-22.

LAB MEMBERS

Research Officers: Dr Christine Neyt, Dr Jessica Frith

Senior Research Assistant: Angela Lawton

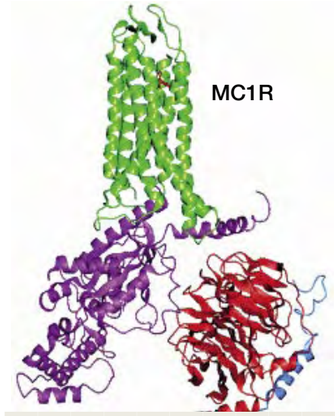
Research Assistants: Aliesha Griffin, Pei Er, Marion Monet

PhD Students: Simon Wilkins, Simon Cridland, Michael Tallack, Paulo Amaral, Tom Whittington

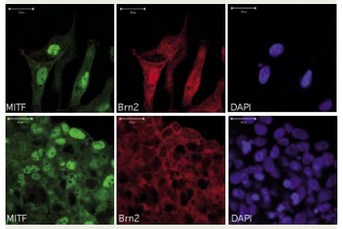
Honours Students: Anne Gisik, Wai Shan Yuen

RICK STURM

Molecular and cellular biology of the pigmentary system



Proposed MC1R structure (green) with g proteins.



BRN2 and MITF staining in melanoma.

LAB MEMBERS

Research Officers: Dr Anthony Cook, Dr Don Roberts, Dr Aaron Smith, Dr Shu Shyan Wong

Research Assistants: Sathiya Ramakrishnan, Darren Smit, Caroline Sturm, Amy Thurber

PhD Students: Helene Johanson, Luke Kirkwood, Kimberley Beaumont, Stephen Ainger

Honours and Masters Students: Wen Lim, Kasturee Jagirdar, Yan Yan Liu, Simon Teng

We have utilised primary cultures of human melanocytes and melanoblasts, as well as numerous melanoma cell lines grown as adherent cultures or induced to form non-adherent spheroids, in our investigations into melanocytic cell growth and transformation. Recent publications have suggested that melanoma may arise from the malignant transformation of melanocytic precursor cells resident in the skin. Our proposal is to study potential differences in the transcriptional and signalling network of skin-derived precursor (SKP) cells, when grown in vitro as spheroids and differentiated into melanocytes. We aim to identify the differentiation and regulatory pathways active in normal melanocyte growth that differ to those responsible for melanoma development, and the formation of spheroids from melanoma cell lines.

Fine association mapping of blue/brown eye colour-related SNPs in an adolescent twin collection from South-East Queensland has been performed within the intergenic region upstream of the *OCA2* and within the neighboring *HERC2* gene. We reported that a single SNP in intron 86 of *HERC2*, *rs12913832 C/T*, predicted eye colour with almost perfect correlation. Comparison of sequence alignments of multiple species showed this SNP lies in the centre of a short highly-conserved sequence, and the blue-eye associated allele breaks up this conserved sequence, part of which forms a consensus binding site for the helicase-like transcription factor (HLTF). We conclude that the conserved region around *rs12913832* represents a regulatory region controlling constitutive expression of *OCA2*, and that the *C* allele at *rs12913832* leads to decreased expression of *OCA2*, particularly within iris melanocytes, which we postulate to be the ultimate cause of blue eye colour.

The occurrence of red hair and pale skin in individuals, which is associated with UV-radiation sensitivity and increased skin cancer risk, is mainly due to polymorphisms in the melanocortin-1 receptor (MC1R) expressed in melanocytes. A serum-free human melanocyte–keratinocyte coculture system has been established to study the behaviour and functional abilities of melanocytes expressing MC1R red hair colour (RHC) variants in order to identify differences from their wild-type counterparts. Formation of dendrites following NDP-MSH peptide agonist activation of the MC1R receptor was markedly enhanced in wild-type melanocytes in comparison to RHC strains. Analysis of mRNA expression and protein levels of the major pigmentation markers following NDP-MSH treatment distinguished the enzyme dopachrome tautomerase (DCT) as being preferentially upregulated in cocultures of wild type strains, with negligible or a much-reduced response in melanocytes with RHC variant alleles.

Recent evidence suggests that MC1R plays a photoprotective role in the cellular response of melanocytes to UV irradiation. We have identified the induction of the NR4A nuclear receptor transcription factors as an important step in MC1R-mediated DNA repair in melanocytes. Furthermore, impaired induction in primary human melanocytes harbouring homozygous RHC variant MC1R alleles may underlie an increase in melanoma susceptibility in these individuals.

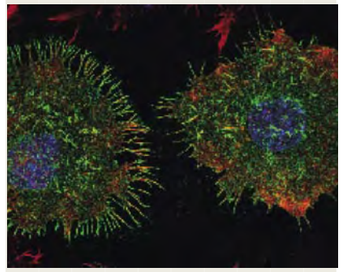
RESEARCH PROJECTS

- Understanding skin cancer risk phenotypes through studying the interaction of genes involved in skin, hair and eye colour
- Undertaking parallel genetic and cellular analysis of human melanogenesis
- Investigating eye colour as a genetic trait
- Researching melanocytic spheroids as a model for melanoma development and metastasis
- Role of NR4A nuclear hormone receptors in melanocytic cells

Further information and publications are available at www.imb.uq.edu.au/index.html?id=11690

MATT SWEET

Pathogen surveillance, innate immunity and inflammation



Plasma membrane localisation of a macrophage-specific protein.

The major research themes of this group are innate immunity and inflammation. In innate immunity, we are elucidating mechanisms by which macrophages sense invading pathogens. We focus on the recognition of individual microbial components (e.g. bacterial CpG-containing DNA), as well as the interactions between macrophages and whole pathogens (e.g. *Salmonella typhimurium*). In 2008, we identified a novel cytoplasmic recognition system for foreign DNA, and we will continue to focus on this pathway in 2009. We also performed comparative genomics studies on primary human and mouse macrophage populations; which has enabled us to identify species-specific innate immune responses. In 2009, we will use this knowledge to focus on novel human-specific immune pathways. This will ultimately increase our understanding of infectious disease processes that are directly relevant to human health.

Macrophages are not only important for anti-microbial responses, but also contribute to the pathology of both acute and chronic inflammatory diseases. Our recent work has focused on the involvement of a family of enzymes, the histone deacetylases (HDACs), in promoting inflammation. Our goals for 2009 are to characterise the mechanisms by which individual HDAC family members regulate macrophage inflammatory responses.

This laboratory was a key participant in the CRC for Chronic Inflammatory Diseases, which was completed in mid-2008. This CRC focused on the involvement of macrophages, as well as osteoclasts (a closely related cell type), in rheumatoid arthritis and chronic obstructive pulmonary disease. In 2008, we identified novel macrophage-specific cell surface proteins as potential regulators of inflammation. In 2009, we will continue our studies on some of these molecules, with a focus on validating their involvement in specific inflammatory pathways.

RESEARCH PROJECTS

- Histone Deacetylases as regulators of inflammation
- A cellular recognition system for detection of foreign DNA in the cytoplasm
- Novel macrophage-specific cell surface proteins as regulators of inflammation
- Species differences in anti-microbial effector mechanisms

KEY PUBLICATIONS

Irvine, K.M., *et al.* (2008). Colony Stimulating Factor-1 (CSF-1) delivers a pro-atherogenic signal to human macrophages. *Journal of Leukocyte Biology* Nov, Epub ahead of print.

Schroder, K., *et al.* (2007). Differential effects of CpG DNA on IFN-beta induction and STAT1 activation in murine macrophages versus dendritic cells: alternatively activated STAT1 negatively regulates TLR signaling in macrophages. *Journal of Immunology* **179**: 3495-3503.

Ripoll, V.M., *et al.* (2007). Gpnmb is induced in macrophages by IFN-gamma and lipopolysaccharide and acts as a feedback regulator of proinflammatory responses. *Journal of Immunology* **178**: 6557-6566.

Irvine, K.M., *et al.* (2006). A CSF-1 receptor kinase inhibitor targets effector functions and inhibits pro-inflammatory cytokine production from murine macrophage populations. *FASEB Journal* **20**: 1921-1923.

Aung, H.T., Schroder, K., Himes, S.R., Brion, K., van Zuylen, W., Trieu, A., Suzuki, H., Hayashizaki, Y., Hume, D.A., Sweet, M.J., and Ravasi, T. (2006). LPS regulates proinflammatory gene expression in macrophages by altering histone deacetylase expression. *FASEB Journal* **20**:1315-1327.

LAB MEMBERS

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Senior Research Officers: Dr Kate Stacey, Dr Ian Ross

Research Officers: Dr Kate Irvine, Dr Kate Schroder, Dr Allison Pettit, Dr Liza-Jane Raggatt, Dr Dmitry Ovchinnikov

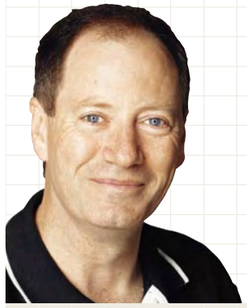
Administrative Officer: Dr Julie Osborne

Lab Manager: Greg Kelly

Research Assistants: Jasmyn Dunn, Stephen Cronau, Larisa Labzin, Nilesh Bokil, Erin Maylin, Lani Hardy

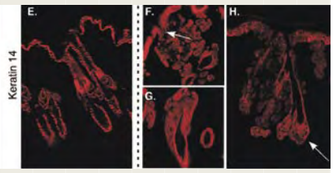
PhD Students: Melanie Andrews, Wendy van Zuylen, Ming Chang, Jane Lattin, Felicia Goh, Adi Haji Idris, Kylie Alexander, Joao Fidalgo

Undergraduate Students: Nabilah AhmadKamal, Ernest Tee

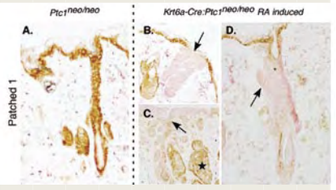


BRANDON WAINWRIGHT

Tissue repair and cancer



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
- Controlling lung regeneration following injury

KEY PUBLICATIONS

Yang, Z.J., Ellis, T., Markant, S.L., Read, T.A., Kessler, J.D., Bourboulas, M., Schüller, U., Machold, R., Fishell, G., Rowitch, D.H., Wainwright, B.J., and Wechsler-Reya, R.J. (2008). Medulloblastoma can be initiated by deletion of Patched in lineage-restricted progenitors or stem cells. *Cancer Cell* **14**: 135-145.

LAB MEMBERS

Senior Research Officer: Dr Tammy Ellis

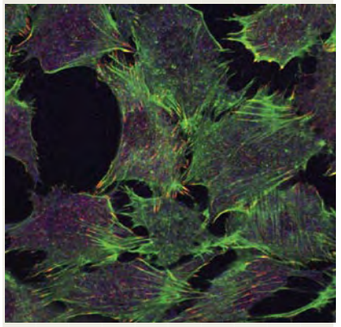
Research Officers: Dr James Palmer, Dr Richa Dave, Dr Elaine Costelloe, Dr Karen McCue

Research Assistants: Ailsa McCormack, Melissa Bourboulas

PhD Students: Rehan Villani, Uda Ho, Elaine Haase, Jonathan Robson, Lena Constantin, Rhonda Kan, Peter Yee

CAROL WICKING

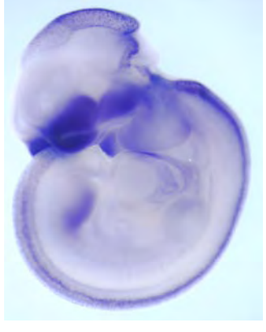
Developmental genes and human disease



Immunofluorescence analysis to reveal subcellular localisation of proteins can provide insight into function.

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. Using the mouse as a model system, we aim to identify and characterise novel molecules contributing to the development of the limb and face, with particular emphasis on genes regulated by the hedgehog signalling pathway. Because of the importance of hedgehog and other developmental signalling pathways in tumorigenesis, many of these genes will also be important in cancer.

Using genomics-based approaches we have identified a number of novel or poorly characterised genes with potential roles in embryonic development and disease. For those genes of interest we are undertaking a more detailed characterisation at both the cell and whole-organism level. We employ standard cell biology and biochemical techniques to shed light on the cellular role of these molecules, and in some cases are using transgenic or knockout approaches in the mouse to elucidate function. Our ultimate aim is to correlate the genes we identify with human disease, and we are currently analysing a number of genes for a role in tumour formation and/or progression.



Whole mount in situ hybridisation is used to reveal gene expression in developing mouse embryos.

The limb bud has long been considered a paradigm for analysis of embryonic development, and hedgehog signalling is a key determinant of patterning in the vertebrate limb. We are using a number of mouse models of hedgehog signalling to further explore the function of this pathway in limb development. In addition to patterning defects, a conditional limb specific knockout of the hedgehog receptor patched has revealed a novel role for this pathway in the very earliest stages of chondrogenesis.

RESEARCH PROJECTS

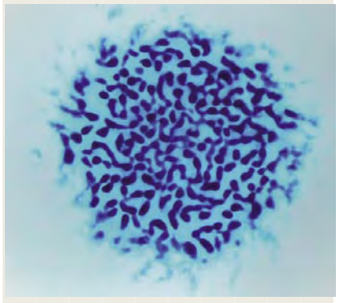
- Conditional knockout of the hedgehog receptor patched in the developing mouse limb causes novel patterning defects
- A novel role for hedgehog signalling in the very early stages of chondrogenesis in the limb
- Identification and analysis of genes regulating limb and face development

KEY PUBLICATIONS

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.

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.



High density micromass culture established from limb mesenchymal cells and stained with Alcian blue to detect sulfated proteoglycans associated with cartilage. This method is used to study chondrogenesis in vitro.

LAB MEMBERS

Senior Research Officer: Dr Fiona Simpson

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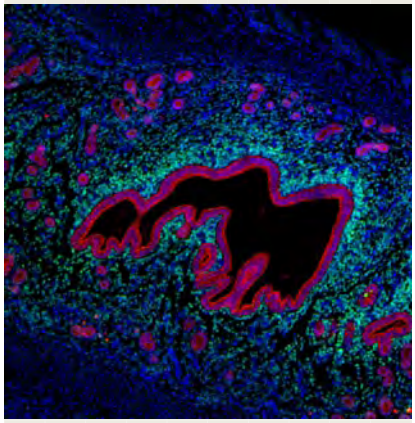
PhD Students: Liam Town, Vicki Metzis

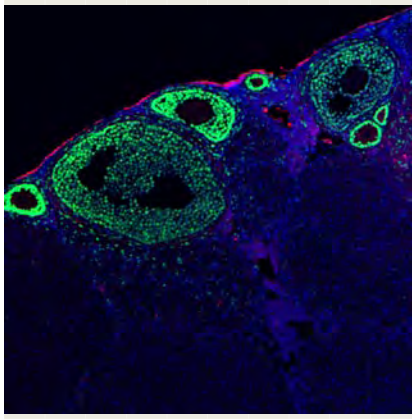
Honours Student: Rachael Barry

DAGMAR WILHELM

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



Uterus stained for FOXL2 and e-cadherin.



Ovary stained for FOXL2 and e-cadherin.

LAB MEMBERS

Research Assistants: Vy Truong, Huijun Chen

Honours Student: Elanor Wainwright

Undergraduate Students: Rebecca Cuskelly, Yoke Ying Tung

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 caused 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 display a highly regulated stage- and sex-specific expression pattern during embryogenesis.

Our research uses mouse as a model system and integrates molecular, developmental, and cancer 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 reproductive system with emphasis on ovarian development?
2. What are the roles of ncRNAs, specifically uaRNAs and microRNAs, a) during the development of testes and ovaries; and b) in tumour formation?
3. How does testicular and ovarian cancer develop?

RESEARCH PROJECTS

- Characterising the role of miR-202 during embryonic development
- Identification and analysis of upstream regulators and downstream target genes of miR-202
- Functional characterisation of uaRNAs during embryonic development and possible implications in cancer
- Studying the cellular and molecular regulation of foetal ovary development

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.

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

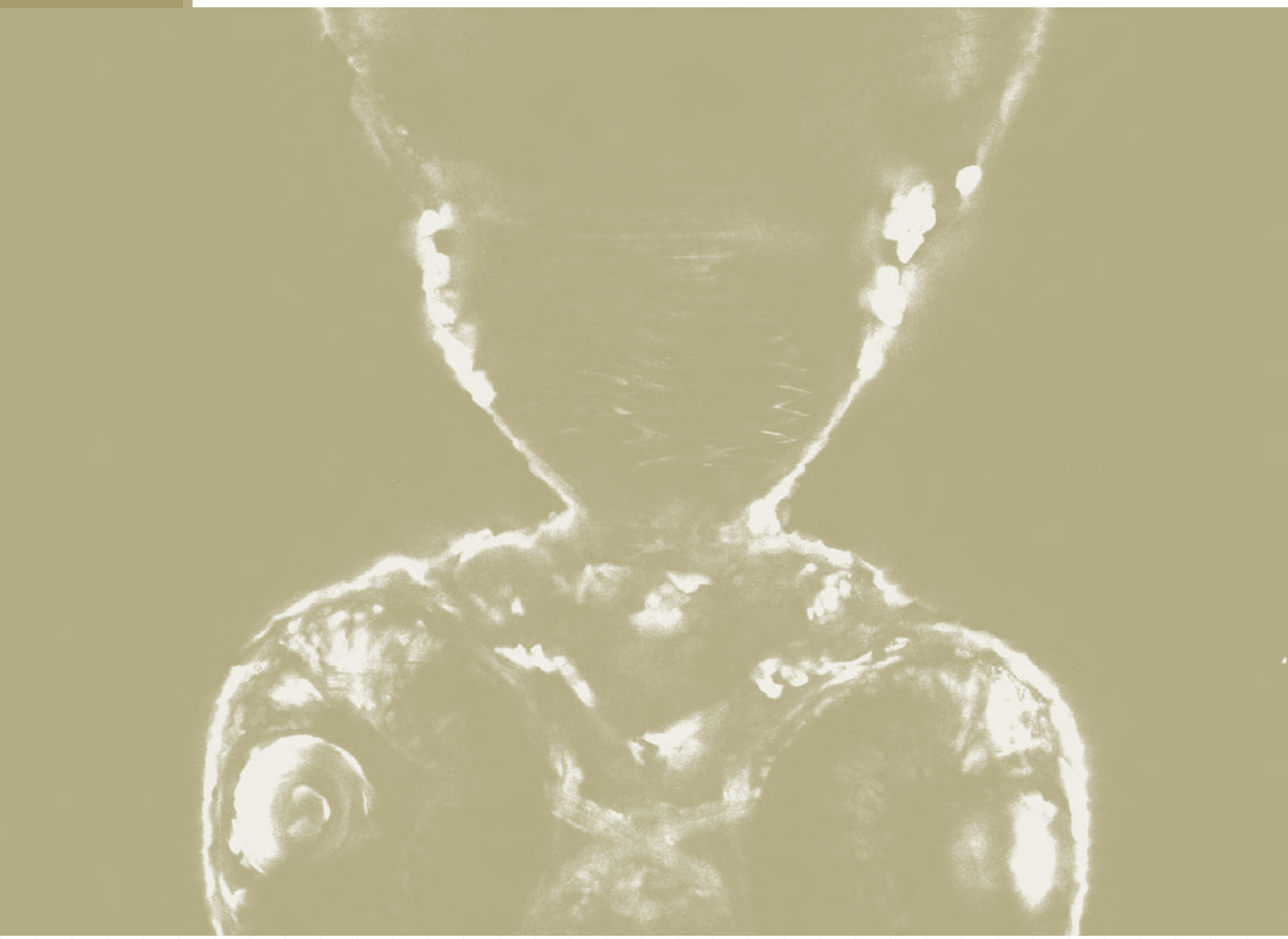
Wilhelm, D., Martinson, F., Bradford, S., Wilson, M.J., Combes, A., Beverdam, A., Bowles, J., Mizusaki, H., and Koopman, P. (2005). Sertoli cell differentiation is induced both cell-autonomously and through prostaglandin signalling to activate Sox9 during mammalian sex determination. *Developmental Biology*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

Division of Molecular Cell Biology

RESEARCH FOCUS

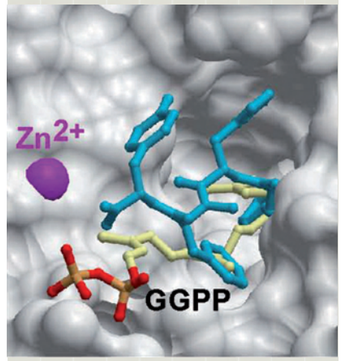
This program has received considerable support from the AMMRF Major National Research Facility; the Australian Cancer Research Foundation; Juvenile Diabetes Research Foundation International; and NIH. It is a major initiative of the IMB with the application of cryo-electron microscopy, cellular tomography, advanced visualisation and high-performance computing. It also includes the ARC Centre of Excellence in Bioinformatics. It focuses on the Visible Cell Project®; and cell architecture and trafficking.

Research Group Leaders
Kirill Alexandrov
Brett Collins
John Hancock
Brad Marsh
Rob Parton
Jenny Stow
Mike Waters
Alpha Yap

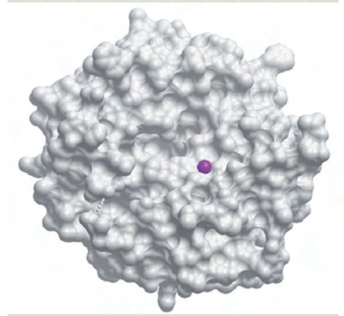


KIRILL ALEXANDROV

Biochemistry of protein prenylation



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



Surface representation of structure of β-subunit of RabGGTase.

Over the past 15 years, it has become increasingly clear that post-translational modification with isoprenoids is a widespread phenomenon, affecting up to 2 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. Much of our attention is focused on the understanding of prenylation of RabGTPases – the largest group of orenylated proteins. RabGTPases are modified by Geranylgeranyltransferase type II (RabGGTase) - a 100 kDa heterodimer that catalyses the transfer of two 20-carbon geranylgeranyl groups from geranylgeranyl pyrophosphate (GGpp) onto C-terminal cysteine Rab's C-terminus GTPases.

The remarkable feature of RabGGTase is its ability to interact with more than 70 different Rab proteins. At the same time, the enzyme is strictly specific for the Rab family and no unspecific activity could be detected. RabGGTase is composed of tightly associated alpha and beta subunits and belongs to the family of protein prenyltransferases together with farnesyl transferase (FTase) and geranylgeranyl trsnsferase I (GGTaseI).

Our aim is to understand the molecular mechanisms underlying specificity of RabGGTase and the evolution of protein prenylation mechanisms. 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 complete mechanistic model of protein prenylation.

RESEARCH PROJECTS

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

KEY PUBLICATIONS

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.

Dursina, B., Reents, R., Delon, C., Wu, Y., Kulharia, M., Thutewohl, M., Veligodsky, A., Kalinin, A., Evstifeev, V., Ciobanu, D., Szedlacsek, S.E., Waldmann, H., Goody, R.S., and Alexandrov, K. (2006). Identification and specificity profiling of protein prenyltransferase inhibitors using new fluorescent phosphoisoprenoids. *Journal of the American Chemical Society* **128**: 2822-2835.

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.

Rak, A., Pylypenko, O., Niculae, A., Pyatkov, K., Goody, R.S., and Alexandrov, K. (2004). Structure of the Rab7:REP-1 complex: insights into the mechanism of Rab prenylation and choroideremia disease. *Cell* **117**: 749-760.

LAB MEMBERS

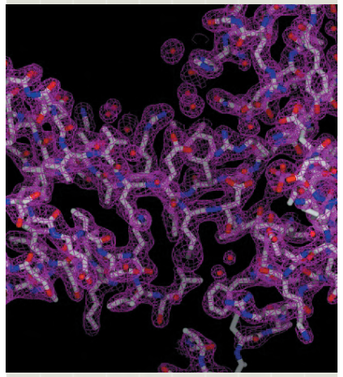
Research Officers: Dr Daniel Abankwa, Dr Sergey Mureev

Research Assistants: Martina Franke, Virajitha Rajagopalan, Veronika Schreiber

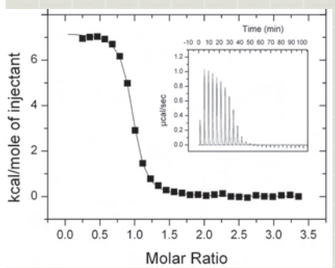
PhD Students: Oleksiy Kovtun, Zakir Tnimov, Marta Kubala

BRETT COLLINS

The endosome at atomic resolution: structural studies of the endosomal trafficking machinery



Electron density for the VPS26B subunit of retromer.



Binding of retromer subunit VPS29 to VPS35 measured by Isothermal Titration Calorimetry.

Our lab is focused on understanding the basic processes of intracellular membrane trafficking within the secretory and endocytic systems of the human cell. We do this using a multidisciplinary approach that integrates 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, lysosomal storage disease and hypercholesterolemia, and it is also exploited by bacterial toxins and viral pathogens such as HIV to gain entry into the cell.

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

RESEARCH PROJECTS

- Structure and function of the retromer protein complex
- Analysing the interaction of retromer with cargo proteins and regulatory molecules
- Membrane remodelling by the SNX protein family
- Structural studies of PX-domain proteins and complexes with effector molecules
- Structure and function of arrestin-related proteins

KEY PUBLICATIONS

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.

LAB MEMBERS

Research Officers: Dr Suzanne Norwood, Dr Catherine Latham

PhD Student: Daniel Shaw

Masters Student: Rajesh Ghai

JOHN HANCOCK

Plasma Membrane Nanostructure and Signal Transduction

Our group studies mammalian intracellular signalling. We are especially interested in the function of Ras proteins. These small GTP binding proteins operate as molecular switches in signal transduction pathways and are present in a mutant, activated state in many human tumours. Understanding the basic biology of Ras has major implications for the development of novel anticancer therapeutics.

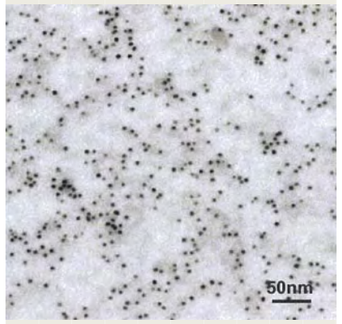
Specifically, we are investigating how the Ras membrane anchors cooperate with the G-domain and peptide sequences flanking the anchor to drive lateral segregation. Our work suggests new models are needed to explain how lipidated proteins interact with, and use, the plasma membrane to generate signalling platforms.

We remain interested in how confinement of signalling complexes onto a 2D surface in general, and in plasma membrane nanodomains in particular, regulates the kinetics and sensitivity of Raf/MEK/Erk signal output. Similarly, as we develop our spatial and proteomic maps of the plasma membrane, we can address how the composition and organisation of the membrane alters in response to specific growth factors. The integration of complex spatial, kinetic and biochemical data sets increasingly requires mathematical modelling to generate and test our novel hypotheses of nanodomain structure and function.

We also have a major interest in characterising the K-ras ER to plasma membrane trafficking pathway and studying the biology of Ras prenyl binding proteins such as PDE delta.

RESEARCH PROJECTS

- Molecular mapping of the proteins and lipids of plasma membrane nanodomains
- Electron microscopic visualisation and quantitative characterisation of surface nanodomains to build up a high-resolution 2D map of the nanodomains of the inner plasma membrane
- Investigating the dynamic regulation of nanodomain localization of Ras and Ras interacting proteins in response to physiological stimuli
- Characterising the mechanism(s) whereby K-ras is transported to the plasma membrane
- Mathematically modelling Ras signal transduction
- Monte Carlo modelling of plasma membrane nanodomain dynamics



Cholesterol depletion also causes the lipid raft marker protein GFP-Th, imaged on intact plasma membrane sheets by immunogold labelling to de-cluster.

LAB MEMBERS

Research Officers: Dr Sarah Plowman, Dr Daniel Abankwa, Dr Michael Hanzal-Bayer, Dr Michelle Hill, Dr Kerry Inder

Research Assistants: Natasha Chaudray, Nick Ariotti, Annette Lane, Dorothy Loo

PhD Students: Kwang-Jin Cho, Andy Goodall

KEY PUBLICATIONS

Tian, T., Harding, A., Inder, K., Plowman, S.J., Parton, R.G., and Hancock, J.F. (2007). Plasma membrane nanoswitches generate high-fi delity Ras signal transduction. *Nature Cell Biology* **9**: 905-914.

Abankwa, D., Hanzal-Bayer, M., Ariotti, N., Plowman, S.J., Gorfe, A.A., Parton, R.G., McCammon, J.A., and Hancock, J.F. (2008). A novel switch region regulates H-ras membrane orientation and signal output. *EMBO Journal* **27**: 727-735.

Inder, K., Harding, A., Philips, M.R., Parton, R.G., and Hancock, J.F. (2008). Activation of the MAPK module from different spatial locations generates distinct system outputs. *Molecular Biology of the Cell* **19**: 4776-4784.

Shalom-Feuerstein, R., Plowman, S.J., Rotblat, B., Ariotti, N., Tian, T., Hancock, J.F., and Kloog, Y. (2008). K-Ras nanoclustering is subverted by over-expression of the scaffold protein galectin-3. *Cancer Research* **68**: 6608-6616.

Harding, A., and Hancock, J.F. (2008). Using plasma membrane nanoclusters to build better circuits. *Trends in Cell Science* **18**: 364-371.

Plowman, S.J., Ariotti, N., Parton, R.G., and Hancock, J.F. (2008). Electrostatic interactions positively regulate K-Ras nanocluster formation and function. *Molecular and Cellular Biology* **28**: 4377-4385.

BRAD MARSH

Structure-function studies of the endocrine pancreas – comparative studies of mouse and human pancreatic islet biology

The ß-cells of the endocrine pancreas are the sole source of insulin in mammals. Death of the ß-cells, or their abnormal processing, trafficking and/or secretion of insulin, results in the disease commonly known as *diabetes*. This disease is one of Australia's national health priority areas and represents the fastest-growing epidemic internationally. More than 230 million people worldwide currently live with the disease, but this number is expected to rise to 350 million within 20 years. In 2007, the world spent an estimated US$215-375 billion to care for diabetes and its complications. In particular, *type 1 diabetes* is one of Australia's fastest-growing chronic diseases, and represents a life-long autoimmune disease that usually begins in childhood and results in premature death through health complications. Type 1 diabetes cannot be prevented, and a cure remains to be found.

Our group's research is focused on understanding the basic mechanisms related to ß-cell function and dysfunction from a structural cell biology perspective, so that we can precisely identify how and where defects in these steps occur. By necessity, this work has led us to develop or advance techniques for the improved preservation and imaging of pancreatic ß-cells *in situ* within pancreatic *islets of Langerhans* isolated from both mice and humans, so that we are positioned to reliably elucidate the basic cell biology and physiology of the ß-cell — and islet biology more generally — through comparative studies of islet cell structure-function.

To complement our move toward an integrated or more *holistic* approach to understanding cells as examples of complex systems, we have undertaken a multi-scale/multi-resolution approach whereby we have started reconstructing entire mammalian (ß) cells in 3D at both high (≤5nm) and intermediate (15-20nm) resolutions. These approaches underpin the Visible Cell® project (www.visiblecell.com) coordinated between the IMB and the Australian Centre of Excellence in Bioinformatics (ACB) at The University of Queensland. Our group's data will uniquely inform advanced *in silico* studies of 3D cell and molecular organisation in mammalian cells that are focused on developing the capacity to model and predict cellular differentiation during normal development, as well as the pathophysiology of chronic diseases like type 1 diabetes.

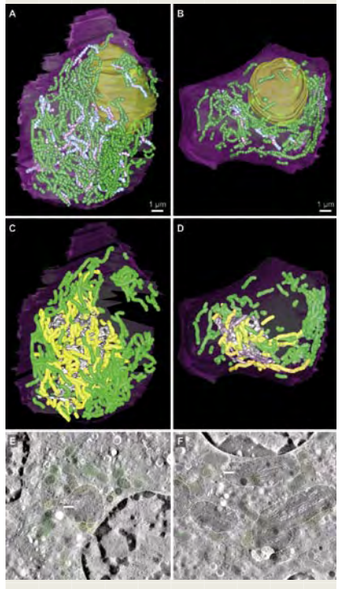
New Research Project: Correlative structure-function studies of cis- and trans-Golgi membrane traffic in mammalian cells

This project combines imaging by light and electron microscopy with additional techniques for studying protein function at the molecular level, to elucidate how changes in the 3D organisation of cellular machinery can lead to fundamental changes in the function and health of mammalian cells. Although this work includes detailed investigation of the 'insulin factory', it has the potential to modify established concepts on membrane traffic and protein secretion well beyond the field of diabetes.

KEY PUBLICATIONS

Noske, A.B., Costin, A.J., Morgan, G.P., and Marsh, B.J. (2008). Expedited approaches to whole cell electron tomography and organelle mark-up in situ in high-pressure frozen pancreatic islets. *Journal of Structural Biology* **161**: 298–313.

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



LAB MEMBERS

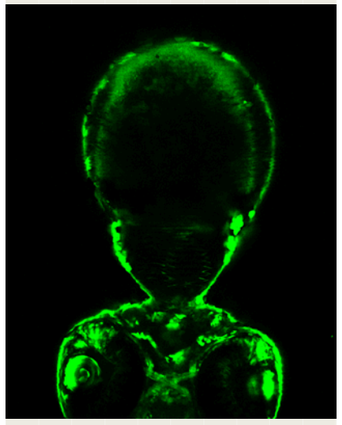
Research Officers: Dr Isabel Morrow, Dr Tobias Richter, Dr Neelima Pottekkat Sidharthan

Research Assistants: Janette Galea, Garry Morgan

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

Visiting Scholars: Meike Leuger, Dr Bo Zhang

ROB PARTON



The cell surface in health and disease

Our group is interested in the organisation, dynamics, and functions of the plasma membrane. The properties of the plasma membrane rely on the specialisation of the plasma membrane into microdomains of specific function. We 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 have shown that caveolins are essential for the formation of lipid droplets during liver regeneration.

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*: characterising novel nanovesicles

KEY PUBLICATIONS

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.

Parton, R.G., and Simons, K. (2007). The multiple faces of caveolae. *Nature Reviews Molecular Cell Biology* **8**: 185-194.

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 Michelle Hill, Dr Susan Nixon, Dr Tobias Richter#, Dr Piers Walser, Dr Lars Kuerschner, Dr Harriet Lo

Research Assistants: Rachel Hancock, Charles Ferguson#, Robert Luetterforst#, James Rae#, Satomi Okano#, Nicole Schieber#, Alejandra Castillo#,

PhD Students: Mark Howes, Michele Bastiani, Samantha Murphy, Carol Kistler

Visiting Scientist: Dr Katia Cortese#

part of year

Protein trafficking in human disease

Our research group studies protein trafficking in human and animal cells with the aim of mapping the cellular organelles and molecules that function in the secretion and endocytosis of disease-related proteins. In this work we use a range of cellular, molecular and biochemical approaches. Trafficking is a highly-dynamic process and studies in this field have been greatly enhanced by the development of fluorescent probes and microscopic techniques for imaging in living cells. Live cell imaging, combined with other forms of microscopy, has thus become a major core technology for the research in our group.

In epithelial cells we are studying E-cadherin, an essential adhesion protein and a vital tumour suppressor. E-cadherin is trafficked to and from the cell surface to regulate cadherin-based cell–cell adhesion and cell polarity. A main goal of this work is to understand how E-cadherin trafficking functions in morphogenesis and cancer progression. As a model system we grow epithelial cells in mini-organ cultures where the effects of gene expression or gene silencing can be analysed.

Cells of the immune system secrete tightly orchestrated arrays of cytokines to control immune responses. In macrophages we are studying the secretion of pro-inflammatory cytokines that contribute to the onset and progression of chronic inflammatory diseases. Understanding how they are trafficked and secreted may lead to the development of new therapeutic strategies in inflammation. Gene expression arrays, live cell imaging, FACS and biochemical approaches are used to map out intracellular pathways for cytokine trafficking and secretion. Recent progress has shown that we can manipulate cytokine secretion in mice and current efforts are focused on using this approach in the treatment of arthritis and inflammation of the stomach and bowel. Based on recent findings, we are now also studying the pathways for phagocytosis or ingestion of different microbes by macrophages.

RESEARCH PROJECTS

- Imaging live cells to create 3D and 4D maps of trafficking pathways: fluorescence imaging and computer modelling
- E-cadherin trafficking in epithelia: morphogenesis and tumorigenesis in cyst cultures
- E-cadherin and growth factor signalling in cancer cells
- Secretion of inflammatory cytokines in macrophages
- Secretion of cytokines in mouse models of inflammatory disease
- Phagocytosis and trafficking of microbes

KEY PUBLICATIONS

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.

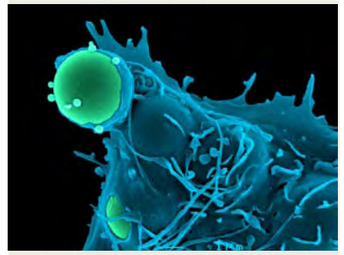
Bryant, D.M., Kerr, M.C., Hammond, L.A., Joseph, S.R., Mostov, K.E., Teasdale, R.D., and Stow, J.L. (2007). EGF induces macropinocytosis and SNX1-modulated recycling of E-cadherin. *Journal of Cell Science* **120**: 1818-1828.

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

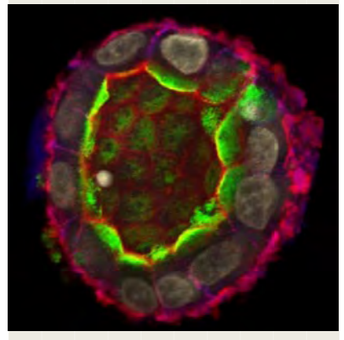
Stow, J.L., Manderson, A.P., and Murray, R.Z. (2006). SNAREing immunity: the role of SNAREs in the immune system. *Nature Reviews Immunology* **6**: 919-929.

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.

JENNY STOW



Scanning electron microscope image of a macrophage ingesting foreign particles.



Confocal microscopy image through a human breast cancer cyst.

LAB MEMBERS:

Senior Research Officer: Dr Tom Taguchi

Research Officers: Dr Marion Desclozeaux, Dr Ryo Misaki, Dr Esther Reefman, Dr Jason Kay

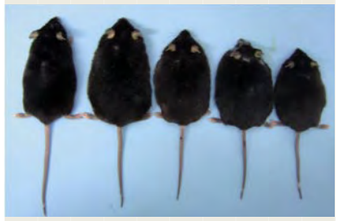
Research Assistants: Darren Brown, Tatiana Khromykh, Juliana Venturato, Teresa Munchow, Luke Hammond

Research Coordinator: Dr Fiona Wylie

PhD Students: Carolin Offenhauser, Regine Low, Daniele Sangermani, Stephanie Wood

MIKE WATERS

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



Marked adiposity in mature male mice lacking growth hormone receptor (GHR-/-), lacking ability of GHR to activate JAK2 (box1), or lacking ability to generate STAT5 in response to GH (receptor truncated at 391), or able to generate only 30% of the normal STAT5 response to GH (receptor truncated at 569).

Diagrammatic representation of mechanism of growth hormone receptor action through binding to CoAA, an important transcriptional coactivator which regulates the direct actions of the GH receptor in the nucleus.

LAB MEMBERS

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

Visiting Research Fellow: Dr Mayumi Ishikawa

Research Assistants: Kathryn Tunny, Linda Kerr

Adult height is determined by the actions of growth hormone (GH) during childhood and adolescence. In the adult, growth hormone is an important metabolic agent regulating body composition, opposing the actions of insulin. In old age, growth hormone status determines lifespan, at least in animal models. We study the means used by growth hormone to achieve these changes, using a variety of approaches directed to the growth hormone receptor, from high-resolution protein structures to genetically-engineered animals.

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

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

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 secretion and action
- Establishing the molecular basis for GH-dependent liver regeneration
- Investigating the feasibility of using GH receptor antagonists to block breast and prostatic cancer

KEY PUBLICATIONS

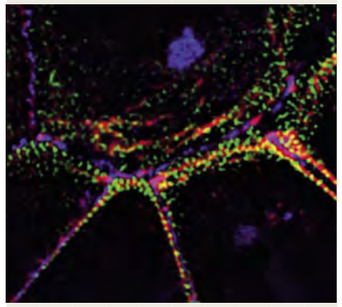
Conway-Campbell, B.L., *et al.* (2008). The extracellular domain of the growth hormone receptor interacts with coactivator activator to promote cell proliferation. *Molecular Endocrinology* **22**: 2190-2202.

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

Rowlinson, S.W., *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.

ALPHA YAP

Cadherin adhesion and tissue organisation: molecular mechanisms and morphogenetic consequences



LAB MEMBERS

Research Officers: Dr Eva Kovacs, Dr Nicole den Elzen, Dr Gang Albert Ren, Dr Matthew Crampton, Dr Michael Smutny

Research Assistants: Suzie Verma, Carmen Buttery

PhD Students: Angela Jeanes, Robert McLachlan, Sabine Mangold

Honours Student: Hayley Cox

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. 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 that are 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.

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 signaling to Src family kinases: defining the pathway(s)
- The morphogenetic consequences of cadherin-activated cell signalling and cooperativity with the actin cytoskeleton

KEY PUBLICATIONS

Akhmanova, A., and Yap, A.S. (2008). Organizing junctions at the cell-cell interface. *Cell* (Invited Preview; in press).

Kovacs, E.M., and Yap, A.S. (2008). Cell-cell contact: Cooperating clusters of actin and cadherin. *Current Biology* **18**: R667-R669.

Maddugoda, M.P., Crampton, M.S., Shewan, A.M., and Yap, A.S. (2007). Myosin VI and vinculin cooperate during the morphogenesis of cadherin cell-cell contacts in mammalian epithelial cells. *Journal of Cell Biology* **178**: 529-540.

McLachlan, R.W., Kraemer, A., Helwani, F.M., Kovacs, E.M., and Yap, A.S. (2007). E-Cadherin adhesion activates c-Src signaling at cell-cell contacts. *Molecular Biology of the Cell* **18**: 3214-3223.

Scott, J.A., Shewan, A.M., den Elzen, N.R., Loureiro, J.J., Gertler, F.B., and Yap, A.S. (2006). Ena/VASP proteins critically determine distinct modes of actin organization that can coexist at cadherin adhesive contacts. *Molecular Biology of the Cell* **17**: 1085-1095.

Stehbens, S.J.*, Paterson*, A.D., Crampton, M.S., Shewan, A.M., Ferguson, C., Akhmanova, A., Parton, R.G., and Yap, A.S. (2006). Dynamic microtubules regulate the local accumulation of E-cadherin and activity of Myosin 2 at cell-cell contacts. *Journal of Cell Science* **119**: 1801-1811. (*Equal contributions.)

Division of Chemical & Structural Biology

RESEARCH FOCUS

This program has some of the most advanced equipment for structural biology in Australia, used in the development of new medicines and technologies, especially through exploration of Queensland's biodiversity. It has been responsible for a number of IMB spin-out companies based on new platform technologies for drug discovery, as well as developing novel drugs for human disease. It focuses on membrane protein structures; soluble protein and nucleic acid structures; and new drugs and therapies.

Research Group Leaders
Paul Alewood
Rob Capon
David Craik
David Fairlie
Ben Hankamer
Glenn King
Richard Lewis
Jenny Martin
Mark Smythe

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

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.

Poth, A.G., Deeth, H.C., Alewood, P.F., and Holland, J.W. (2008). Analysis of the Human Casein Phosphoproteome by 2-D Electrophoresis and MALDI-TOF/TOF MS Reveals New Phosphoforms. *Journal of Proteome Research* **7**: 5017-5027.

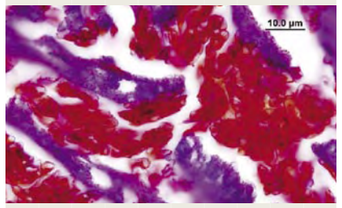
Yan, W.X., Armishaw, C., Goyette, J., Yang, Z., Cai, H., Alewood, P., and Geczy, C.L. (2008). Mast cell and monocyte recruitment by S100A12 and its hinge domain. *Journal of Biological Chemistry* **283**: 13035-13043.

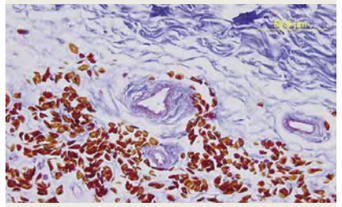
Dutertre, S., Ulens, C., Büttner, R., Fish, A., van Elk, R., Kendel, Y., Hopping, G., Alewood, P.F., Schroeder, C., Nicke, A., Smit, A.B., Sixma, T.K., and Lewis, R.J. (2007). AChBP-targeted a-conotoxin correlates distinct binding orientations with nAChR subtype selectivity. *EMBO Journal* **26**: 3858-3867.

Lewis, R.J., Schroeder, C.I., Ekberg, J., Nielsen, K.J., Loughnan, M., Thoma, 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.





LAB MEMBERS

Research Manager: Dianne Alewood

Senior Research Officer: Dr John Holland

Research Officers: Dr Aline Dantas, Dr Andrea Vernal, Dr Tom Durek, Dr Lachlan Rash, Dr Jean Jin

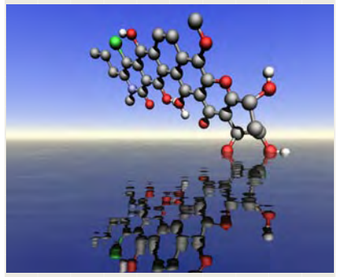
Research Assistants: Aaron Poth, Zoltan Dekan

PhD Students: Marcus Muttenthaler, Rod Morales, Jen Smith, Kalyani Abondi, Simone Vink

Visiting Students: Julie Klint and Christine Ussing (Danish Pharmaceutical University),

Visiting Fellow: Mehdi Varidi (University of Mashhad)

ROB CAPON



Biodiscovery: from biodiversity and biology, to bioactives and beyond

Our research centres 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, have potential as molecular probes to better interrogate and understand living systems, and could find application as biological control agents.

The research group coordinates an extensive network of collaborators across many scientific disciplines, in industry, academia and government, both in Australia and overseas, which allows us to target such therapeutic indications as infectious and neurodegenerative diseases, cancer, inflammation, pain, diabetes and obesity, as well as invasive animal and pest control through chemical ecology, and gene-activated microbial biodiscovery.

RESEARCH PROJECTS

- Marine biodiscovery: discovering new drugs to control neurodegenerative diseases
- Cephalopod biodiscovery: exploring chemical ecology as a source of new pain drugs
- Microbial biodiscovery: Exploring the microbial genome for bioactive metabolites with application against infectious and neurodegenerative diseases, diabetes, obesity, atherosclerosis, inflammation, pain and cancer
- Chemical synthesis: Developing “natural” antihelmintics to combat parasitic infection in livestock
- Chemical ecology: Developing new “natural” strategies for controlling cane toads
- Biomimetic synthesis: Developing new “natural” routes into bioactive chemical space

KEY PUBLICATIONS

Capon, R.J., Peng, C., and Dooms, C. (2008). Trachycladindoles A-G: Novel cytotoxic heterocycles from an Australian marine sponge, *Trachycladus laevispirulifer*. *Organic & Biomolecular Chemistry* **6**: 2765-2771.

El-Naggar, M., Piggott, A.M., Capon, R.J., Bistellettazines, A.-C., and Bistellettazole, A. (2008). New Terpenyl-Pyrrolizidine and Terpenyl-Imidazole Alkaloids from a Southern Australian Marine Sponge, *Stelletta* sp. *Organic Letters* **10**: 4247-4250.

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Zhang, H., and Capon, R.J. (2008). Phorbasins D-F: Diterpenyl-taurines amines from a southern Australian marine sponge, *Phorbas* sp. *Organic Letters* **10**: 1959-1962.

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 & Biomolecular Chemistry* **6**: 3811-3815.

LAB MEMBERS

Personal Assistant: Nadine Coleman

Postdoctoral Fellows: Dr Frank Fontaine, Dr Angela Salim, Dr Andrew Piggott, Dr Hua Zhang, Dr Andrew Hayes, Dr Cedric Dooms

Research Assistant: Melissa Conte

PhD Students: Leith Fremlin, Mohamed El-Naggar, Walter Balansa, Raju Ritesh, Soumini Vijayasarathy, Fabien Plisson

Undergraduate Students: Kristian Dalle, Nathan Boase, Michael Auld

International Occupational Trainees: Kenneth Johansen (Denmark), Monika Hermann (Germany)

International Visiting Scientist: Professor David Myers (USA)

DAVID CRAIK

Violet flowers with the structures of cycloviolacin O1.

NMR and protein structure in drug design

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 can 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.

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?

Amongst the highlights of last year included our isolation and characterisation of a pair of key cyclic peptide-processing enzymes (asparaginyl endoprotease and peptide disulfide isomerase) and our identification of potential common processing mechanisms of circular proteins across divergent plant families.

To read more details about other projects we are working on, please see: www.imb.uq.edu.au/index.html?id=11695

RESEARCH PROJECTS

- Bioengineering circular proteins
- Discovering new circular proteins
- Studying the structure-activity relationship of toxins
- Development of new drugs for pain
- Development of new anticancer drugs
- Investigating plant proteinase inhibitors
- Conducting metabolomic screening

KEY PUBLICATIONS

Gruber, C.W., Elliot, A., Ireland, D.C., Trabi, M., Göransson, U., Delprete, P.G., Dessein, S., Robbrecht, E.F., and Craik, D.J. (2008). Distribution and evolution of circular mini-proteins in flowering plants. *The Plant Cell* **20**: 2471-2483.

Saska, I., and Craik, D.J. (2008). Protease catalysed protein splicing – a new post translational modification? *Trends in Biochemical Sciences* **33**: 363-368.

Simonsen, S.M., Sando, L., Rosengren, K.J., Colgrave, M.L., Daly, N.L., and Craik, D.J. (2008). Alanine scanning mutagenesis of the prototypic cyclotide reveals a cluster of residues essential for bioactivity. *Journal of Biological Chemistry* **283**: 9805-9813.

Craik, D.J., and Adams, D.J. (2007). Chemical modifications of conotoxins to improve stability and activity. *ACS Chemical Biology* **2**: 457-468.

Craik, D.J., Cemazar, M., and Daly, N.L. (2007). The chemistry and biology of cyclotides. *Current Opinion in Drug Discovery and Development* **10**: 176-184.

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Greenwood, K.P., Daly, N.L., Brown, D.L., Stow, J.L., and Craik, D.J. (2007). The cyclic cystine knot miniprotein MCoTI-II is internalized into cells by macropinocytosis. *International Journal of Biochemistry and Cell Biology* **39**: 2252-2264.

Gruber, C.W., Cemazar, M., Clark, R.J., Horibe, T., Renda, R.F., Anderson, M.A., and Craik, D.J. (2007). A novel plant protein disulfide isomerise is involved in the oxidative folding of cystine knot defense proteins. *Journal of Biological Chemistry* **282**: 20435-20446.

LAB MEMBERS

Research Officers: Dr Norelle Daly, Dr Richard Clark, Dr Horst Schirra, Dr Masa Cemazar, Dr Joshua Mylne, Dr Quenkin Kaas, Dr Jan Westerman, Dr Ute Marx, Dr Sonia Henriques

Research Assistants: Dr Shane Simonsen, Chia-Chia Tan, Emily McCallum, Ashley Cooper

PhD Students: Laura Cascales, Philip Nguyencong, Sunithi Gunasekara, Christian Gruber, Crystal Yen-Hua Huang, David Ireland, Conan Wang, Reena Halai, Kathryn Greenwood, Louise Thorstholm, Phillippa Smith, Basar Oku, Muhareem Akcan, Angeline Chan, Aaron Poth

Honours Students: Andrew Kinghorn

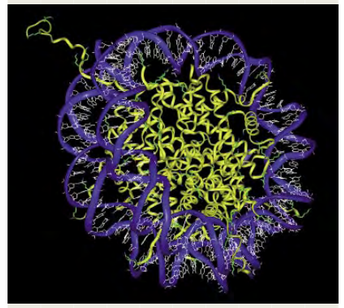
Masters Students: Martin Poms, Lisbeth Sorum, Bodil Carstens, Tilman Plass

Undergraduate Students: Reynold Philips, Yee Chng, Soumya Krishna Moorthy

Visitor: Dr Terry Qin

Chemistry and human therapeutics

DAVID FAIRLIE



DNA-wrapped histone.

LAB MEMBERS

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

Research Officers: Dr Grant Barry, Dr Tim Hill, Dr Huy Hoang, Dr Fredrik Lindahl, Dr Rink-Jan Lohman, Dr Andrew Lucke, Dr Reik Löser, Dr Praveen Madala, Dr Gloria Ruiz-Gómez, Dr Conor Scully

PhD Students: Jade Blakeney, Renee Beyer, Russell Driver, Maria Halili, Dhiraj Hans, Rose Harrison, Ranee Singh, Jacky Suen

Masters Students: Steven Pace, Nicole Wheatley

Honours Students: Patricia Garcia, Pei'e Han, Junxian Lim, Mark Matthew, Vernon Seow

Undergraduate Students: Peifei Chu, Kelly Collins, Anneke Dorgelo, Johan Hamidon, Nor Hana Hamzah, Kinitra Hutchinson, Karen Yong

Our group works at the interface of chemistry, biology and disease. Our researchers study chemistry, biology, or chemistry and biology to better understand the detailed processes of life, ageing, disease and death.

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

Our *biology researchers* use our new compounds to interrogate human protein and cellular function and to elucidate mechanisms of protein activation, biological/physiological processes, disease development, and drug action. Researchers gain insight to processes pivotal to human physiology or aberrant in disease, and develop interdisciplinary skills in enzymology, biochemistry, pharmacology, immunology, oncology, parasitology, virology and neurobiology.

RESEARCH PROJECTS

- Designing and discovering drugs (e.g. for GPCRs, proteases, enzymes)
- Synthetic organic or medicinal chemistry (solution & solid phase)
- Determining structure using 2D NMR spectroscopy
- Enzymology & protein-protein interactions
- Pharmacology: molecular (cellular) and experimental (animal models)
- Structural and functional mimicry of protein surfaces by small molecules
- Mechanisms of disease development & drug action in human inflammatory disorders, cancers, viral and parasitic infections, neurodegenerative and cardiovascular diseases

KEY PUBLICATIONS

Blakeney, J.S., Reid, R.C., Le, G.T., and Fairlie, D.P. (2007). Nonpeptidic Ligands For Peptide-Activated GPCRs. *Chemical Reviews* **107**: 2960-3041.

Chappell, K.J., Stoermer, M.J., Fairlie, D.P., and Young, P.R. (2006). Insights to Substrate Binding and Processing by West Nile Virus NS3 Protease through Combined Modelling, Protease Mutagenesis, and Kinetic Studies. *Journal of Biological Chemistry* **281**: 38448-38458.

Kahnberg, P., Lucke, A.J., Glenn, M.P., Boyle, G.M., Tyndall, J.D.A., Parsons, P., and Fairlie, D.P. (2006). Design, Synthesis, Potency and Cytoselectivity Of Anticancer Agents Derived By Parallel Synthesis From Alpha-Aminosuberic Acid. *Journal of Medicinal Chemistry* **49**: 7611-7622.

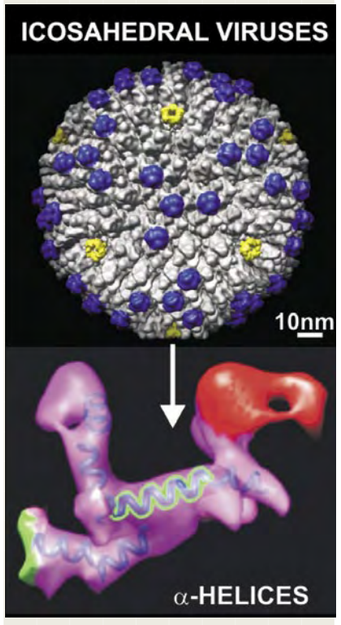
Levick, S., Loch, D., Rolfe, B., Reid, R.C., Fairlie, D.P., Taylor, S.M., and Brown, L. (2006). Antifibrotic Activity of an Inhibitor of Group IIa Secretory Phospholipase A_2 in Young Spontaneously Hypertensive Rats. *Journal of Immunology* **176**: 7000-7007.

Shepherd, N.E., Hoang, H.N., Desai, V.S., Letouze, E., Young, P.R., and Fairlie, D.P. (2006). Modular Alpha Helical Mimetics With Antiviral Activity Against Respiratory Syncitial Virus. *Journal of the American Chemical Society* **128**: 13284-13289.

Singh, Y., Stoermer, M.J., Lucke, A.J., Guthrie, T., Fairlie, D.P. (2005). Structural Mimicry of Two Cytochrome b_{562} Interhelical Loops Using Macrocycles Constrained By Oxazoles and Thiazoles. *Journal of the American Chemical Society* **127**: 6563-6572.

Structural biology of membrane proteins, macromolecular assemblies and viruses

BEN HANKAMER



LAB MEMBERS

Research Officers: Dr Ian Ross, Dr Michael Landsberg

Research Assistant: Rosalba Rothnagel

PhD Students: Evan Stephens, Erin Ahern, Drew Ringsmuth, Emily Knauth, Winnie Waudo, Matthew Timmins

MSc Student: Malte Kock

Honours Student: Hong Wai Tham

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 about 70 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, physics and software development
- The Visible Cell® Project: resolving the 3D structure of the macromolecular assemblies
- 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

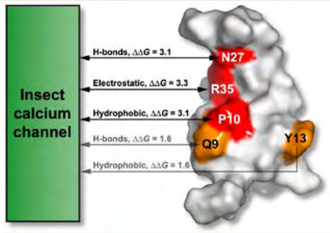
KEY PUBLICATIONS

Landsberg, M.J., Vajjhala, P.R., Rothnagel, R., Munn, A.L, and Hankamer, B. (2008). 3D structure of the AAA ATPase Vps4: Advancing structural insights into the mechanisms of endosomal sorting and enveloped virus budding.*Structure* **17**: 427-437.

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.

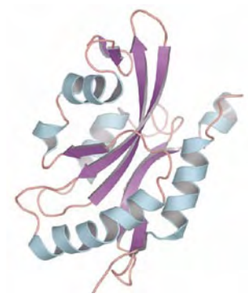
Bugs and drugs: rational development of novel antibiotics, analgesics, and environmentally-friendly insecticides

GLENN KING

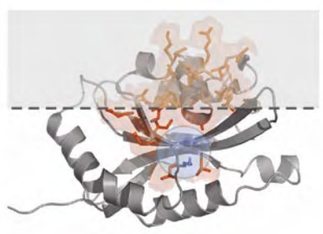


Model of the interaction between the spider toxin ω-ACTX-Hv1a and insect voltage-gated calcium channels.

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.



Three-dimensional structure of chick cofilin.



Model of the interaction of cofilin with lipid bilayers.

RESEARCH PROJECTS

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

KEY PUBLICATIONS

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.

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

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.

Szeto, T.H., Rowland, S.L., Rothfield, L.I., and King, G.F. (2002). Membrane localization of MinD is mediated by a C-terminal motif that is conserved across eubacteria, archaea, and chloroplasts. *Proceedings of the National Academy of Sciences USA* **99**: 15693–15698.

LAB MEMBERS

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

Research Officers: Dr Volker Herzig, Dr Rikki Hvorup, Dr David Wilson, Dr Brit Winnen

Research Assistants: Lindsey Long, Alysha Elliott

PhD Students: Margaret Gentz, Sandy Gonzalez, Jonas Jensen, David Morgenstern, Natalie Saez, Kimberly Wadsworth

MSc Students: Radha Seshadri, Virajitha Rajagopalan

Undergraduate Interns: Tomas Miljenovic, Darshani Rapasinghe, Mitchell Sullivan

Molecular pharmacology of venom peptides

RICHARD LEWIS

My research focuses on the discovery and characterisation of venom peptides, especially the conotoxins produced by the predatory cone snail. 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, which was developed from χ-MrIA, originally discovered by my group.

A major focus of the group is to discover new protein targets and develop peptides able to act at these targets to reduce pain sensation. 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 simulations of the peptide target interaction.

RESEARCH PROJECTS

- Discovering conopeptides that modify pain pathways (NHMRC Program Grant)
- Determining sites of conotoxin action at the α1-adrenoceptor and noradrenaline transporter
- Studying interactions of conotoxins at ion channels including the nicotinic acetylcholine receptors and calcium and sodium channels
- Discovering and characterising novel bioactives using high-content screening
- Developing mass spectrometric approaches to unravel the peptide diversity of cone snail venoms

KEY PUBLICATIONS

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 α-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.

Paczkowski, F.A., Sharpe, I.A., Dutertre, S., and Lewis, R.J. (2007). χ-Conopeptide and tricyclic antidepressant interactions at the norepinephrine transporter define a new transporter model. *Journal of Biological Chemistry* **282**: 17837-17844.

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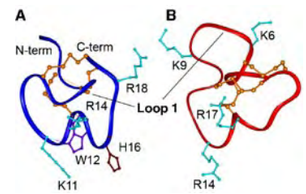
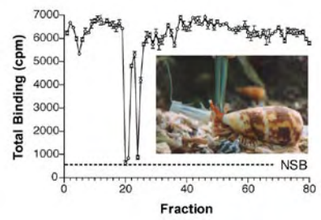
Lewis, R.J., and Garcia, M.L. (2003). Therapeutic potential of venom peptides. *Nature Reviews Drug Discovery* **2**: 790-802.

Sharpe, I.A., Gehrmann, J., Loughnan, M.L., Thomas, L., Adams, D.A., Atkins, A., Palant, E., Craik, D.J., Adams, D.F., Alewood, P.F., and Lewis, R.J. (2001). Two new classes of conopeptides inhibit the α1-adrenoceptor and noradrenaline transporter. *Nature Neuroscience* **4**: 902-907.



Comparison of μ-conotoxin (A) μ-SIIIA and (B) μ-TIIIA structures determined using NMR techniques.



Identification of native μ-SIIIA and SIIIB in milked crude C. striatus *venom. Active fractions eluting from RP-HPLC using a 1% gradient from 0–80% ACN displaced 125I-TIIIA(2-22) binding to rat brain (downward peaks).*

LAB MEMBERS

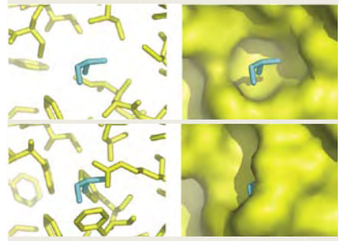
Research Officers: Dr Irina Vetter, Dr Anderson Wang, Dr Lotten Ragnarsson-McGrath, Dr Marion Loughnan, Dr Fil Paczkowski, Dr Aijun Yang

Research Assistants: Dianne Alewood, Jodie Major, Asa Anderson, Jasmine Davis

PhD Students: Marco Inserra, Vu Bach, Josh Wingerd

MSc Students: Nausad Shaikh, Uru Malik, Hareshwar Goswarmi, Mercy Gunnampaty

JENNY MARTIN

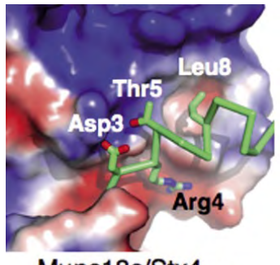


Protein structure and drug design

Our work aims to better understand the role of proteins in disease and to develop novel chemicals to modify the functions of disease-causing proteins. We use a range of techniques to investigate the structure, function and interactions of proteins. Our research has been enhanced enormously through the recent ARC LIEF-funded automation upgrade of the UQ ROCX Facility.

A major outcome over the past years has been the advance in our understanding of 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 (Latham et al. Traffic 2006). 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 has been recognised by the award of a 2009 NHMRC program grant between James and Martin and other diabetes researchers at the Garvan Institute.

Our long-running interest in bacterial redox folding factors has led us to focus our attention on developing inhibitors of DsbA as potential antibacterial agents, using the technique of fragment-based screening. We have already successfully applied this approach to the study of inhibitors of PNMT, using our new automated UQ ROCX facility. PNMT crystals were used to screen 400 drug-like fragments: 12 hits were identified and confirmed by isothermal calorimetry. Six elaborated compounds were designed and synthesised and these are currently being tested for inhibitory activity. This whole procedure from first crystal soak to final chemical synthesis step has taken one PhD student just 18 months, demonstrating the strength of structure-based approaches for drug lead discovery.



Munc18c/Stx4$_{1-19}$

RESEARCH PROJECTS

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

KEY PUBLICATIONS

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

Sabbatical Visitors: Professor Ted Baker, Dr Heather Baker (Both University of Auckland)

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

Research Officers: Dr Gordon King (SRC crystallisation officer), Dr Gautier Robin, Dr Stephen Shouldice (UQ Postdoctoral Fellow)

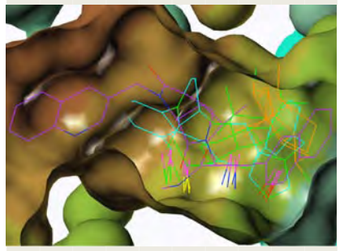
UQ ROCX X-ray Lab Manager: Karl Byriel

Research Assistant: Russell Jarrott

PhD Students: Mareike Kurz, Nyssa Drinkwater, Michelle Christie, Kevin Chen, Nurliyana Ahmad Zawawi

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

MARK SMYTHE



A conserved surface patch in unrelated proteins, and a diverse set of ligands bound to this common surface patch.

Combinatorial chemistry and molecular design

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

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

RESEARCH PROJECTS

- Modulating hematopoietic 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

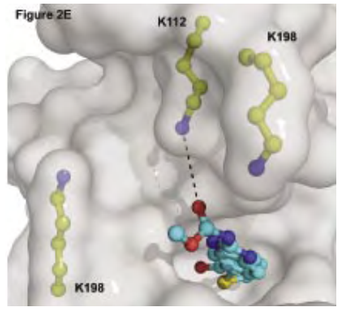
Horton, D.A., Horton, G.T., Coughlan, J., Kaiser, S.M., Jacobs, C.M., Jones, A., Ruhmann, A., Turner, J.Y., and Smythe, M.L. (2008). Cyclic tetrapeptides via the ring contraction strategy: chemical techniques useful for their identification. *Organic & Biomolecular Chemistry* **6**: 1386-1395.

Severinsen, R., Bourne, G.T., Tran, T.T., Ankersen, M., Begtrup, M., and Smythe, M.L. (2008). Library of Biphenyl Privileged 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.



Crystal structure revealing binding mode of an inhibitor and key electrostatic interaction.

LAB MEMBERS

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

Research Officers: Dr Rena Hirani, Dr Peter Bain, Dr Jenny Zhang

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

PhD Students: Christina Kulis, Matt Daley

Joint appointments at the IMB

RESEARCH FOCUS

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.

Research Group Leaders
Alan Mark
Geoffrey McLachlan

Molecular dynamics of biomolecular systems

ALAN E. MARK

The group, with members based both at The University of Queensland (UQ) and the University of Groningen (RUG), The Netherlands, 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 some 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 of 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. On one hand 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.

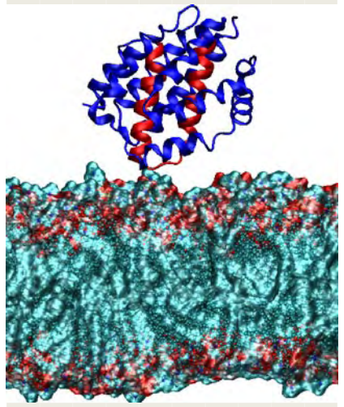
RESEARCH PROJECTS

- 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

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.

Wassenaar, T.A., Quax, W.J., and Mark, A.E. (2008). The conformation of the extracellular binding domain of Death Receptor 5 in the presence and absence of the activating ligand TRAIL: A molecular dynamics study. *Proteins: Structure, Function, and Bioinformatics* **7**: 333-343.



The initial stage of the binding of the pore-forming toxin Colicin to a model membrane.

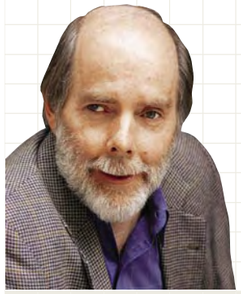
The lateral assembly of the amyloid-forming peptide SUP-35.

LAB MEMBERS

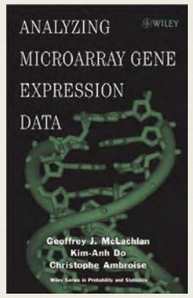
Research Officers: Dr David Poger (UQ), Dr Itamar Kass (UQ), Dr Aldo Rampioni (RUG), Dr Semen Yesylevskyy (RUG), Dr Alpesh Malde (UQ), Dr Maria Ratajczak (UQ), Dr Zuo Le (UQ)

Administration: Sophie Turner (UQ)

PhD/Masters Students: Ajinkya Joshi (UQ), Matthew Breeze (UQ), Daniela Mueller (RUG), Ying Xue (RUG), Jelger Risselada (RUG)



GEOFFREY MCLACHLAN



Covers from books to which Professor McLachlan has contributed.

Applied statistics and bioinformatics

My research in applied statistics is in the related fields of classification, cluster and discriminant analyses, data mining, image analysis, intelligent systems, machine learning, neural networks, and pattern recognition, and in the field of statistical inference. The focus in the latter field has been on the theory and applications of finite mixture models and on estimation via the E(expectation)- M(maximization) 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. However, the complexity of tumours makes it likely that a diagnostic test will be based on marker profiles rather than individual markers. But the identification of relevant subsets of the genes has its challenges, because typically thousands of gene expression levels are available from only tens of patients. It means that off-the-shelf methods of statistical analysis cannot be implemented, at least not without serious modifications. Thus, there is a need for new methodologies to be able to process thousands of genes with the aim of finding those genes that are biologically heterogeneous and therefore potential markers for cancer type, treatment therapies, or clinical outcomes.

RESEARCH PROJECTS

- Statistical modelling via finite mixture models, including methods for the detection of differentially expressed genes in different treatment classes or in time-course studies
- Analysing the statistics of microarray gene-expression data for the development of disease diagnostics
- Developing diagnostic methods for cancer, using multiple molecular indices in conjunction with clinical factors
- Developing statistical methodology for the next generation of high-throughput technology with fast sequencing platforms

KEY PUBLICATIONS

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., *et al*. (2008). Clustering. In Bioinformatics, Vol. 2: Structure, Function, and Applications, J.M. Keith (Ed.). Totowa, New Jersey: Humana Press, pp. 423-439.

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

Wu, X., Kumar, V., Quinlan, J.R., Ghosh, J., Yang, Q., Motoda, H., McLachlan, G.J., *et al*. (2008). Top 10 algorithms in data mining. *Knowledge and Information Systems* **14**: 1-37.

Zhu, J.X., McLachlan, G.J., *et al*. (2008). On selection biases with prediction rules formed from gene expression data. *Journal of Statistical Planning and Inference* **38**: 374-386.

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 Officers: Dr Kim-Anh Le Cao, Dr Lloyd Flack

PhD Students: Justin Zhu, Katrina Monico, Leesa Wockner

AFFILIATE APPOINTMENTS









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

PROFESSOR MATT BROWN
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

PROFESSOR IAN FRAZER
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

ASSOCIATE PROFESSOR STUART KELLIE
School of Molecular and Microbial Sciences

PROFESSOR BOSTJAN KOBE
School of Molecular and Microbial Sciences

ASSOCIATE PROFESSOR FRED MEUNIER
Queensland Brain Institute

ASSOCIATE PROFESSOR JOE ROTHNAGEL
School of Molecular and Microbial Sciences

PROFESSOR ISTVAN TOTH
School of Molecular and Microbial Sciences

DR JON WHITEHEAD
Diamantina Institute for Cancer, Immunology and Metabolic Medicine

ASSOCIATE PROFESSOR PAUL YOUNG
School of Molecular and Microbial Sciences

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 fifteen 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 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. During the first five years, IMBcom 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 50 individuals in R&D and commercialisation. These spinouts have gone on to develop strategic relationships in their own right with many other Australian and international biotechnology and pharmaceutical companies, and have encouraged the growth and establishment of service providers, adding to the fabric and critical mass of the industry in Queensland. The companies continue to mature under their own management once substantial investment is raised. IMBcom has 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.

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 with the inclusion of commercial and ethical dimensions. IMBcom delivers this objective through the provision of workshops throughout the training period. 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 Queensland agenda. IMBcom showcases not only the IMB and the University to industry and investment, but also Queensland as an industry destination.

POSTGRADUATE RESEARCH

It has been another productive year for the IMB postgraduate program! Our number of RHD students has stabilised at around 130 students and, again, over 20 students completed their PhD degree in 2008 (for a full list see page 64). An additional 15 students submitted their theses for assessment in 2008 and we are looking forward to a high number of graduations in 2009. 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, in locations such as Europe and the States (for details see page 64). As noted in the previous report, the number of international students within our cohort is growing, with approximately 38 percent of our current students being international students representing 20 different countries! This year we welcomed students from Guatemala, Turkey, Israel and Poland as well as Malaysia, India, France, Denmark, USA, Egypt and Singapore.

The Dean's list for 2007 was announced in the first half of 2008, further verifying that our graduates are producing high-quality research outcomes. Of the 22 students who had their degrees conferred in 2007, eight appeared on the Dean's list, which is particularly impressive as this represents the top 10 percent of theses for any given year. Congratulations must go to Melissa Davis (Teasdale group), Christian Gruber (Craik group), Julita Imperial (Alewood group), David Ireland (Craik group), Jason Kay (Stow group), Marion Loughnan (Lewis group), Ranjala Ratnayake (Capon group) and David Woolford (Hankamer group) for their outstanding theses.

A number of other students also received accolades throughout the year. Some of the highlights are given in table 2 on page 65. Of particular note were the achievements of Ms Maggie Gentz from King group. Mid-year, she was chosen to become a "2008 Young Science Ambassador" by the Australian Academy of Technological Sciences and Engineering and in this role has already visited Rosewood, Cunnamulla and Charleville State High Schools to bring her research to the next generation of young scientists. Together with Michael Tallack (Perkins group), she was chosen as an IMB finalist in the inaugural UQ Graduate School "3 Minute Thesis" competition and together with Caroline Hopkins (Little group) was a "Women in Technology" award finalist for the Griffith Biotech PhD Career Start Award. In July this year she was an Invited speaker at the International Congress on Entomology, Durban, South Africa and in November was an invited speaker at the Entomological Society for America, receiving the Feir Graduate Student Award in Insect Physiology, Biochemistry, or Molecular Biology. In addition, she was instrumental in instigating the IMB Science Ambassadors Program, which will have its pilot year in 2009. Twenty-four Early Career Researchers (ECRs) at IMB have been chosen to take part in the program, which aims to both develop a training program for ECRs to heighten communication skills, useful when dealing with both the media and members of the public, and provide a vehicle for formally acknowledging those young researchers who regularly assist in showcasing the IMB's research to the community. There will be more about this exciting new initiative in the 2009 annual report!

Our honours cohort was again smaller than usual for 2008 and, as with our RHD students, was distributed such that nearly half the students commenced their honours study mid-year. We had 15 students commencing in February 2008, six students who carried over from July 2007 and six others who commenced July 2008.

As in previous years, 80 percent of those students completing their year in 2008 obtained a grade of First class honours. The Amgen Award, for the most outstanding honours student at the IMB in 2007, was presented in 2008 by Ms Bronwyn Shanahan from AMGEN Australia Pty Ltd to Ms Pei Ching Regine Low from Professor Jenny Stow's group. Regine, whose honours project involved establishing and optimising a high-content screening assay for TNF trafficking and secretion in macrophages, completed her honours year in mid-2007 and commenced a PhD in the Stow group later that year. 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 continued the Undergraduate Research Scholarship Scheme (URSS) in 2008, placing 22 second- and third-year students in laboratories within 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 12 students in summer projects of 6-10 weeks duration as part of newly launched UQ Summer Vacation program, which attracted students from as far afield as New Zealand to the IMB. Once again, we 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 throughout Queensland to undertake a brief period of work experience within research laboratories.

Our IMB Student Association, SIMBA, continued to organise a host of social events and bonding exercises, which reinforced our student body's cohesive identity within the institute. These included the SIMBA- and IMBcom-sponsored "Great Debate" which, much to everyone's delight, questioned whether we should "Bring the sexy back into science". The affirmative team, comprising PhD student Rehan Villani and group leaders Professor Glenn King and Dr Matt Sweet narrowly defeated the negative team of PhD student Kate Ewen, group leader Professor Jenny Martin and IMBcom's Zachary King. Many thanks to Andrew Noske (2007 SIMBA secretary) and Dr Peter Isdale (CEO IMBcom) for instigating the debate, which we now hope will become an annual event! Just prior to this, SIMBA ushered in a new Executive at their AGM in July and we welcomed to the helm: Jonathan Robson (President), Rathi Thiagarajan (Vice President), Erin Ahern (Secretary), Lena Constantin (Treasurer), Emily Knauth (SIMBAlize Editor-in-Chief) and Robert McLeay (Webmaster). This Executive continued with the energy of the last, hosting the second annual IMB/AIBN inter-institute Trivia Evening, this year sponsored by Invitrogen (which AIBN won) and providing opportunities to collectively celebrate the Olympics and Halloween. They also became involved with the honours recruitment session held in September, running tours and providing information for prospective students. The IMB Early Career Researcher (ECR) Committee also had a very active year. In addition to running a mentoring afternoon tea in May, they devised and conducted an ECR survey of the IMB research culture and successfully hosted the inaugural IMB ECR Symposium in December. This poster session provided a great opportunity for IMB postdocs and students to showcase their research, fostering further collaborations within the Institute. 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 as part of a new IMB-funded initiative. During 2008, the members of the ECR committee were postdocs Dr Johanna Barclay, Dr Michael Hanzal-Bayer, Dr Mathias Francois, Dr Andrew Brooks, Dr Richa Dave, Dr Karin Kassahn, and PhD students Evan Stephens and Simon Wilkins.

The Postgraduate Program continued to run a set of workshops designed to assist students in overall career development. These included IMBcom's three-day "BioBusiness Retreat" for the third-years, which was held in 2008 from April 2 to April 4 at Noosa Springs Resort, Noosa Heads. Once again, feedback from the retreat was extremely positive, with students really enjoying the mentoring sessions, the networking opportunities and career advice. We ran both a basic and advanced statistics course with Carl Sherwood and re-initiated the Bioethics Workshop for first-years, run by Dr Lucy Carter and Ms Angela Wallace, which this year discussed "Tissue Engineering: some ethical considerations". An information session covering fellowship applications was conducted by our Grants Officer, Michelle Foley, in November, and Bronwyn Adams, our Communications Officer, organised a half-day workshop on communication skills and media training, run by Ms Jan King, the UQ Communications Manager, and her team.

2008 continued to be a time of change for the UQ Graduate School, with the RHD offices initiating further changes in practice, which are set to continue in 2009. One of the biggest changes for 2008 was the move to compulsory electronic thesis submission, a first for an Australian university. Students now lodge their thesis for assessment in electronic form only and the final approved copy, housed by UQ, is also kept in this form (no longer hard copy). Assessors may of course request a hard copy of the thesis for examination, which is supplied by the Theses Office, but the student is no longer required to supply this at any stage during the assessment process. Other noted changes impacted positively on our international students. Due to a change in the way UQ handles international student costs, it has become more straightforward for schools to apply for fee-waiver scholarships (UQIRTA) for those high-calibre students who are in receipt of merit-based stipend scholarships. In the past, because the number of IPRS and UQIRTA scholarships was restricted to a total of 50 university-wide and assigned as part of the annual IPRS round, many gifted students were not funded by this scheme. The ability of a school to apply for an UQIRTA, through a nomination process, has relieved research budgets from the cost of student fees for many of our best students. In addition, as of September 2008, the IPRS/IRTA/UQRS scholarship round became continuous. Students can apply for scholarships at any time throughout the year provided they have an unconditional offer of entry into the RHD program. This is in line with changes made to the APA/UQRS scheme in late 2007. Another major change, which will be incepted in 2009, is the introduction of the Candidature Milestones, which are set to replace annual progress reports. During 2008, after much discussion at the Academic Board's UQ RHD Committee, in which our Postgraduate Coordinator, Professor Rob Capon, took an active role, UQ policies were formulated to cover both the Milestones and RHD recruitment. A letter from SIMBA was lodged with (and well received by) the committee as part of the ongoing debate during the development process. Schools are now developing guidelines defining how the Milestones will best be implemented for their research discipline.

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. Rob's commitment to and vision for the IMB Graduate Program has ensured that it continues to move forward in a proactive and directed way to help deliver to our students the best possible research experience.

TABLE 1: PhD CONFERRALS FOR 2008

Last Name	First Name	Group	Degree	Thesis Title	Where are they now?
Aturaliya	Rajith	Teasdale	PhD	The Subcellular Localisation of Typell Membrane Proteins	Pfizer Animal Genetics, formerly Catapult Genetics Brisbane, Australia
Barry	Grant	Fairlie	PhD	Agonists and Antagonists of Protease Activated Receptor-2 (PAR2)	IMB Fairlie group in 2008, joining patent attorney, Davies, Collison and Cave, Melbourne, in 2009
Beyer	Renee	Fairlie	PhD	Towards Constrained α-Helical Peptides	Australian Institute for Bioengineering & Nanotechnology, UQ, Brisbane, Australia
Blakeney	Jade	Fairlie	PhD	Ligands for C3a and C5a Receptors	Graduate Medical Programme, UQ
Bradford	Stephen	Koopman	PhD	The Regulation and Action of SRY	INSERM U636 Centre de Biochemie, Nice, France
Butterfield	Natalie	Wicking	PhD	Contribution of Patched1 and the Sonic hedgehog pathway to vertebrate limb development	IMB Wicking group in 2008, joining National Institute for Medical Research, London, UK in 2009
Chan	Cheong Xin	Ragan	PhD	Units of genetic transfer in prokaryotes	University of Iowa, Iowa City, U.S.A.
Downes	Meredith	Koopman	PhD	The Role of Sox18 in Blood Vessel Development	School of Health & Rehabilitation Science, UQ, Brisbane, Australia
Fleming	Jennifer	Hall	PhD	Biobanks: professional, donor & public perception of tissue banks & the ethical & legal challenges of consent, linkage & the disclosure of research results	Queensland Health, Centres for Health Research, Princess Alexandra Hospital, Brisbane, Australia
Hartig	Gerald	Smythe	PhD	Drugs for undruggable targets and other impossibilities: the development of molecular scaffolds for more efficient drug design and devleopment	Telecom, Brisbane, Australia
Kurz	Mareike	Martin	PhD	Structural and functional characterization of DsbA homologues from *Wolbachia pipientis*	University of Zürich, Zürich, Switzerland
Lusis	Michael	Little	PhD	Isolation of Stem Cells from Murine Embryonic Kidney	Wilson HTM Investment Group, Brisbane, Australia
Madala	Praveen Kumar	Fairlie	PhD	Computer Aided Drug Design: GPCRs And Proteases	IMB Fairlie group, Brisbane, Australia
Maddugoda	Madhavi	Yap	PhD	The Role of Myosin VI in E-cadherin Adhesive Contact Biogenesis	Mediterranean Research Centre for Molecular Medicine, Nice, France
Pantelic	Radosav	Hankamer	PhD	Enhanced filter algorithms and application of Single Particle Analysis to the study of Ovine atadenovirus	Max-Planck-Institut für Biochemie, Munich, Germany
Pelekanos	Rebecca	Waters	PhD	Determining the Mechanism of Growth Hormone	Mater Medical Research Institute, Brisbane, Australia
Polanco-Barerro	Juan-Carlos	Koopman	PhD	Analysis of SRY and SOX Gene Activities in the Regulation of Testis Formation in the Mouse	IMB Koopman group, Brisbane, Australia
Roberts	Donald	Sturm	PhD	A Melanocyte-Keratinocyte Coculture Model to Study MC1R Dependent Pigmentation Responses	Family business
Simons	Cas	Mattick	PhD	Transposon free regions in vertebrate genomes	The Queensland Facility for Advanced Bioinformatics (QFAB), Brisbane, Australia
Stehbens	Samantha	Yap	PhD	Cadherin-Microtubule Cooperativity	University of California San Francisco, USA
Stephen	Stuart	Mattick	PhD	Ultraconserved Elements and Non-coding RNAs in Mammals	University of California, San Francisco, USA
Trieu	Angela	Sweet	PhD	The Function and Regulation of TLR9	Queensland Institute of Medical Research, Brisbane, Australia
Wang	Bo (Josh)	Stow	PhD	The regulators of E-cadherin trafficking in polarized epithelial cells	Baker IDI Heart and Diabetes Institute, Melbourne, Australia
Wheatley	Nicole	Fairlie	MPhil	Design & Synthesis of HDAC inhibitors derived from α-aminosuberic acid	IMB Fairlie group, Brisbane, Australia
Wooh	Jong Wei	Waters	PhD	The role of the nuclear growth hormone receptor in cell proliferation and tunorigenesis	Australian Institute for Bioengineering & Nanotechnology, UQ, Brisbane, Australia

Table 2: Non-IMB Awards received by PhD Students in 2008

Recipient	Award
Erin Ahern (Hankamer group)	Highly Commended, Postgraduate Student - Science, Smart Women: Smart State Awards
Denis Bauer (Bailey group)	Best Student Paper, Third IAPR International Conference on Pattern Recognition in Bioinformatics
Michelle Christie (Martin group)	UQ Graduate School Research Travel Grants - University of Sydney
Alex Combes (Koopman group)	David Walsh Student Symposium Prize, Combio
Marianne Diaz (Muscat group)	Smart State PhD Top-Up Scholarship
Nyssa Drinkwater (Martin group)	Kansas University & Indianapolis University Purdue University Indianapolis (IU-PUI)
Yen-Hua Crystal Huang (Craik group)	UQ Graduate School Research Travel Grants - University of Southern Denmark
Carol Kistler (Parton group)	Smart State PhD Top-Up Scholarship
Emily Knauth (Hankamer group)	Highly Commended, Postgraduate Student - Science, Smart Women: Smart State Awards
Jane Lattin (Sweet group)	2nd prize, Oral Presentation, Australian Society for Medical Research Queensland Postgraduate Student Conference
Robert McLeay (Bailey group)	Smart State PhD Top-Up Scholarship
Andrew Noske (Marsh group)	Young Investigator Award, Queenstown Molecular Biology Meeting
Elizabeth Skippington (Ragan group)	Smart State PhD Top-Up Scholarship
Dr Amanda Carozzi	IMB Postgraduate Administrative Officer
Conan Wang (Craik group)	UQ Graduate School Research Travel Grants - ISIS, Rutherford Appleton Laboratory, UK

VISITING SPEAKERS

PROFESSOR TED BAKER
University of Auckland, New Zealand
"Crystallography and the world around us"

DR SURESHKUMAR BALASUBRAMANIAN
School of Integrative Biology, The University of Queensland
"Exploiting natural variation to dissect the genetic basis of complex developmental traits"

DR GARY BROOKE
Mater Medical Research Institute, Brisbane
"Mesenchymal stem cells: from bench to clinic"

ASSOCIATE PROFESSOR BERNIE CARROLL
School of Land, Crop and Food Sciences, The University of Queensland
"Intercellular RNA signalling in plants"

DR SHARON CLARK
Australian Institute of Bioengineering and Nanotechnology, The University of Queensland
"Extracellular regulators of mesenchymal stem cell morphology"

PROFESSOR ELIZABETTA DEJANA
University of Milan, Italy
"The role of endothelial cell to cell junctions in the development of the vascular system"

PROFESSOR BEN DUNN
University of Florida, Gainesville, USA
"Global infectious diseases: the potential for protease inhibitors in developing new therapeutics"

PROFESSOR IAN FRAZER FAA
Diamantina Institute for Cancer, Immunology and Metabolic Medicine, The University of Queensland
"Controlling cancer through immunisation: a glass half full?"

PROFESSOR ROBERT FREEDMAN
Warwick University, Coventry, United Kingdom
"Protein disulphide-isomerase – still trying to find how it works!"

DR BRYAN FRY
QEII Research Fellow, Department of Biochemistry and Molecular Biology, Bio21 Institute, Melbourne, Victoria
"Central role for venom in predation by the Komodo Dragon and extinct giant Megalania"

PROFESSOR JOHN FUNDER AO
Prince Henry's Institute of Medical Research, Melbourne, Victoria
"Translational research goes both ways: lessons for basic biology from clinical studies"

DR MAXIMILLIAN FÜRTHAUER
University of Geneva, Switzerland
"Cell division and signaling: a relationship in development"

DR TOMAS GANZ
Department of Medicine, University of California Los Angeles, USA
"Iron is hot: the molecular basis of iron regulation and its disorders"

ASSOCIATE PROFESSOR JOZEF GECZ
Women's and Children's Hospital and University of Adelaide, South Australia
"The genetic landscape of learning and memory: what do we learn from naturally occurring mutations?"

PROFESSOR PAUL GLEESON
Bio21 Institute, University of Melbourne, Victoria
"In and out of the Golgi apparatus: manipulation of membrane trafficking pathways in vivo using RNAi"

DR LUKE GUDDAT
School of Molecular and Microbial Sciences, The University of Queensland
"Branched-Chain amino acid biosynthesis: structural studies"

DR NATASHA HARVEY
Hanson Institute, Adelaide, South Australia
"Defining the signals important for embryonic development of the lymphatic vasculature"

PROFESSOR RICHARD HARVEY
Victor Chang Cardiac Research Institute, Sydney, New South Wales
"Molecular pathways in heart developmental and congenital heart disease"

PROFESSOR JAY HINTON
Norwich Research Park, United Kingdom
"The secret life of salmonella in epithelial cells: unexpected insights from a transcriptomic approach"

DR BEN HOGAN
Hubrecht Institute for Developmental and Stem Cell Biology, Utrecht, The Netherlands
"Embryonic lymphangiogenesis: new insights from zebrafish"

DR PAUL HORTON
Computational Biology Research Centre, Tokyo, Japan
"Mitochondrial beta-signal; the end of the story?"

DR CAI HUANG
Department of Cell and Developmental Biology, University of North Carolina at Chapel Hill, USA
"Talin phosphorylation by Cdk5 regulates Smurf1-mediated talin head ubiquitination and cell migration"

DR MICHAEL J. KELSO
University of Wollongong, New South Wales
"Combating antimicrobial drug resistance – looking to nature for clues"

PROFESSOR LEVON KHACHIGIAN
Centre for Vascular Research, University of New South Wales, Sydney
"Immediate-early genes as master regulators of angiogenic, inflammatory and proliferative disorders"

DR STEPHEN KIDD
School of Molecular and Microbial Sciences, The University of Queensland
"A role in pathogenesis for the transcription factor NmIR: oxidative and nitrosative stress response"

DR BENJAMIN KILE
Walter and Eliza Hall Institute, Melbourne, Victoria
"The molecular regulation of platelet life span"

KATE KOLLAR
Mater Medical Research Institute, Brisbane
"Determining the molecular mechanisms of mesenchymal stem cell homing to acute myocardial infarct"

DR WERNER KÜHLBRANDT
Director, Department of Structural Biology, Max-Planck-Institute of Biophysics, Frankfurt am Main, Germany
"Molecular mechanisms of membrane transport studied by cryo-EM"

PROFESSOR DEBORAH LECKBAND
University of Illinois, Urbana, USA
"Nanomechanics of cell adhesion: single molecules to cell"

ASSOCIATE PROFESSOR JEAN-PIERRE LEVESQUE
Mater Medical Research Institute, Brisbane
"Behaviour of haematopoietic stem cells is governed by their niches"

PROFESSOR ROB LEWIS
Director, Monash Centre for Synchrotron Science, Monash University, Melbourne
"The use and importance of synchrotrons in biomedical research"

PROFESSOR CHRIS MARSHALL
Institute of Cancer Research, Chester Beatty Laboratories, London, UK
"Rho family GTPases, actomyosin contractility and cell migration"

PROFESSOR KLAUS MATTHAEI
John Curtin School of Medical Research, Australian National University, Canberra, Australian Capital Territory
"Genetically manipulated mice: providing all the answers, or just more problems?"

DR JACQUELINE MATTHEWS
University of Sydney, New South Wales
"Out on a LIM: protein interactions in disease and development"

DR BETH MCGRAW
School of Integrative Biology, The University of Queensland
"Beyond the gonads: a broader view of the *Wolbachia* by insect host interaction"

DR ALBERT S. MELLICK
School of Medical Science, Griffith University, Brisbane
"Small non-coding RNAs, bone marrow stem cells and cancer"

PROFESSOR CHRISTINA MITCHELL
Head, Department of Biochemistry, Monash University, Melbourne, Victoria
"Regulation of PI 3-kinase signalling in macrophages"

DR GRANT MONTGOMERY

Queensland Institute of Medical Research, Brisbane

"Genomics and genetic architecture in common complex diseases"

DR ROBERT L. MORITZ

Ludwig Institute for Cancer Research and Walter and Eliza Hall Institute, Melbourne, Victoria

"Utilising a large computing resource for your proteomics research: the Australian Proteomics Computational Facility – using the APCF for biomarker discovery for new diagnostic/prognostic markers for colorectal cancer"

DR ELIZABETH MURCHISON

Australian National University, Canberra, Australian Capital Territory

"Dicing with the devil: small RNAs and genomics in mammals"

and

"piRNAs, miRNAs and siRNAs: small RNA pathways in mammals"

DR SERGE NEF

Department of Genetic Medicine and Development and National Centre of Competence in Research – Frontiers in Genetics, University of Geneva, Switzerland

"Sertoli cell Dicer is essential for spermatogenesis in mice"

DR DAVID NEWMAN

National Cancer Institute, Bethesda, Maryland, USA

"Natural products as biological probes and leads to drugs"

DR TIM NEWSOME

University of Sydney, New South Wales

"Navigating the subcellular space: lessons from vaccina virus"

JULIE NIELSEN

Regional Director, Workplace Health and Safety Queensland

"General workplace safety"

ASIAH OSMAN

Griffith University, Brisbane

"Structure-function studies of annexins in infectious diseases"

DR MARIE-ODILE PARAT

School of Pharmacy, The University of Queensland

"Caveolin-1 in endothelial cell migration and angiogenesis"

DR TEIJA PEURA

Australian Institute for Bioengineering and Nanotechnology, The University of Queensland

"Disease-specific human embryonic stem cell lines obtained by Preimplantation Genetic Diagnosis"

DR MARIA RATAJCZAK

School of Molecular and Microbial Sciences, The University of Queensland

"Keeping cholesterol under control"

DR TONI REVERTER

CSIRO, Brisbane

"Elevated rates of expression and network connectivity among housekeeping and disease-associated tissue-specific genes"

PROFESSOR PHILIP J. ROBINSON

Children's Medical Research Institute, Sydney, New South Wales

"Dynamin's role in synaptic transmission: a target for anti-epileptic drug discovery"

DR PERNILLE RØRTH

Temasek Lifesciences Laboratory, Singapore

"Guiding cell migration: the individual and the collective"

DR JAMIE ROSSJOHN

Monash University, Melbourne, Victoria

"Immune recognition and the Atkins diet"

DR MICHAEL RYAN

La Trobe University, Melbourne, Victoria

"Mitochondria: dynamic protein complexes within a dynamic organelle"

DR RENAE RYAN

Bosch Institute, The University of Sydney, New South Wales

"Structure and function of a glutamate transporter homologue"

ALAN SAWYER

Director, Monash Antibody Technologies Facility, Monash University, Melbourne, Victoria

"Monash Antibody Technology Facility – the development of a high-throughput monoclonals platform"

DR STEFAN SCHULTE-MERKER

Hubrecht Institute, Utrecht, The Netherlands

"Genetic analysis of organ formation in zebrafish"

PROFESSOR MARTIN A. SCHWARZ

University of Virginia, Charlottesville, USA

"Integrins and cancer"

STACY SCOTT

Griffith University, Brisbane

"Two conformations of oxidised human galectin-1 protect against hydrogen peroxide-induced apoptosis of MOLT4 cells"

PROFESSOR LARRY SMARR

Director, California Institute for Telecommunications and Information Technology, San Diego, USA

"Coupling Australia's researchers to the global innovation economy"

PROFESSOR DICK STRUGNELL

The University of Melbourne, Victoria

"Purine metabolism in *Salmonella* pathogenesis"

ASSOCIATE PROFESSOR GILDA TACHEDJIAN

Burnet Institute, Melbourne, Victoria

"HIV reverse transcriptase dimerisation: role in enzyme function and viral replication"

DR STEVEN TAYLOR

Amylin Pharmaceuticals, San Diego, USA

"Mass spectrometry for discovery of peptide-based therapeutics"

DR PAUL THOMAS

School of Molecular and Biomedical Sciences, University of Adelaide, South Australia

"Identifying mechanisms of brain and gonad development using *Sox3* transgenic mice"

PROFESSOR RANJENY THOMAS

Diamantina Institute, The University of Queensland

"Immune deficiency or hyperactivity? NF-kB illuminates autoimmunity"

PROFESSOR WALTER THOMAS

Chair of General Physiology, School of Biomedical Sciences, The University of Queensland

"Complexities in the activation of 7 transmembrane-spanning receptors"

DR PAUL TRAINOR

School of Medicine, University of Kansas, Lawrence, USA

"Making faces: the role of neural crest cells in craniofacial development and congenital birth defects"

DR BRUNO VAN SWINDEREN

Queensland Brain Institute, The University of Queensland

"Attention in the *Drosophila* brain"

DR JONATHAN R. WALLS

Mouse Imaging Centre (MICe), Toronto Center for Phenogenomics, Canada

"Improving optical projection tomography for 3D imaging of the embryonic mouse"

PROFESSOR NEIL WATKINS

Monash Institute of Medical Research, Monash University, Melbourne, Victoria

"Epigenetics and lineage addiction interact with Hedgehog signalling in medulloblastoma"

PROFESSOR EMMA WHITELAW

Queensland Institute of Medical Research, Brisbane

"Epigenetic reprogramming in development"

DR MURRAY WHITELAW

SRC for the Molecular Genetics of Development, University of Adelaide, South Australia

"bHLH/PAS transcription factors: sensors of dioxins, hypoxia and their roles in development and disease"

DR ANDREW WHITTEN

University of Sydney, New South Wales

"Small-angle scattering studies of cardiac myosin binding protein-C: insights into the regulation of muscle contraction"

DR ROHAN WILLIAMS

John Curtin School of Medical Research, Australian National University, Canberra, Australian Capital Territory

"Expression genetics, eQTL and the nature of inter-individual variation in gene expression"

PROFESSOR BOB WILLIAMSON FRCPATH FAA FRS AO

Honorary Senior Principal Fellow, University of Melbourne, Victoria

"Stem cells, cystic fibrosis and why medical research is inherently ethical"

DR ANJA WINTER

Griffith University, Brisbane

"Nature of calcium-binding sites in annexins"

ASSOCIATE PROFESSOR ERNST WOLVETANG

Australian Institute for Bioengineering and Nanotechnology, The University of Queensland

"Elucidating the link between CD30 and genetic stability of hESC"

DR ROBERT YANG

University of New South Wales, Sydney

"Lipotoxicity and lipodystrophy: the role of lipid droplets"

GREG YOUNG

Centre for Clinical Research, The University of Queensland

"Better science and safety while avoiding reinventing the SOP and Risk Assessment Wheel"

XING YU

Griffith University, Gold Coast

"Structural insight into interactions between sialic acid derivatives and porcine rotavirus CRW-8 carbohydrate-recognising domain VP8"

COLLABORATIVE RESEARCH PARTNERSHIPS

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

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

ARC SPECIAL RESEARCH CENTRE FOR FUNCTIONAL AND APPLIED GENOMICS

The ARC Special Research Centre for Functional and Applied Genomics was funded in 2000 to provide and develop technologies that enable world-class research in the field of genomics. An integrated network of core technology units was established and their services have supported the research of local and national researchers and biotechnology companies for the past nine years. Funding for the SRC ended on 31st December 2008 but several of the more established facilities including the Microarray Facility, the Protein Expression Facility, the Biodiscovery Unit, the Mass Spectrometry Facility and TASQ (the Transgenic Animal Service Queensland) will keep operating, allowing researchers continued access to state of the art infrastructure and expertise in these areas.

AUSTRALIAN PHENOMICS FACILITY

The Australian Phenomics Facility (APF) is based at the John Curtin School for Medical Research and is a Major National Research Facility (MNRF) formed by support from the IMB, the Australian National University 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 and 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. 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. The Centre was upgraded to a Centre of Excellence in 2007.

CRC FOR CHRONIC INFLAMMATORY DISEASES

The IMB is a core participant in the CRC for Chronic Inflammatory Diseases (CRC-CID), whose partners are Monash University, The University of Melbourne and AstraZeneca. The major objective of the CRC is to discover new molecular targets involved in the pathogenesis of chronic inflammatory lung and joint disease and use this information to develop novel treatments for these disorders. The CRC is using gene microarrays, proteomics, cell-based assays and genetically-modified animal models of disease to understand how macrophages cause chronic inflammation. The CRC is structured to facilitate the entire drug discovery cycle: primary target identification using functional genomic and proteomic approaches, target validation in disease models and human tissues, high-throughput cell-based assay development, lead target screening, generation of therapeutic and research antibodies, and the development of macrophage-targeted drug delivery strategies.

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 currently serves on the advisory board for 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.

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 MNRF was formed as 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 Biotechnology Centre of Excellence funded by the federal Department of Industry, Innovation and Science and Research and the Australian Research Council and initially created in 2001. While establishing laboratories at Monash University, it has now expanded to create a node of activity at the University of Queensland. The ASCC funds research in both adult and embryonic stem cells, with the long term aim of translating this research to outcomes. The IMB has very close links with the ASCC. Professor Melissa Little was seconded to the ASCC in 2007 as its Chief Scientific Officer, where she was responsible for scientific strategy, scientific review and management. She was also instrumental in the establishment of the Queensland node of the ASCC at the University of Queensland and managed this node until returning to the IMB in late 2008. Funding from the ASCC has supported the work of Associate Professor Andrew Perkins, Associate Professor Sean Grimmond, Dr Rohan Teasdale and Professor Melissa Little. Associate Professor Grimmond's international expertise in expression profiling has enabled ASCC researchers to dissect the genetic hierarchies involved in human ES cell differentiation. This has also been instrumental in the research projects of Professor Martin Pera and Dr Andrew Laslett while dissecting the molecular basis of pluripotency. Associate Professor Sean Grimmond now provides all ASCC-funded researchers with bioinformatics and is applying next-generation sequencing technologies to the analysis of induced pluripotent cells with the support of the Queensland State Government. Professor Melissa Little and Professor Rob Capon have also received leverage from both the ASCC and the Queensland State Government to establish high content screening of embryonic stem cells using the unique chemical compound libraries within the IMB.

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 new 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 also now examine a vast range of proteins at the same time and examine their dynamics in live cells over time.

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. Professor John Mattick has a visiting scientist appointment at RIKEN. The RIKEN Genome Sciences Centre is based at Yokohama and Wako, 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 *Nature Genetics, PLoS Genetics, PLoS Computational Biology, Genome Biology* and *Genomics*.

QUEENSLAND FACILITY FOR ADVANCED BIOINFORMATICS (QFAB)

QFAB was established in 2006 with a $1.9 million Queensland State Government grant and is based at the IMB. 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.

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 remains the main source of information about the Institute for external stakeholders. When 'molecular bioscience' is searched in Google, the IMB is the number one response, a position it has held consistently throughout the past few years. In 2008, the website received over 260,000 visits, resulting in over 1.25 million page views. The IMB website is also a repository for all of IMB's media releases and newsletters. These provide another avenue for disseminating information about the Institute, and during 2008, substantial donations were received to the institute as a result of media coverage.

IMB researchers volunteered at several events organised by UQ throughout the year, notably UQ's Open Day and the Ekka. St Lucia Open Day attracted nearly 16,000 people to the St Lucia campus of the university. IMB staff were on hand to give information to prospective students, and PhD students Rehan Villani (Wainwright group) and Adam Costin (Marsh group) conducted tours of the IMB. An encouraging sign was the fact that tour numbers doubled from the 2007 figures. IMB students also volunteered at the Ekka, or the Royal Brisbane Show as it is officially known, with Denis Bauer (Bailey group), Conor Scully (Fairlie group), Brooke Gardiner (Grimmond group) and Brit Winnen (King group) helping children extract DNA from strawberries at the UQ stand. IMB staff made up 'showbags' for stand visitors to take home, containing IMB merchandise, hand-outs with science activities and information for parents, which proved to be very popular.

Open Day was not the only time that people toured through the IMB. Various interest groups, including primary and high school classes, international university representatives, industry members, dignitaries and politicians came through the facility. IMB welcomes enquiries from groups wishing to tour the Institute; please email imb@imb.uq.edu.au in the first instance.

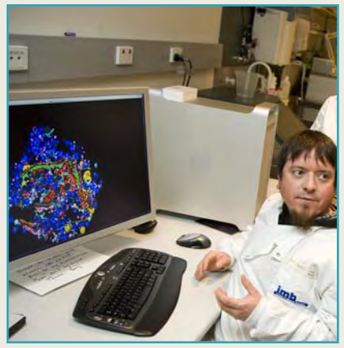
IMB researchers engaged with the community in a number of ways in 2008. Maggie Gentz from the King group was chosen as an Australian Academy of Technological Sciences and Engineering Young Science Ambassador. In this role, she visited Charleville State High School, Cunnamulla State High School and Rosewood State High School, as well as attending a Science-in-Parliament workshop on nanotechnology and speaking at the ATSE Queensland Annual Meeting.

Five IMB scientists participated in the "Scientists in Schools" program, which pairs scientists with teachers and brings real-life science in the classroom. Dr Brad Marsh joined classes at Graceville State School and Richmond State School; Adi Idris went to Wooloowin State School, Dr Horst Schirra teamed with Junction Park State School, Andrew Noske went to Wilston State School and Peter van der Heide partnered with Mansfield State High School.

The Queensland State Government launched a program called 'Talking Scientists' which aimed to link up community groups looking for interesting speakers with scientists. Sixteen IMB researchers signed up for the program, and Professor Brandon Wainwright was asked to give a talk to a Rotary group in Townsville. 2009 should present further opportunities for these scientists to give talks, with Maggie Gentz already scheduled for a talk in Toowoomba.

In the past, IMB has usually engaged with others through existing channels, such as those outlined above, rather than duplicating the efforts of valuable existing programs. However, it was decided in 2008 that the Institute had reached a level of maturity where it would be useful to have its own ambassadors, and to engage proactively with the community. As a result, the IMB Science Ambassadors program was created.

Science Ambassadors will receive training in media and community engagement, and will serve the IMB in a number of ways, for example, participating in outreach activities, taking tours, supervising work experience students and creating educational resources. The pilot cohort of ambassadors will also help shape the program, and make suggestions on how it can be developed in the future. Applications were called for late in 2008 and the first cohort of 24 early career researchers has been chosen. They will begin training early in 2009, and their activities and achievements will be outlined in next year's report.



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Yee Chng
Undergraduate Student


Kwang-Jin Cho
PhD Student


Jooyoung Choi
PhD Student


Angelika Christ
Research Assistant


Michelle Christie
PhD Student


Peifei Chu
Undergraduate Student


Han Chui
Research Assistant


Michael Clark
PhD Student


Richard Clark
Research Officer

Nicole Cloonan
Research Officer

Barb Clyde
HR Consultant

Nadine Coleman
Personal Assistant

Brett Collins
Group Leader

Kelly Collins
Undergraduate Student

Alex Combes
PhD Student

Lena Constantin
PhD Student

Melissa Conte
Research Assistant

Anthony Cook
Research Officer

Ashley Cooper
Research Assistant

Elaine Costelloe
Research Officer

Adam Costin
PhD Student

Hayley Cox
Honours Student

David Craik
Group Leader

Robyn Craik
Purchasing Officer

Matthew Crampton
Research Officer

Simon Cridland
PhD Student

Larry Croft
Research Officer

Stephen Cronau
Research Assistant

Lisa Crowther
PhD Student

Rebecca Cuskelly
Undergraduate Student

Matt Daley
PhD Student

Kristian Dalle
Undergraduate Student

Norelle Daly
Research Officer

Vinh Dang
Honours Student

Aline Dantas
Research Officer

Aaron Darling
Research Officer

Richa Dave
Research Officer

Tara Davidson
Research Assistant

Jasmine Davis
Research Assistant

Melissa Davis
Research Officer

Zoltan Dekan
Research Assistant

Christian de Marco
Computer Systems Officer

Nicole den Elzen
Research Officer

Marion Desclozeaux
Research Officer

Marcel Dinger
Research Officer

Ross Dixon
Level 3 Floor Manager

Cedric Dooms
Research Officer

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Undergraduate Student

Meredith Downes
PhD Student

Nyssa Drinkwater
PhD Student

Russell Driver
PhD Student

Jaimee Duncan
Research Assistant

Jasmine Dunn
Research Assistant

Tom Durek
Research Officer

Alysha Elliot
Research Assistant

Tammy Ellis
Senior Research Officer

Mohamed El-Naggar
PhD Student

Pei Er
Research Assistant

Natalie Eriksson
Research Assistant

Andrés Esteban-Marcos
Honours Student

Calvin Evans
Computer Systems Officer

Katherine Ewen
PhD Student

Henk Faber
Technical Officer

David Fairlie
Group Leader

Diana Farkas
PhD Student

Geoff Faulkner
PhD Student

Barbara Feenstra
Office Manager

Manuel Fernandez
Research Officer

Selene Fernandez Valverde
PhD Student

Allen Feng
Research Assistant

Charles Ferguson
Research Assistant

Joao Fidalgo
PhD Student

Rebecca Fitzsimmons
Research Assistant

Michelle Foley
Grants Officer

Frank Fontaine
Research Officer

Alex Foo
PhD Student

Mathias Francois
Research Officer


Martina Franke
Research Assistant


Leith Fremlin
PhD Student


Jessica Frith
Research Officer


Janette Galea
Research Assistant


Nira Gamage
Research Officer


Patricia Garcia
Honours Student


Brooke Gardiner
Research Officer


Angela Gardner
Finance Manager


Susan Garner
Administrative Assistant


Katrina Garner-Moore
Purchasing Officer


Margaret Gentz
PhD Student


Kylie Georgas
Research Assistant


Rajesh Ghai
Masters Student


Anne Gisik
Honours Student


Felicia Goh
PhD Student


Mei Goh
Administration Assistant


Caraine Gomez
HR Officer


Milena Gongora
Research Assistant


Sandy Gonzalez
PhD Student


Andy Goodall
PhD Student


Dominique Gorse
QFAB Technical Manager


Hareshwar Goswarmi
Masters Student


Jenny Greder
Marketing Manager


Kathryn Greenwood
PhD Student


Aliesha Griffin
Research Assistant


Sean Grimmond
Group Leader


Rowan Gronlund
IT Support Manager


Christian Gruber
PhD Student


Sunithi Gunasekara
PhD Student


Mercy Gunnampaty
Masters Student


Adi Haji Idris
PhD Student


Elaine Haase
PhD Student


Reena Halai
PhD Student


Maria Halili
PhD Student


Johan Hamidon
Undergraduate Student


Nick Hamilton
Group Leader


Luke Hammond
Research Assistant


Nor Hana Hamzah
Undergraduate Student


Pei'e Han
Honours Student


John Hancock
Group Leader

Rachel Hancock
Research Assistant

Ben Hankamer
Group Leader

Dhiraj Hans
PhD Student

Martin Hansen
Research Officer

Michael Hanzal-Bayer
Research Officer

Lani Hardy
Research Assistant

Britney Harrington
Student

Rose Harrison
PhD Student

Gerald Hartig
Research Assistant

John Hawkins
Research Officer

Andrew Hayes
Research Officer

Traci Holland
Finance Officer

Caroline Hopkins
PhD Student

Sonia Henriques
Research Officer

Begoña Heras
Senior Research Officer

Monika Hermann
International Occupational Trainee

Volker Herzig
Research Officer

Michelle Hill
Research Officer

Tim Hill
Research Officer

Ondrej Hlinka
Computer Systems Officer

Rena Hirani
Research Officer

Uda Ho
PhD Student

Huy Hoang
Research Officer

John Holland
Senior Research Officer

Brett Hosking
Research Officer

Gail Howard
Receptionist

Mark Howes
PhD Student

Shu-Hong Hu
Senior Research Officer

Crystal Yen-Hua Huang
PhD Student

Nigel Hughes
Technical Officer

Kinitra Hutchinson
Undergraduate Student

Rikki Hvorup
Research Officer

Kerry Inder
Research Officer

Jess Ineson
Research Assistant

Marco Inserra
PhD Student

David Ireland
PhD Student

Kate Irvine
Research Officer

Kasturee Jagirdar
Student

Russell Jarrott
Research Assistant

Angela Jeanes
PhD Student

Jonas Jensen
PhD Student

Jean Jin
Research Assistant

Helene Johanson
PhD Student

Kenneth Johanson
International Occupational Trainee

James Johnson
Honours Student

Chol Hee Jung
PhD Student

Quenkin Kaas
Research Officer

Rhonda Kan
PhD Student

Seetha Karunaratne
Research Assistant

Ken-ichi Kashimada
Research Officer

Karin Kassahn
Research Officer

Jay Kay
Research Officer

Greg Kelly
Lab Manager

Linda Kerr
Research Assistant

Markus Kerr
Research Officer

Tatiana Khromykh
Research Assistant

Glenn King
Group Leader

Gordon King
Research Officer

Andrew Kinghorn
Honours Student

Wayne Kirby
Technical Officer

Luke Kirkwood
PhD Student

Carol Kistler
PhD Student

Emily Knauth
PhD Student

Deon Knight
Research Assistant

Malte Kock
Masters Student

Gabriel Kolle
Research Officer

Peter Koopman
Group Leader

Darren Korbie
PhD Student


Eva Kovacs
Research Officer


Oleksiy Kovtun
PhD Student


Soumya Krishna Moorthy
Undergraduate Student


Jeremy Kroes
Workshop Manager


Marta Kubala
PhD Student


Elizabeth Kuczek
Project Manager


Lars Kuerschner
Research Officer


Christina Kulis
PhD Student


Krzysztof Kurowski
Research Officer


Mareike Kurz
PhD Student


Larisa Labzin
Research Assistant


Michael Landsberg
Research Officer


Annette Lane
Research Assistant


Ian Lane
Level 7 Floor Manager


Catherine Latham
Research Officer


Jane Lattin
PhD Student


Patrick Lau
Research Officer


Nicole Lawrence
Senior Research Officer


Angela Lawton
Senior Research Assistant


Stephanie Le
Honours Student


Paul Leo
Senior Research Officer


Gary Leong
Senior Research Officer


Emmanuelle Lesieur
Research Assistant


Richard Lewis
Group Leader


Joan Li
Research Officer


Junxian Lim
Honours Student


Wen Lim
Student


Fredrik Lindahl
Research Officer


Melissa Little
Group Leader


Fawang Liu
Research Officer


Ligong Liu
Senior Research Officer


Yan Yan Liu
Student


Harriet Lo
Research Officer


Rink-Jan Lohman
Research Officer


Lindsey Long
Research Assistant


Dorothy Loo
Research Assistant


Reik Löser
Research Officer


Marion Loughnan
Research Officer


Pei Ching (Regine) Low
PhD Student


Andrew Lucke
Research Officer

Robert Luetterforst
Research Assistant

Philip Machanick
Research Officer

Shev MacNamara
Research Officer

Praveen Madala
Research Officer

Stefan Maetschke
Research Officer

Jodie Major
Research Assistant

Igor Makunin
Research Officer

Uru Malik
Masters Student

Lorenzo Malquori
Research Officer

Sabine Mangold
PhD Student

Stratios Manolis
Store Manger

Nelson Marques
Computer Systems Officer

Brad Marsh
Group Leader

Mhairi Marshall
Data Grid Developer

Nick Martel
Research Assistant

Jenny Martin
Group Leader

Sally Martin
Senior Research Officer

Ute Marx
Research Officer

Mark Matthew
Honours Student

John Mattick
Group Leader

Erin Maylin
Research Assistant

Emily McCallum
Research Assistant

Tim McComb
Research Officer

Ailsa McCormack
Research Assistant

Karen McCue
Research Officer

Nicole McDonald
Receptionist

Lindsay McFarlane
PhD Student

Crystal McGirr
Research Assistant

Greg McHugh
Workshop Manager

Robert McLachlan
PhD Student

Robert Mcleay
PhD Student

Tim McPhee
Research Officer

Jeremy Mead
Store Person

Tim Mercer
PhD Student

Vicki Metzis
PhD Student

Tomas Miljenovic
Undergraduate Intern

Ryo Misaki
Research Officer

Mehdi Mobli
Senior Research Officer

Seha Mohammed Suhaimi
Research Assistant

Linda Molloy
Glassware Attendant

Marion Monet
Research Assistant

Rod Morales
PhD Student

Garry Morgan
Research Assistant

David Morgenstern
PhD Student

Isabel Morrow
Research Officer

Duncan Mortimer
PhD Student

Cody Mudgway
Executive Secretary

Sergey Mureev
Research Officer

Craig Murphy
Senior Research Officer

Samantha Murphy
PhD Student

Arief Mulyadi
Research Assistant

Teresa Munchow
Research Assistant

George Muscat
Group Leader

Markus Muttenthaler
PhD Student

Stephen Myers
Research Officer

Joshua Mylne
Research Officer

Satu Nakhuri
PhD Student

Charles Nelson
Safety Officer

Michelle Newman
Level 2 Floor Manager

Christine Neyt
Research Officer

Ee Ting Ng
Research Assistant

Philip Nguyencong
PhD Student

Susan Nixon
Research Officer

Suzanne Norwood
Research Officer

Andrew Noske
PhD Student

Ehsan Nourbkash
Research Officer

Ryan Nugent
Research Assistant

Harald Oey
Research Officer


Carolin Offenhauser
PhD Student


Satomi Okano
Research Assistant


Basar Oku
PhD Student


Julie Osborne
Administrative Officer


Dmitry Ovchinnikov
Research Officer


Steven Pace
Masters Student


Fil Paczkowski
Research Officer


James Palmer
Research Officer


Timothy Pan
PhD Student


Ajay Panwar
Masters Student


Rob Parton
Group Leader


Darren Paul
Microscopy and Laser Safety Officer


Michael Pearen
PhD Student


John Pell
Technical Officer


David Pennisi
Research Officer


Andrew Perkins
Group Leader


Allison Pettit
Research Officer


Michael Pheasant
Research Officer


Reynold Phillips
Undergraduate Student


Yu Leng Phua
Student


Andrew Piggott
Research Officer


Barry Pitt
Store Manager


Tilman Plass
Masters Student


Fabien Plisson
PhD Student


Sarah Plowman
Research Officer


Juan Carlos Polanco
Research Officer


Martin Poms
Masters Student


Aaron Poth
PhD Student


Neelima Pottekkat Sidharthan
Research Officer


Rosanna Quinlivan
Purchasing Officer


Imre Radacs
Technical Officer


Fiona Rae
Research Officer


James Rae
Research Assistant


Chikako Ragan
Scientific Programmer


Mark Ragan
Group Leader


Liza-Jane Raggatt
Research Officer


Lotten Ragnarsson-McGrath
Research Officer


Suryaprakash Raichur
PhD Student


Virajitha Rajagopalan
Masters Student


Sathiya Ramakrishnan
PhD Student

Divya Ramnath
Student

Darshani Rapasinghe
Undergraduate Intern

Lachlan Rash
Research Officer

Lance Rathbone
Database Manager

Felicity Ray
HR Consultant

Esther Reefman
Research Officer

Robert Reid
Senior Research Officer

Gang Albert Ren
Research Officer

Stewart Rice
Technical Officer

Tobias Richter
Research Officer

Drew Ringsmuth
PhD Student

Raju Ritesh
PhD Student

Don Roberts
Research Officer

Alan Robertson
Honours Student

Gautier Robin
Research Officer

Jonathan Robson
PhD Student

Leigh Rose
General Hand

Ian Ross
Research Officer

Rosalba Rothnagel
Research Assistant

Susan Rowland
Senior Research Officer

Sandrine Roy
Research Officer

Kelin Ru
Senior Research Assistant

Gloria Ruiz-Gómez
Research Officer

Bree Rumballe
Research Assistant

Natalie Saez
PhD Student

Angela Salim
Research Officer

Daniele Sangermani
PhD Student

Nicole Schieber
Research Assistant

Horst Schirra
Research Officer

Veronika Schreiber
Research Assistant

Kate Schroder
Research Officer

Conor Scully
Research Officer

Shoaib Sehgal
Research Officer

Vernon Seow
Honours Student

Radha Seshadri
Masters Student

Nausad Shaikh
Masters Student

Desla Shand
Administrative Assistant

Erin Shand
Mailroom Clerk

Daniel Shaw
PhD Student

Chang Jin Shin
PhD Student

Stephen Shouldice
Research Officer

Cas Simons
PhD Student

Shane Simonsen
Research Assistant

Fiona Simpson
Senior Research Officer

Ranee Singh
PhD Student

Elizabeth Skippington
PhD Student

Darren Smit
Research Assistant

Aaron Smith
Research Officer

Jen Smith
PhD Student

Mark Smith
Finance Officer

Martin Smith
PhD Student

Phillipa Smith
PhD Student

Michael Smutny
Research Officer

Mark Smythe
Group Leader

James Sokolich
Intern

Lisbeth Sorum
Masters Student

Cassy Spiller
PhD Student

Josefine Sprenger
PhD Student

James Springfield
Microscopy Technology Facility Manager

Kate Stacey
Senior Research Officer

Stuart Stephen
PhD Student

Evan Stephens
PhD Student

Anite Steptoe
Senior Research Assistant

Martin Stoermer
Senior Research Officer

Jenny Stow
Group Leader

Caroline Sturm
Research Assistant

Rick Sturm
Group Leader

Jacky Suen
PhD Student

Mitchell Sullivan
Undergraduate Intern

Tim Sullivan
Visible Cell Project Officer

Terje Svingen
Research Officer

Matt Sweet
Group Leader

Ryan Taft
PhD Student

Tom Taguchi
Senior Research Officer

Michael Tallack
PhD Student

Chia-Chia Tan
Research Assistant

Ian Taylor
Deputy Director (Systems & Administration)

Rohan Teasdale
Group Leader

Ernest Tee
Undergraduate Student

Simon Teng
Student

Hong Wai Tham
Honours Student

Rathi Thiagarjan
Masters Student

Louise Thorstholm
PhD Student

Amy Thurber
Research Assistant

Matthew Timmins
PhD Student

Zakir Tnimov
PhD Student

Anne Tobin
Level 5 Floor Manager

Liam Town
PhD Student

Vy Truong
Research Assistant

Kathryn Tunny
Research Assistant

Ronda Turk
Receptionist

Jill Turner
Research Assistant

Lang Valentine
Computer Systems Officer

Peter van der Heide
PhD Student

Rebekka van Kampen
Administrative Assistant

Wendy van Zuylen
PhD Student

Juliana Venturato
Research Assistant

Suzie Verma
Research Assistant

Andrea Vernal
Research Officer

Irina Vetter
Research Officer

Soumini Vijayasarathy
PhD Student

Rehan Villani
PhD Student

Simone Vink
PhD Student

Nicola Waddell
Research Officer

Kimberly Wadsworth
PhD Student

Brandon Wainwright
Director

Elanor Wainwright
Honours Student

Logan Walker
Research Officer

Piers Walser
Research Officer

Dawn Walsh
Central Sterilising Facility Manager

Anderson Wang
Research Officer

Conan Wang
PhD Student

Jack Wang
PhD Student

Mary Wang
Research Officer

Shivangi Wani
Research Assistant

Mike Waters
Group Leader

Winne Waudo
PhD Student

Jane Weber
Level 6 Floor Manager

Jan Westermann
Research Officer

Nicole Wheatley
Masters Student

Tom Whitington
PhD Student

Carol Wicking
Group Leader

Dagmar Wilhelm
Group Leader

Simon Wilkins
PhD Student

Lorine Wilkinson
Research Officer

Danielle Wilson
Research Assistant

David Wilson
Research Officer

Josh Wingerd
PhD Student

Brit Winnen
Research Officer

Lanna Wong
Manager, ARC Centre of Excellence in Bioinformatics

Shu Shyan Wong
Research Officer

David Wood
Visible Cell

Stephanie Wood
PhD Student

Chung-Wei (Jimmy) Wu
Computer Systems Officer

Fiona Wylie
Research Co-ordinator

Aijun Yang
Research Officer

Alpha Yap
Group Leader

Peter Yee
PhD Student

Karen Yong
Undergraduate Student

Zheng Yuan
Senior Research Officer

Wai Shan Yuen
Hnoours Student

Hua Zhang
Research Officer

Jenny Zhang
Research Officer

Catherine Benham
Administration Assistant

Lisa Black
Marketing & Events Coordinator

Kellie Broderick
Manager, Infrastructure and Education

Kelly Coomber
Company Accountant

Leah Creed
General Counsel

Ujjwal Dua
Commercialisation Officer

Paul Ellender
Marketing & Events Coordinator

Noi Inthasan
IP & Operations Support

Peter Isdale
Chief Executive Officer

Zachary King
Commercialisation Officer

Andrew Leech
IP Associate

Bridget Maher
Commercialisation Officer

Emma McComb
IP Associate

Jodie McNab
Company Accountant

Lyn Rosen
Executive Assistant

Chris Price
Vice President, Commercial Development

Amanda Smith
Manager, IP & Development

Karen Soxsmith
Systems Administrator

Erin Wansbrough
Business Development Manager

Charlie Widberg
Commercialisation Officer

IMBcom

FINANCIAL STATEMENTS

Statement of Operating Income and Expenditure – Year ended 31 December 2008

INCOME:	NOTE	2004	2005	2006	2007	2008
University of Queensland (Operating Grant)	1	6,877,099	7,225,765	10,767,311	11,087,942	11,062,918
University of Queensland Research Grants		228,999	334,500	252,252	300,436	190,291
State Government		10,000,000	10,425,000	10,175,000	11,127,168	10,857,620
Src Grant (Australian Research Council)		1,117,038	1,137,436	1,159,047	1,182,516	1,206,166
Australian Research Council	2	4,261,849	4,744,519	5,218,279	6,010,239	5,977,542
Arthritis Foundation Of Australia		0	14,950	0	0	0
Australian Cancer Research Foundation		600,000	600,000	0	0	0
Australian Nuclear Science & Technology Organisation		0	85,355	78,757	230,492	61,326
Australian Stem Cell Centre		306,219	161,691	159,780	467,335	770,065
Cancer Council South Australia		30,500	0	0	0	0
Clive and Vera Ramaciotti Foundation		0	0	0	60,000	30,000
Community Health + Tuberculosis Australia		0	0	49,000	0	0
CRC for Discovery of Genes for Common Human Diseases		0	0	0	0	
CRC for Chronic Inflammatory Diseases		1,261,017	1,367,457	1,326,058	1,462,776	1,214,510
CRC for Pest Animal Control		0	0	122,210	0	47,952
Dairy Australia		338,779	203,765	167,644	700,321	333,084
Department Industry Science & Resources		0	0	0	200,000	135,000
Department of Primary Industries		0	0	0	50,000	0
Diabetes Australia Research Trust		0	0	45,000	0	50,008
Department of Industry Science and Technology		0	0	0		
Human Frontiers Science Program		138,057	0	0	81,783	58,180
Glaxo Welcome Australia		0	0	0		
Government Employees Medical Research Fund		0	0	0		
Japanese Science & Technology Agency		0	0	0	0	106,462
The John Trivett Foundation		0	0	0	267,817	0
Juvenile Diabetes Foundation International		151,732	177,814	178,634	147,708	110,723
Mayne Bequest Foundation		0	0	0	0	
The Merck Genome Research Institute		0	0	0	0	
The Mazda Foundation		0	0	0	0	150,000
The Murdoch Institute		0	0	0	347,527	235,515
National Institute of Health (US)		1,475,684	1,132,358	1,176,642	969,415	561,829
National Health and Medical Research Council	2	6,438,350	9,819,880	7,888,967	11,054,142	12,445,955
National Heart Foundation		50,000	50,000	0	0	65,800
New Zealand Dept Science & Technology		0	0	0	81,392	40,738
Novartis		0	0	0	0	
Post Graduate Scholarships		91,968	140,237	261,263	305,255	234,520
QIMR		0	0	0	0	
Queensland Cancer Fund		140,000	215,100	148,700	312,000	554,000
Sylvia and Charles Viertel Charitable Foundation		0	0	0	0	
Wellcome Trust		180,706	150,311	0	0	0
Commercial Income		1,473,905	1,856,012	2,018,054	4,880,234	4,585,955
Cross-institutional Contributions to Lief or Facilities		192,800	60,000	509,472	188,000	50,000
University of Newcastle (Re Arc Centre)		127,893	47,727	252,562	128,218	153,218
QBP Recoveries		312,979	316,211	386,092	371,257	363,065
Shared Grants		128,764	262,062	234,685	4,000	40,772
Conference Income		25,501	73,032	66,615	184,340	70,558
QBPstore		44,021	247,890	276,819	314,057	326,215
Wesley Research Institute		0	0	20,000	93,645	98,423
Miscellaneous Income		355,652	416,707	399,887	357,293	391,776
TOTAL INCOME:		**36,349,512**	**41,265,778**	**43,338,729**	**52,967,307**	**52,580,186**
Funds brought forward from previous year	3	6,746,999	6,557,150	9,050,612	11,441,270	15,641,004
TOTAL FUNDS AVAILABLE		**43,096,511**	**47,822,929**	**52,389,341**	**64,408,577**	**68,221,189**
EXPENDITURE:						
Salaries -Research		16,195,354	18,430,158	20,110,376	22,878,237	24,750,517
-Administration		1,243,375	1,343,782	1,205,466	1,349,056	1,345,709
-Infrastructure		2,131,608	2,383,622	2,673,620	2,368,795	2,862,623
Research Services		7,667,863	9,976,365	10,995,871	13,099,865	13,091,734
Education Programs	4	418,784	375,177	358,445	332,919	380,733
Administration	5	383,224	379,317	529,612	521,743	496,666
Corporate Services (UQ)	1	0	0	0	0	
Infrastructure	6	1,772,942	1,287,442	1,295,139	1,862,212	2,160,052
Capital Equipment	7	5,521,066	3,389,715	2,569,801	5,156,825	3,438,525
IMBcom		1,205,144	1,206,738	1,209,741	1,197,920	1,198,528
TOTAL EXPENDITURE:		**36,539,360**	**38,772,316**	**40,948,071**	**48,767,573**	**49,725,426**
Funds carried forward:	**8**	**6,557,150**	**9,050,612**	**11,441,270**	**15,641,004**	**18,495,763**

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

B) GROSS INCOME & CORPORATE SERVICES CHARGE

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

2/ FELLOWSHIP/PROJECTS FROM GOVERNMENT AGENCIES

Australian Research Council	
Projects	4,830,361
Fellowships	1,147,181
	5,977,542
National Health and Medical Research Council	
Projects	10,243,979
Fellowships	2,201,977
	12,445,955

3/ FUNDS CARRIED FORWARD TO 2008

University of Queensland Operating Grant	7,468,461
University of Queensland Research Grants	53,647
Post Graduate Scholarships	84,768
State Government	3,036,824
SRC Grant	-292,297
Fellowships (as approved by funding bodies)	541,148
Overseas Grants funded mid year	294,675
Contract Research	2,639,402
Project Grants (as approved by funding) bodies)	1,814,376
	15,641,004

4/ EDUCATION PROGRAMS

Postgraduate scholarships	303,623
Postgraduate recruitment and training	77,110
Total Education Services	**380,733**

5/ ADMINISTRATION

Annual Report	9,720
Marketing	48,954
Personnel Recruitment and Training	74,824
Visiting Scientists/Seminars	36,293
Fees	9,499
Quinquennial Review	-
Entertaining	50,555
Photocopying	114,879
Postage and Freight	7,247
Printing and stationery	38,454
Telephone	65,482
Travel Expenses	15,521
Board Fees	25,240
Total Administration	**496,666**

6/ INFRASTRUCTURE

Building Maintenance	189,656
Rental -Storage	8,085
Safety Equipment	55,824
Laundry	4,552
Minor Equipment & Furniture	28,752
Equipment Maintenance	307,481
Animals	281,366
Computer Services	577,507
Glass washing and replacement	50,344
Reticulated gases, RO water and dry ice	54,306
Cost Recovery	-140,623
Stores	742,802
Total Infrastructure	**2,160,052**

7/ CAPITAL EQUIPMENT

Scientific Equipment	2,655,867
Minor Equipment	782,658
Total Capital Equipment	**3,438,525**

8/ 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
	18,495,763

Of this, $1.8m is the carry forward on IMB Group Leader core accounts & $0.7m relates to oustanding 2008 equipment commitments. There is also a significant committment regarding orders placed in 2008 whose payment has timeshifted into 2009 due to the introduction of a new financial system. This is also the reason for the significantly higher activity in 2008 through Stores.

GLOSSARY OF TERMS

Ab initio A calculation made from 'first principles', rather than experimental data.

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

Actin Nucleators Proteins that increase the rate of growth of actin fibrils.

Adipose Fat or fatty tissue.

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.

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

Antihelminthics Anything that rids the body of parasitic intestinal worms.

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

Apoptosis Programmed cell death.

ARC Australian Research Council.

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

Atherosclerosis The process whereby arteries harden and narrow over time.

Bioinformatics The collection, organisation and analysis of large amounts of biological data using networks of computers and databases.

Bilayer Two layers of molecules.

Bioactive Has an effect on a living organism.

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

Biomimetic synthesis An artificial process for synthesising chemicals that is inspired by biochemical processes.

Bioscience Any of the branches of science dealing with the structure and behaviour of 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, which ensure cells adhere to one another within a tissue.

Caveolae A small pocket extending from the outside to the inside of a cell. Sites of uptake and expulsion of materials into and out of the cell.

Cephalopod Organisms in the class Cephalopoda, which includes octopus and cuttlefish.

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

Chelate An organic molecule that has bonded to a metal to form a ring-shaped structure.

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.

Clathrin The protein that largely forms the vesicle responsible for transportation of proteins into and out of the cell.

CNS Central Nervous System

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

Conopeptide Peptides found in the marine cone snail.

Conotoxin A group of toxic peptides isolated from the venom of the marine cone snail.

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.

Cytotoxin A toxin harmful to cells.

De novo Not previously present.

Dendrites Branches of a neuron cell that receive nerve impulses from other neurons.

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

Diabetes A disease that occurs when the body cannot produce or cannot use insulin, which regulates blood sugar levels.

Differentiation The process of specialisation from a general precursor cell into a cell with a specific role.

Dimer An organic molecule formed by combining two smaller molecules.

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.

Electrolyte The dissolved form of a mineral, capable of conducting an electrical current. Helps regulate the proper balance of body fluids.

Electron tomography A method of obtaining a 3D image using an electron microscope.

Embryogenesis The development of an embryo.

Endocytosis Uptake of material into a cell.

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.

Epidermis The outer layer of skin.

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.

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.

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.

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.

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.

Glucose A six-carbon sugar that is a major energy source for the body.

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

Gram-positive Bacteria that have a single cell wall; many species are pathogenic.

GTPase A large family of enzymes that can bind and break down GTP, a type of nucleotide. GTPase is involved in a number of processes, including translation, transport, signal transduction and cell division.

Haemoglobin A protein in red blood cells that carries oxygen around the body.

Heterodimer An organic molecule formed by combining two smaller, different molecules.

Heterogeneous Comprised of more than one type of element.

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

Homeodomain A protein motif in a homeobox (a highly-conserved DNA sequence) found in genes that regulate embryo development.

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

Homology Similarity due to common ancestry.

Homozygous Refers to a gene in which both copies of an allele are the same.

Hyperplasia The multiplication of cells beyond that which is normal.

Icosahedron A structure with twenty equal faces.

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

In silico A process that has been simulated on a computer.

In situ In its natural place.

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

In vivo A process occurring within an organism.

Insulin A hormone that regulates sugar concentration in the blood.

Ion Channels Proteins that act as gates in order to control the flow of ions across cellular membranes.

Islet Clusters of cells in the pancreas that secrete insulin.

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.

Locus The location of a gene on a chromosome.

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.

Mass spectrometry A method of studying the structure and composition of molecules.

Mechanosensitive channels Proteins in the membrane that open and close in response to mechanical force.

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

Melanoblast Precursor of a melanocyte.

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

Melanogenesis The production of 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.

Metabolomic Relating to all of the metabolites in a sample at any given time.

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.

Microtubules Tiny tubes found in most cells.

Mimetics A molecule with similar effects to the molecule under consideration.

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

Morphogenesis The process where cells differentiate into different structures.

Motif A repeating element.

mRNA Messenger RNA. Contains the information on how to make a protein, and takes it from the genes in DNA to the site of protein synthesis.

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

Mutant A gene or an organism that has experienced a mutation (a change in its genetic sequence).

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

Nanovesicles Small, dense vesicles.

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.

Nucleic Acid A molecule consisting of a chain of organic molecules that are sequenced with one another to create genetic information.

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.

Oncoprotein A protein involved in the formation and growth of tumours.

Organelle A discrete subcellular structure with a specialised function.

Orthologous Any gene found in more than one species that can be traced back to the same common ancestor.

Osteoclast A large, multinuclear cell involved with the absorption and removal of bone.

Paralogous Two genetic sequences that have the same evolutionary ancestor and arose through gene duplication.

Pathogen A disease-causing organism.

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.

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.

Phosphatase An enzyme that removes a molecule containing phosphorous acid from a nucleic acid or protein.

Phosphoregulators All mouse protein kinase and phosphatase genes.

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.

Polymer A large molecule consisting of repeated subunits.

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.

Proteome The complete set of proteins being expressed at any one time by a cell, tissue or organism.

Quantitative An attribute that is clearly measurable.

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

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

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.

Scission Splitting.

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

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.

Stochastic A process that is governed by random chance.

Teleosts A class of bony vertebrate fish.

Tomography The process of creating a series of detailed pictures of areas inside the body, created by a computer linked to an X-ray machine.

Transcription The formation of RNA from a DNA template.

Transcriptome All of the messenger RNA transcribed from genes within a given genome.

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

Triplex Consisting of three parts.

Tumorigenesis The formation of a tumour.

Upregulated When the production of a substance, or the rate of a process, is increased.

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

Vesicle A closed membrane shell.

Zinc finger A DNA-binding protein domain in which the zinc ion is crucial.

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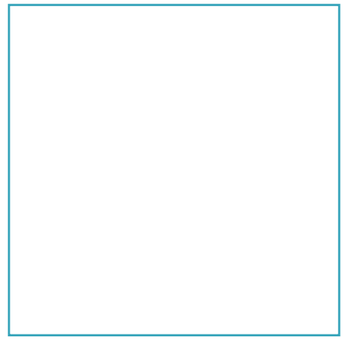

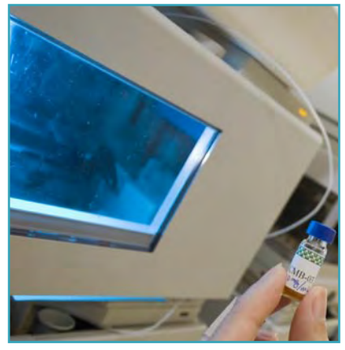

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