Creativity, motivation and intellectual freedom are the vital components of scientific discovery and technological progress, 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 our 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.

"Cubist Crystal" by Jenny Martin is one of a series of prints available for purchase from the IMB's Angstrom Art Series. Prints can be ordered online at www.imb.uq.edu.au

Contents

The IMB acknowledges and thanks our supporters and partners.

Queensland Government

Australian Cancer Research Foundation

Cooperative Research Centre for Chronic Inflammatory Diseases

National Institutes of Health

Australian Government
National Health and Medical Research Council

Australian Government
Australian Research Council

1.

Professor John Hay AC

CHAIR'S MESSAGE

I am delighted with the progress and achievements of The University of Queensland's Institute for Molecular Bioscience (IMB).

The IMB's growth and success is a vindication of the faith shown by UQ and important funders, the Queensland and Federal governments, and The Atlantic Philanthropies, in investing in the vital area of biotechnology research. UQ and its partners recognise that the health of Australia's economy rests partly on the outcomes and achievements of research in the fields of molecular and biomedical research.

As Chair, I thank the members of the IMB Board and Scientific Advisory Committee for the time, skills and energy they dedicate to manage and develop the Institute.

The collaborative environment and work which IMB's world-class researchers are carrying out at the state-of-the-art Queensland Biosciences Precinct at UQ's St Lucia campus is inspiring. Their considerable achievements are listed in this Annual Report.

UQ is building one of the largest concentrations of biological scientists in the world, and the IMB is at the centre of these developments. The Australian Institute for Bioengineering and Nanotechnology (AIBN) and Queensland Brain Institute (QBI) are also being advanced to contribute to UQ's vision of creating a strategic cluster of world-class research centres. Construction of the $60million AIBN building is underway, and this will be followed by a new building for the QBI.

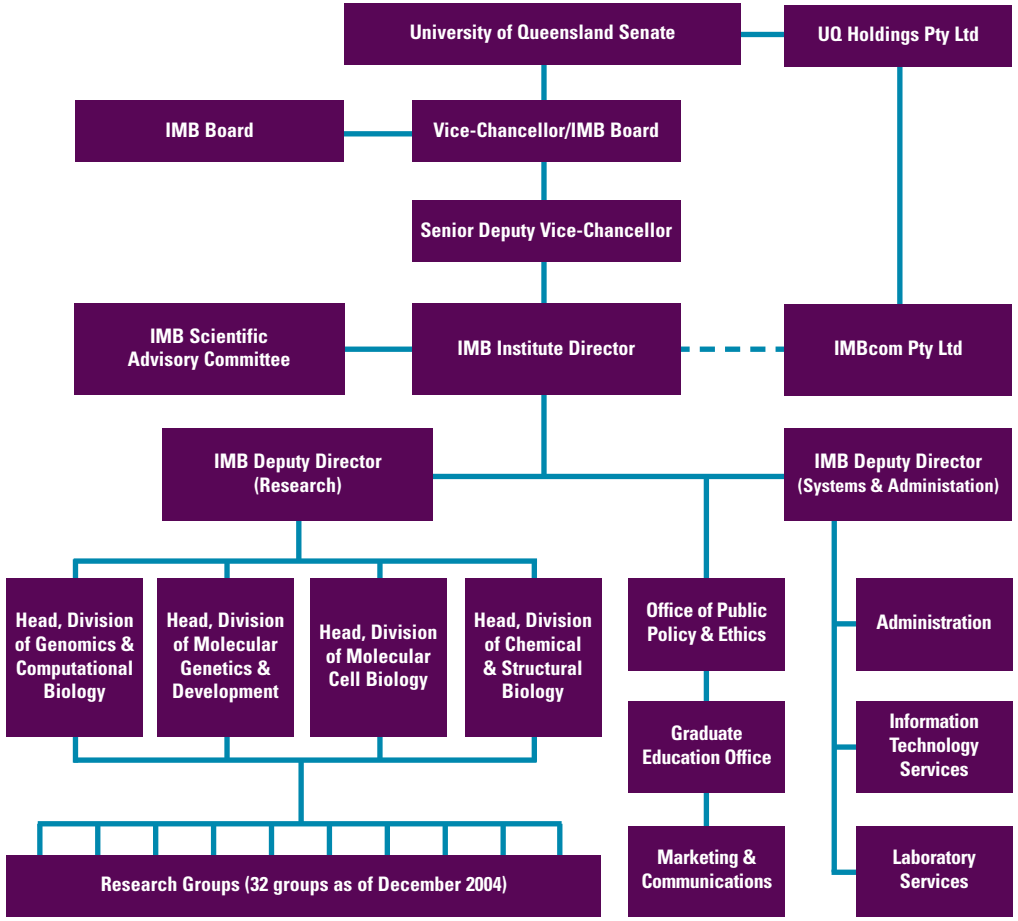
In addition, UQ has invested strategically in the areas of mining and minerals to create the Sustainable Minerals Institute which recently moved into a new high-tech building.

All of these initiatives have been made possible with the support of our generous donors, and we acknowledge the foresight of the Queensland Government in supporting UQ through its Smart State strategy. These are smart investments for our State, and are laying the foundation for the University to continue to play a central role in research and innovation in Australia.

Professor John Hay AC
Vice-Chancellor
The University of Queensland

2.

Organisational Chart



3.

IMB Advisory Board

Professor John Hay AC (Chair) *(Pictured 1)*

Professor John Hay has been Vice-Chancellor and President of The University of Queensland since 1996. He is a graduate of the University of Western Australia and Pembroke College, Cambridge where he held a Hackett Research Fellowship. He held the Chair of English and was Head of the Department in the University of Western Australia where he was also Deputy Chair of the Academic Board. At Monash University, he was Dean of Arts and Chair of the National Key Centre for Australian Studies and was then appointed Senior Deputy Vice-Chancellor of Monash University. In 1992 Professor Hay was appointed Vice-Chancellor and President of Deakin University in Victoria. In 2002 Professor Hay was appointed to the Higher Education Review Reference Group. Professor Hay was Chair of the Group of Eight, Australia's leading research-intensive universities from January 2002 to May 2003. He is currently Chair of the Australian Universities Teaching Committee, and Universitas 21, a consortium of international research-intensive universities.

Professor John Mattick AO (Director) *(Pictured 2)*

Professor Mattick is the Foundation Professor of Molecular Biology and the Director of the Institute for Molecular Bioscience at the University of Queensland. Professor Mattick completed his first degree at the University of Sydney (1972), followed by a PhD at Monash University (1977). He has subsequently worked at Baylor College of Medicine in Houston (1977-81), at the CSIRO Division of Molecular Biology in Sydney (1982-88), as well as at the University of Cambridge (1993), the University of Oxford (2000) and the University of Cologne (2002). He joined the University of Queensland in 1988.

Professor Mattick was the Foundation Director of the Australian Genome Research Facility (1996-2002), a major national research facility based in Brisbane, Melbourne and Adelaide. He was Chair of the Organising Committee of the 1999 Human Genome Meeting (HGM'99) and a Member of the Scientific Organising Committees of HGM'98 and HGM 2000. He serves on the Advisory Boards of several major research institutes in Australia and abroad. In 2001 Professor Mattick was appointed an Officer in the Order of Australia for his services to molecular biology and biotechnology, and in 2002 he was elected as an Honorary Fellow of the Royal College of Pathologists of Australasia.

Professor Mattick's research interests are in the molecular genetics of bacterial pathogenesis and the role of noncoding RNA in the evolution and development of complex organisms. He has published over 120 scientific papers. He has recently developed a new theory of the structure of genetic information in the higher organisms, and which may explain the purpose of the so-called junk DNA in the human genome as the control architecture for human development.

Mr Paul Fennelly *(Pictured 3)*

Appointed as Director-General, Department of State Development and Co-ordinator General of Queensland in February 2002. Mr Fennelly has recently been appointed as Director-General of the newly established Department of State Development and Innovation. The Department is responsible for driving the economic development of Queensland and the delivery of the Government's Smart State Strategy.

The Department's activities involve:
- Major Projects & Infrastructure
- Investment Attraction
- Public Private Partnerships
- Industry Development
- Innovation
- Small Business

From January 2000 to January 2002, Mr Fennelly was the State Director of Australian Industry Group, Victoria's largest business organisation, representing approximately 6,000 companies. Mr Fennelly was also the Queensland Director of MTIA / Australian Industry Group from 1993 - 1999. Mr Fennelly holds degrees in Law and Arts, as well as a Graduate Diploma in Industrial Law.

Professor Frank Gannon *(Pictured 4)*

Since 1994, Frank Gannon has been 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 at Laboratory (EMBL) in Heidelberg, Germany. His major research interest is the Estrogen Receptor as a Transcription Factor. He is also Senior Editor of EMBO Reports and Associate Editor of the EMBO Journal and of Molecular Systems Biology. He serves on a number of scientific advisory boards at institutes throughout the world.

Professor Paul Greenfield *(Pictured 5)*

Professor Greenfield is Senior Deputy Vice-Chancellor of the University of Queensland. After graduating Bachelor of Engineering, first-class honours in chemical engineering, from the University of New South Wales (UNSW), Professor Greenfield worked in the private sector before completing a PhD at UNSW. He 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. Currently, he chairs the Scientific Advisory Committee overseeing the $5.2 million Moreton Bay and Brisbane River Wastewater Management Study (since 1994); the Waste Technical Working Group, Basel Convention (since 1995); and the Advisory Board of I.P. Australia (since 1999).

He is also a Director of several University companies including UniQuest Pty Ltd. 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.

Dr Russell Howard *(Pictured 6)*

Dr. Howard is CEO OF Maxygen (NASDAQ: MAXY) and one of the company's founders. Since creation of Maxygen in 1997, its core technologies were used to create several independent businesses. The industrials business opportunity, Codexis, develops enhanced processes for pharmaceutical intermediates manufacture and was spun out with private financing in 2002. The business opportunity for improved genes in agricultural applications, Verdia, was sold in 2004 to Dupont. Today Maxygen is focused on discovery and development of protein pharmaceuticals.

Originally trained in biochemistry and chemistry at Melbourne University, Australia, Dr. Howard spent over 20 years studying infectious diseases, primarily malaria. Before joining Maxygen, Dr. Howard served as the president and scientific director of Affymax Research Institute, employing combinatorial chemistry and high throughput target screening to discover drug leads (1994-96). Prior to joining Affymax, Dr. Howard held various research positions at DNAX Research Institute and the National Institutes of Health, MD, where he received tenure. In addition to numerous patents, Dr. Howard has over 140 publications in peer-reviewed journals.

Dr Peter Isdale *(Pictured 7)*

Dr Isdale is the CEO of IMBcom Pty Ltd. the University of Queensland's commercialisation company for its Institute for Molecular Bioscience. He is a former Business Director at the Australian Institute of Marine Science, Australia's national marine research agency, and directed the strategic development of AIMS' business and commercial interests, and managed the Institute's legal and intellectual property affairs. He is also a former Principal Research Scientist at AIMS who is the author or co-author of more than 30 papers in his special field of research.

He has 18 years experience in the operation and governance of both 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 the positions of non-executive Director, Great Barrier Reef Research Foundation, non-executive Director of ElaCor Pty Ltd, Chairman of The Wetlands and Grasslands Foundation, Senior Fellow of the Chaiyong Limthongkul

Members of the IMB Advisory Board: *Professor John Hay AC, Professor John Mattick AO, Mr Paul Fennelly, Professor Frank Gannon, Professor Paul Greenfield, Dr Russell Howard, Dr Peter Isdale, Ms Helen Lynch AM, Professor Mick McManus, Mr Ross Rolfe, Sir Sydney Schubert.*

Foundation, Bangkok, Thailand and Adjunct Professor, Department of Land Development and Environmental Planning, School of Architecture, Texas A&M University.

He holds a B.A. with First Class Honours and a PhD in Marine Geomorphology, (1982) from James Cook University of North Queensland.

Ms Helen Lynch AM *(Pictured 8)*

Helen Lynch AM is Deputy Chairman of Pacific Brands Limited, Chairman of the Sydney Symphony Orchestra, and a Non-Executive Director of Southcorp Limited, Westpac Banking Corporation. Helen Lynch's previous directorships include Chairman of OPSM Group Limited until 2003, Director of Coles Myer Ltd.1995-2003, Chairman of the Superannuation Funds Management Corporation of South Australia 1995-2000. Current involvements include member of Advisory Board Caliburn Partnership and External Advisor Mallesons Stephen Jaques. External Board Member Institute of Molecular Bio-Science University of Queensland. Helen Lynch had a distinguished career, spanning 35 years, in the Banking and Finance Industry at Westpac Banking Corporation including being a member of the Bank's executive committee. She left Westpac in 1994 and was appointed a Non-Executive Director of the Bank in 1997. In 1990 Helen Lynch was the Bulletin/Qantas Business Woman of the Year. Helen was made a member of the Order of Australia in 1994 for services to the Banking and Finance Industry. In 2003, Helen received the Centenary Medal in recognition of her service to Australia: Society in Business Leadership.

Professor Mick McManus *(Pictured 9)*

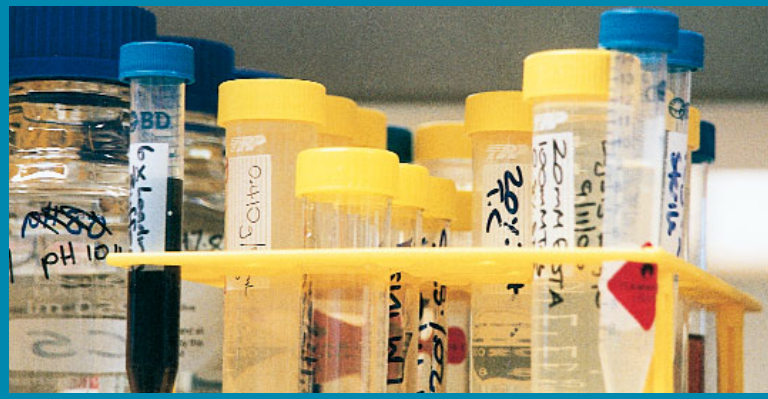
In 1998, Mick McManus was appointed Executive Dean of the Faculty of Biological & Chemical Sciences and prior to this he was Head of the Department of Physiology & Pharmacology from 1993 to 1997. Mick's initial appointment to the university was as Foundation Professor of Pharmacology and he was President of the Australasian Society of Clinical & Experimental Pharmacologists & Toxicologists from 2000 - 2001. He came to the University from a National Health & Medical Research Council Principal Research Fellowship position in the Department of Clinical Pharmacology at Flinders University in Adelaide. He was initially trained as a pharmacist at Curtin University of Technology and completed his PhD at the University of Western Australia in 1978. Mick has held research positions at the Royal Postgraduate Medical School, University of London and the National Cancer Institute, National Institutes of Health in Bethesda, Maryland, USA. He continues to have a strong research interest in the area of xenobiotic metabolism, especially on the role human sulfotransferases play in this process.

Mr Ross Rolfe *(Pictured 10)*

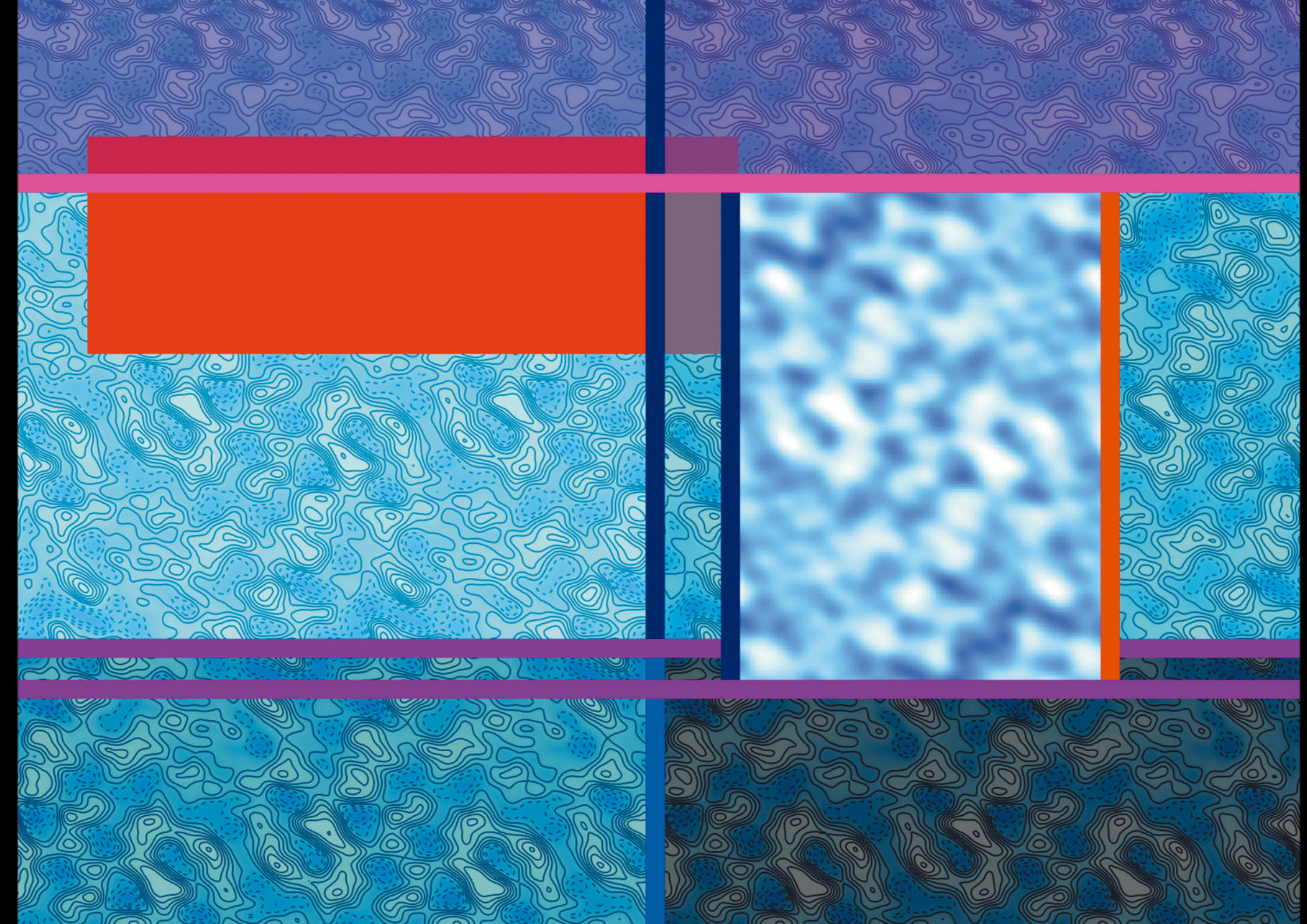
Ross Rolfe was appointed the Director-General of the Department of State Development and Co-ordinator General in 1998. In 1996, he was the Director-General of the Department of Environment and Heritage, under the previous Labor Government. Mr Rolfe has a background in issues relating to land management, the energy industry and the environment. Mr Rolfe's expertise and knowledge has been utilised by such companies as Chevron Asiatic, Powerlink Queensland, BHP - Coal Division, industry associations and a range of development companies.

Sir Sydney Schubert *(Pictured 11)*

Sydney Schubert has had a career spanning 40 years with the Queensland Government, including Co-ordinator General and Director-General between 1976 and 1988. He was Executive Chair of Daikyo Group of Companies, Australia and New Zealand, from 1988 to 2000. Currently he is Chair of the CRC for Great Barrier Reef World Heritage Area, CRC for Tropical Rainforest Ecology and Management and CRC for Torres Strait.



The IMB is part of a strategic cluster of research excellence at UQ - the Australian Institute for Bioengineering and Nanotechnology (AIBN) and the Queensland Brain Institute (QBI) currently under development are modelled on the successful IMB.



4.

Director's Report

Professor John Mattick AO

At the close of 2004 the Institute for Molecular Bioscience has been in operation for five years. In this time the Institute has grown from the initial 17 research groups of the Centres for Drug Design and Development and Molecular and Cellular Biology to the cohesive systems biology research institute of 32 research groups that is the IMB.

In addition to the many achievements highlighted in the following pages, it is the continued growth and development of our intellectual and physical resources that are pivotal to the IMB's ongoing success.

We are fortunate to be co-located in the Queensland Bioscience Precinct with the CSIRO Divisions of Livestock Industries and Plant Industries, and it is the maturation of our association with CSIRO that is one of the most pleasing aspects of 2004. This association includes the establishment of joint CSIRO-IMB postgraduate scholarships, a joint proteomics facility, and a joint AccessGrid node for high resolution video conferencing and data sharing.

IMB looks forward to further developing this relationship with CSIRO as both organisations collaboratively identify strategic goals in our efforts to understand and apply the information contained in genes and proteins, especially in the areas of comparative genomics, bioinformatics and pharmaceutical development.

In 2004 three new research groups commenced operations at the IMB with the arrival of Drs Alan Munn from Singapore, Andrew Perkins from Melbourne and Brad Marsh from Colorado. Each bring with them unique skill sets and research foci that strategically enhance the IMB's research objectives in cell, developmental structural biology. We also appointed Dr Martin Frith as a joint UQ Postdoctoral Fellow with the RIKEN Genome Sciences Center in Yokohama, Japan, an appointment which strengthens the strategic relationship between IMB and RIKEN in mammalian genomics.

We were also delighted to announce the appointment of three new Honorary Professors to the Institute: Professor Vicki Sara, formerly of the Karolinska Institute and the Queensland University of Technology, until recently the CEO of the Australian Research Council and now Chancellor of the University of Technology Sydney; Professor Frances Brodsky, a noted cell biologist at the University of California San Francisco; and Professor Peter Visscher, a noted animal geneticist, formerly of the University of Oxford and now at the Queensland Institute of Medical Research. They join Professor David Weisbrot, Head of the Australian Law Reform Commission in Sydney, Professor Nic Nicola, Assistant Director of the Walter and Eliza Hall Institute of Medical Research in Melbourne, Professor Yoshihide Hayashazaki, RIKEN Genomic Sciences Centre in Tokyo and Professor Gene Myers, University of California at Berkeley, who were appointed as Honorary Professors in 2003.

Other points of note in 2004 were our continued successes in ARC, NHRMC and NIH grant funding, as well as funding from industry and our commercial activities. We have established a Centre for Molecular Diversity under the direction of Professor Rob Capon, which will integrate natural product discovery with advanced screens based on IMB's cell biological expertise, which we expect will fuel the next round of pharmaceutical development arising from our research.

The IMB was also successful in 2004 in the formation and continuation of a range of research partnerships including the ARC Centre of Excellence in Biotechnology and Development, the Australian Stem Cell Centre, the ARC Centre in Bioinformatics, the Australian Phenomics Facility, the Australian Genome Research Facility, the Cooperative Research Centre for Chronic Inflammatory Diseases and the Cooperative Research Centre for Australasian Invasive Animals. The ARC Centre for Bioinformatics hosted the first Winter School in Mathematics and Computational Biology in conjunction with the Australian Mathematical Sciences Institute (AMSI). Lead by Professor Mark Ragan, the IMB now has the largest bioinformatics capability in Australia, enhanced by the appointment of Dr Lindsay Hood as IT and high performance computing manager. Dr Hood joins IMB after many years experience in advanced computing and the computer industry.

In 2004 the IMB commissioned a new $3m cryo-electron microscope, which was acquired in partnership with the NANO major national research facility program and the Centre for Microscopy and Microanalysis. We also commissioned the Dynamic Imaging Facility for Cancer Biology, supported by a $1.2m grant from the Australian Cancer Research Foundation. These facilities are the most advanced in Australia and significantly enhance our pre-eminent position in cell biology and cell structural analysis.

The IMB is fortunate to have as a partner IMBcom, which we consider to be the best biotechnology transfer and commercial development group in the country. We thank the CEO of IMBcom Dr Peter Isdale, and the Deputy-Director Dr Peter Riddles, and their staff, for their energy and success in the development of IMB research, and in assisting IMB to meet its key performance indices.

In 2004 IMB completed its strategic plan and performance review criteria, as a platform for the future. As I write we are preparing for our first major quinquennial review, which will examine the IMB's research performance and its financial and strategic contributions to the development of a strong biotechnology industry and knowledge-based economy in Queensland and Australia.

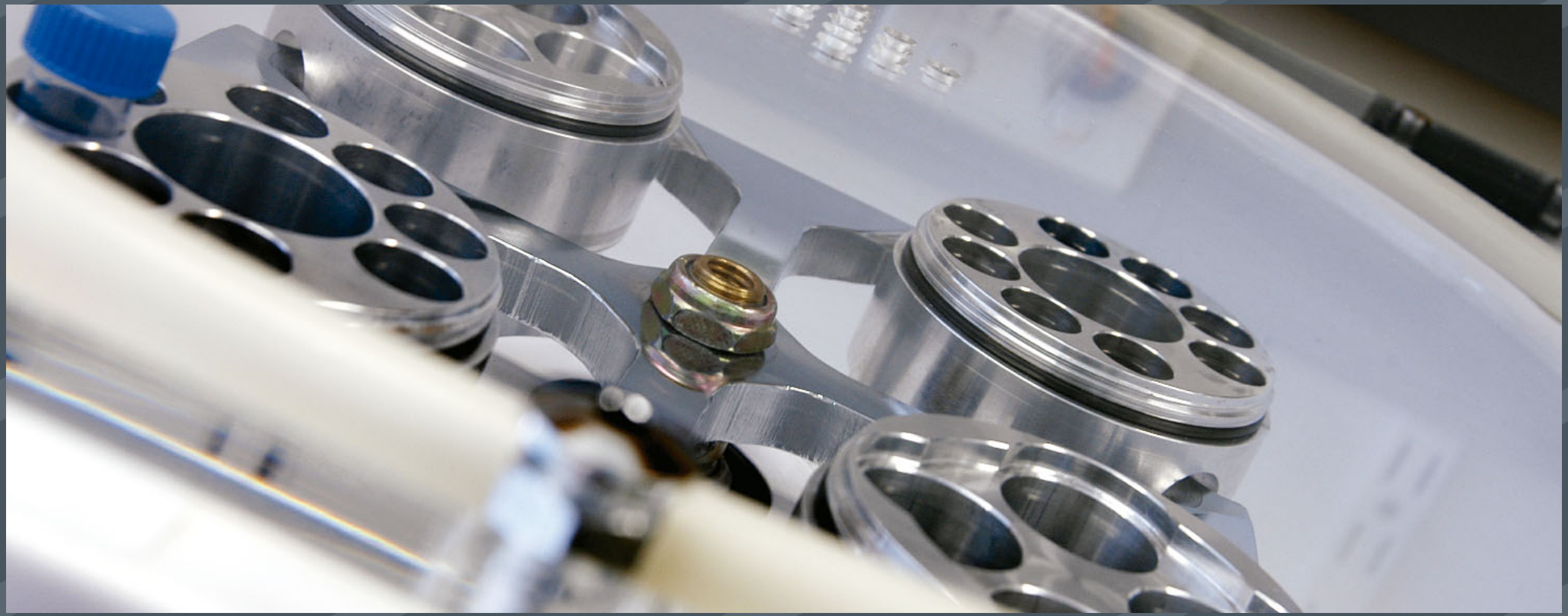
Once again I thank the IMB's senior executive team, particularly Professor Brandon Wainwright (Deputy Director, Research) and Dr Ian Taylor (Deputy Director, Systems and Administration). Both have tirelessly contributed to the growth and development of the IMB in their areas of responsibility. I also thank IMB's Divisional Heads, Professors Mark Ragan, George Muscat, John Hancock, and Paul Alewood, as well as Professor David Hume, Director of the ARC Special Research Centre for Functional and Applied Genomics, and Professor Wayne Hall, Director of the Office of Public Policy and Ethics, for their leadership and strong contributions to the management and development of the IMB. The IMB is well supported by outstanding IT, administrative, postgraduate, marketing communication and technical support staff under the leadership of Lindsay Hood, Chris Barnett, John Spooner, Barbara Clyde, Andrea Sackson and Amanda Carozzi, whom we thank sincerely.

I also thank the Vice Chancellor Professor John Hay, the Senior Deputy Vice Chancellor Professor Paul Greenfield, the Deputy Vice Chancellor (Research) Professor David Siddle, the Dean of the Faculty of Biological and Chemical Sciences Professor Mick McManus and our other senior colleagues at the University of Queensland for their continued support of the IMB and its development.

In addition the IMB is in the enviable position of having a very experienced and committed Board and Scientific Advisory Committee members. These extremely busy people give freely of their time and expertise to benefit the governance and strategic development of our organization, for which we remain most grateful.

Finally the IMB acknowledges the extensive support of the Queensland and Australian governments, without which we could not function and who invest in us because of their belief that we will deliver benefits to the national and international community. We continue to try to do so.

Professor John Mattick AO
Director
Institute for Molecular Bioscience



5.

IMB Research Highlights

The year in review.

Professor John Mattick (left) and Dr Craig Venter

RESEARCH

IMB scientists discover new class of genetic elements in humans

In a world first, IMB scientists uncovered a new class of genetic elements with the potential to radically alter our notions of how the genome "comes to life" to form humans.

In conjunction with the University of California at Santa Cruz, IMB's Professor John Mattick and Michael Gagen discovered that, despite hundreds of millions of years of divergent evolution, there are thousands of these genetic elements in humans, rats and mice that have remained identical.

Patching up skin burns and skin cancer

Burns patients could potentially benefit from a world-first discovery from the labs of the IMB.

By discovering the link between a vital cell signalling pathway and stem cells of the skin, the research team of IMB's Professor Brandon Wainwright produced skin containing up to four times as many stem cells and capable of producing more skin tissue in less time than current methods.

Eye colour, pigmentation genes and ancestry

New research from the IMB demonstrated that one of the classic examples of genetic inheritance taught in schools is wrong.

No longer is it true to say there is a single gene influencing the colour of our eyes according to IMB's Dr Rick Sturm and DNAprint Genomics' Dr Tony Frukadis in their review article published in the respected journal *Trends in Genetics*.

IMB collaborates with world-renowned genetic expert

Researchers from UQ's IMB are collaborating with Dr Craig Venter, the US scientist who helped crack the human genetic code, during his six-month visit to Queensland as part of his quest to define the origins and diversity of life.

Dr Venter and a research team from the Venter Institute are circling the globe in his yacht and floating laboratory, *Sorcerer II*, to collect marine samples and analyse their genetic data. Australia is the 14th country the team has visited.

Scientists tackle the decline in male fertility

Australian scientists gathered at IMB to discuss the causes of an alarming decline in male fertility in Australia and worldwide.

Professor Peter Koopman, head of the Brisbane node of the Australian Research Council's Centre of Excellence in Biotechnology and Development said there had been a huge increase in male infertility in the past thirty years.

GRANTS

Snakes and ladders – Taipan venom in the fight against heart failure

A venom compound from the world's deadliest snake, the Taipan, is being developed by IMB in partnership with the Brisbane biotechnology company ElaCor, as a new drug to treat heart failure.

Congestive heart failure (CHF) claims the lives of over 3,000 Australians each year with a further 300,000 people affected by the disease.

The project's principal researcher, IMB's Professor Paul Alewood, said current treatments for CHF had serious side effects and rarely combated the progression of the disease.

"The team has isolated a unique set of active molecules from Taipan venom and research shows they are extremely effective at easing the heart's workload," he said.

Year of Success for Nephrogenix

IMB start-up company Nephrogenix received a $250,000 grant from the Federal Government's Biotechnology Innovation Fund to further its ground-breaking work on renal disease and kidney regeneration.

Established by IMBcom and Monash Commercial, the commercialisation companies at the University of Queensland and Monash University respectively, Nephrogenix aims to translate basic research in kidney disease into applied and commercial outcomes.

Nephrogenix's Chief Scientific Advisor, Associate Professor Melissa Little said the grant enabled further advances on stem cell markers and methods for generating cell types needed to develop cellular therapies and therapeutics for renal disease.

Furthermore, in a bid to offer relief to patients affected by kidney, blood and heart disease, Nephrogenix also signed a collaborative research agreement with Australia's National Stem Cell Centre (NSCC).

Seeking to maximise the existing synergies that exist between the two companies, NSCC and Nephrogenix signed a collaborative agreement to explore the common ancestry of interrelated systems involved in forming kidneys, bone and bone marrow.

Program Grant Success

IMB scientists researching safer and more effective drugs to treat pain and understanding sexual development disorders will share $11.4 million over five years as part of the latest round of National Health and Medical Research Council Program Grants.

In a collaborative grant IMB's Associate Professor Richard Lewis and Professor Paul Alewood along with the team from the Pain Management Research Institute at the University of Sydney, will work on developing new drugs derived from the venom of one of Australia's most poisonous creatures.

Meanwhile patients with disorders of sexual development stand to benefit from a collaborative research program between IMB, the Murdoch Children's Research Institute and Prince Henry's Institute of Medical Research, both in Victoria.

IMB's Professor Peter Koopman said the incidence of intersex disorders was surprisingly common among the population with about four percent of live births affected by disorders resulting in infertility, genital abnormalities, gender mis-assignment and long-term psychological trauma.

Cancer research boosted in Queensland

IMB was one of just three recipients of the largest research grant ever given by the Australian Cancer Research Foundation (ACRF).

Announcing the 2004 funding allocation today, ACRF Chairman Tom Dery said $3.3 million would be provided for three major research projects now taking place at Australia's foremost cancer research centres - the Institute for Molecular Bioscience in Brisbane, Garvan Institute in Sydney and Peter MacCallum Cancer Centre in Melbourne.

IMB scientists are already utilising the Facility to further our understanding of the complex mechanisms by which cells communicate with each other, the factors influencing cellular differentiation and the methods by which cells move around the body, both normally during development and abnormally in the case of cancer.

AWARDS

World Top 10 for Queensland Scientist

Research by IMB's Professor John Mattick has been recognised as one of the top ten discoveries of 2004 by the world-leading journal *Science*.

His work investigating the role of 'junk' DNA in genetic programming and regulation is leading to a reappraisal of the central dogma of molecular biology.

Professor Mattick said sequencing of the human genome, as well as other organisms like mouse and bacteria, allowed scientists to compare and contrast features like the complexity of organisms and the role of non-protein coding DNA; the DNA between the 'genes'.

HIV drug research boosted by UQ Foundation

A promising lead in developing anti viral drugs with the potential to fight human immunodeficiency virus (HIV) and herpes simplex virus (HSV) has been boosted by a University of Queensland Foundation Research Excellence Award.

The $50,000 award enables IMB's Dr Norelle Daly to determine the molecular structure of retrocyclin, a molecule with the ability to protect human cells from HIV infection.

Given the worldwide increase in the incidence of AIDS, as well as the projected US$61 billion market for anti-HSV drugs there is enormous interest in identifying naturally occurring antiviral molecules.

IMB researcher joins Fellowship of the Smart State

A Smart State Fellowship awarded Dr Horst Schirra has significantly advanced IMB research into the control of crop damaging pests.

Dr Schirra is developing new ways of pest control by determining how plant proteins block the digestive enzymes of insect pests.

"The aim is to structurally characterize the interactions between the digestive enzymes of insects with proteinase inhibitors from plants," he said.

Professor David Siddle, UQ's Deputy Vice-Chancellor (Research), said the fellowships scheme was a manifestation of the government's commitment to Research and Development, and to the development of a knowledge economy.

Top: University of Queensland Foundation Research Excellence Award winner Norelle Daly
Bottom: Smart State Fellow Horst Schirra (right) with UQ's Deputy Vice Chancellor (Research) Professor David Siddle and other Smart State Fellows.

ANZAC spirit to flourish with biotech agreement

The ANZAC spirit of the Australian and New Zealand biotech industries was boosted with the arrival of one of New Zealand's premier agricultural scientists at IMBcom, UQ's commercialisation company for the IMB.

Dr Warren Parker, until recently Chief Operating Officer with NZ's AgResearch an independent Crown-owned research and development company protecting intellectual property and commercialising New Zealand research, commenced his 12 month secondment in September.

Molecular bioscience reveals its artistic appeal

'Sweetbox', a delicious image illustrating the pollen from a pigeon pea flower, was just one of the spectacular images born from the research labs of UQ and IMB (see page 57).

IMB will release ten images for sale as prints to raise awareness of the work of its scientists and contribute funds to IMB research.

6.

IMB Researchers

The people and their passion.

The highly integrated research environment at the IMB facilitates the fertile exchange of ideas and experimental approaches across the broad spectrum of molecular biological sciences.

This enables a whole of system approach to understanding the basis of human and mammalian growth and development at the molecular, cellular and organ levels.

Only by understanding the complex molecular and cellular events that occur throughout a normal human life can scientists begin to understand abnormalities responsible for many common human diseases and to find treatments for them. IMB researchers are particularly interested in the genetic programming of mammalian development and variation, the mapping of the structure, growth and dynamics of mammalian tissues and cells, and the development of new medicines and technologies, as well as research into the issues in genetic and cellular medicine and technologies through its Office of Public Policy and Ethics.

This research will lead to new pharmaceuticals, gene therapies, technologies and diagnostics capable of identifying, halting or even reversing the progress of many diseases.

The following pages briefly outline the research interests and achievements of the IMB's 32 research groups.

More information can be found on the IMB website www.imb.uq.edu.au.

DIVISION OF GENOMICS AND COMPUTATION BIOLOGY

Research focus:

This program includes the ARC Centre in Bioinformatics and intersects with the Department of Mathematics and School of Information Technology and Electrical Engineering.

It focuses on comparative mammalian and vertebrate functional genomics; rnomics; and computational modelling of genetic and cellular regulatory networks.

Research Group Leaders:

- Tim Bailey
- Sean Grimmond
- Jennifer Hallinan
- John Mattick
- Mark Ragan
- Rohan Teasdale

Joint Appointments

- Kevin Burrage
- Geoff McLachlan

Research

New computational algorithms are required for the analysis of high-throughput biological data and for modeling biological systems. My group applies expertise in the development of computer algorithms using machine learning, data mining, pattern recognition and statistical analysis to biological problems. Using these technologies, we develop computational tools to help biologists make predictions from data.

Our recent work has focused mainly on analyzing protein, DNA and RNA sequence data. We have developed tools for making predictions in several biological domains:

- Identifying protein families
- Discovering protein domains
- Discovering transcription factor binding sites
- Predicting clusters of interacting transcription factors
- Predicting protein flexibility and accessible surface area
- Detecting errors in protein databases

One current focus is on using the evolutionary signal present in orthologous genes from multiple species to improve the sensitivity and accuracy of these predictions.

We place a strong emphasis in delivering useful computational tools to biologists. Most of the algorithms we have developed are available as interactive tools over the web. We support these tools via websites located at IMB, UCSD, Boston University and the Pasteur Institute. These include MEME, a tool for discovering motifs (sequence patterns) in protein and DNA sequences; MAST, a tool for scanning sequence databases for matches to known patterns; MCAST, Comet and ClusterBuster, tools for scanning sequences for clusters of transcription factor binding sites; and Meta-MEME, a general purpose sequence modeling too. Some of these tools are among the most widely used bioinformatics algorithms. For example, the MEME algorithm is used via the UCSD website by over 450 biologists around the world each month. Maintaining these websites and supporting the biologists who use them is an important commitment for us.

Lab members

Research Officers:
Martin Frith
Richard Davis

Students:
Vacation scholar: Emma Redhead

Research Projects

- Developing HMMs that utilize evolutionary information
- Developing a scanning algorithm utilizing evolutionary information for detecting transcription factor binding sites
- Improving the accuracy of motif discovery algorithms
- Improved statistics for motif discovery
- Using Support Vector Machines (SVMs) for prediction of protein characteristics

External Duties

Member ISMB 2005 program committee

Internal Duties

Coordinator of Combio, IMB's internal weekly research seminar in bioinformatics and computational biology

Course coordinator for BIOL3014, Advanced Bioinformatics

Key Publications Since 2000

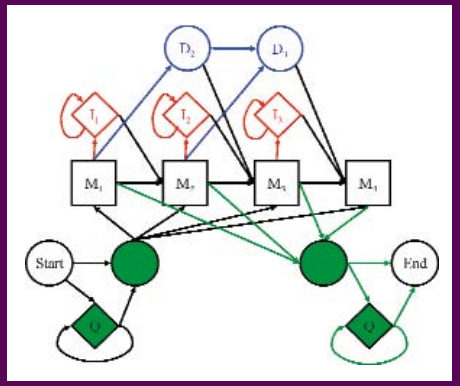
Martin Tompa, Nan Li, Timothy L. Bailey, George M. Church, Bart De Moor, Eleazar Eskin, Alexander V. Favorov, Martin C. Frith, Yutao Fu, W. James Kent, Vsevolov J. Makeev, Andrei A. Mironov, William Stafford Noble, Giulio Pavesi, Graziano Pesole, Mireille Régnier, Nicolais Simonis, Saurabh Sinha, Gert Thijs, Jacques van Helden, Mathias Vandenbogaert, Zhiping Weng, Chun Ye and Zhou Zhu (2005) Assessing Computational Tools for the Discovery of Transcription Factor Binding Sites, *Nature Biotechnology*, 23:137-144.

Zheng Yuan, Timothy L. Bailey and Rohan Teasdale, (2005) Prediction of protein B-factor profiles. *Proteins*. 58:905-12.

Timothy L. Bailey and William Noble, (2003) Searching for statistically significant regulatory modules, *Bioinformatics*, Suppl 2:II16-II25.

Timothy L. Bailey and Michael Gribskov, (2002) Estimating and evaluating the statistics of gapped local-alignment scores, *Journal of Computational Biology*, 9:575-593.

Timothy L. Bailey and Michael Gribskov, (2000) Concerning the accuracy of MAST E-values, *Bioinformatics*, 16:488-489.



Timothy Bailey

Sean Grimmond

Research

The central focus of my research is to capture information associated with global gene expression and use it to define the key gene that control important biological processes and pathological conditions. Undertaking this sort of research requires an integrated pipeline that uses:

- Microarray technology to capture all transcriptional consequences of a challenge to a biological system (eg chemical, environmental, genetic mutation, growth factor),
- Bioinformatics for ascribing putative functions to all active genes,
- Computational tools to identify genes whose expression pattern correlates with the challenge, and
- High throughput functional genomic assays for validating the role of lead genes generated by this and other pipelines. Once established this pipeline is a powerful tool for lead gene discovery in almost any biological system.

Since the completion of mammalian genome and transcriptome sequencing projects, the full complement of genes in the mouse and the human have been elucidated. The key challenges for my laboratory are to catalogue putative roles for all gene products, exploit genomic tools to fast track the discovery of lead genes and develop better understanding of the networks that control key processes. Integrating global assays of promoter activity, globally defined gene expression and phenotypic events attain these insights.

Research Projects

- Annotating the mammalian transcriptome
- Temporal and spatial profiling of kidney development

External Duties

Member, Organising Committee, Lorne Genome Conference.

Lab members

Senior Research Officers:
Tina Maguire, Mark Crowe

Research Officers:
Brooke Gardiner, Nic Waddel

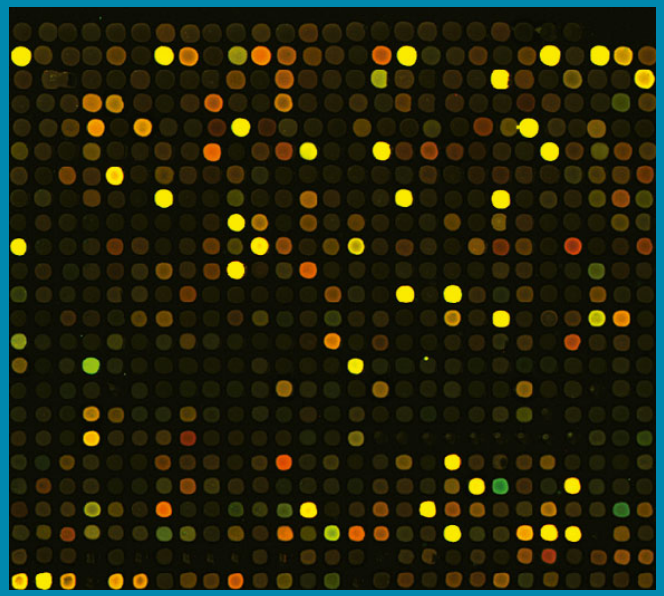
Research Assistants:
Milena Gongora, Phil Huggard, Rowena Cecil

Bioinformatician:
Darrin Taylor

PhD student:
Alistair Forrest

MSc student:
Yuma Nakagawa

Honours students:
Rowena Cecil, Suwarni Haji, Modh Diah, Ehsan Nourbakhsh



Awards

Eppendorf Australian Researcher Award 2004.

Key Publications Since 2000

Grimmond S, Van Hateren N, Siggers P, Arkell R, Larder R, Soares MB, Bonaldo M, Smith L, Tymowska-Lalanne Z, Wells C, Greenfield A. (2000) Sexually dimorphic expression of protease nexin-1 and Vanin-1 in the developing mouse gonad prior to overt differentiation suggests a role in mammalian sexual development *Human. Mol Genet.* 9:1553-1560.

The FANTOM Consortium and The RIKEN Genome Exploration Research Group Phase I & II Team (Grimmond. SM) (2002) Analysis of the Mouse Transcriptome based upon Functional Annotation of 60,770 full length cDNAs *Nature.* 420: 563-73.

Forrest A, Ravasi T, Hume D, Taylor D, Huber T, RIKEN Members, Grimmond SM. (2003) Protein Phosphoregulators: Protein Kinases and protein phosphatases of the mouse. *Genome Res:* 13:1443-54.

Grimmond, S Miranda K, Yuan Z, RIKEN GER Group Members, R.D.Teasdale. (2003) The mammalian secretome. *Genome Res.* 13:1350-1359.

Challen GA, Martinez G, Davis MJ, Taylor DF, Teasdale RT, Grimmond SM, Little MH (2004) Identifying the molecular phenotype of renal progenitor cells. *J Am Soc Nephrol.* 15:2344-57.

Sean Grimmond

Research

The cell is a complex system containing a myriad of different interacting molecules. DNA, RNA, proteins and biochemicals interact to maintain the cell in a robust, dynamic non-equilibrium state.

We are interested in the structure, dynamics and evolution of intracellular interaction networks ranging from metabolic networks through protein/protein interaction networks to the intricate networks of genetic regulation, responsible for the type and activity of the cell.

Our research aims to understand how critical biological phenomena, such as homeostasis, mutational robustness and flexible gene regulation arise from interactions between the components of a complex biological system.

We use the techniques of network analysis, already applied in fields as diverse as sociology, economics, physics, computer science and mathematics, to pursue this goal.

We have designed and implemented a suite of computational tools for the generation and analysis of networks. Processing can be performed on either a single machine or a cluster, permitting the analysis of large numbers of networks with clearly defined characteristics, as well as in-depth investigation of specific individual networks.

Using this tool we have extended the RBN algorithm to make it more biologically plausible, incorporating asynchronous dynamics, constitutive gene activation, fast-acting RNA control layers and the ability to "evolve" using a genetic algorithm.

We have also designed and implemented a database of genetic regulatory interactions, which is currently being populated with data on the p53 oncogene network underlying many cancers. Preliminary analysis of the cancer network has been carried out using tools developed via RBN modelling.

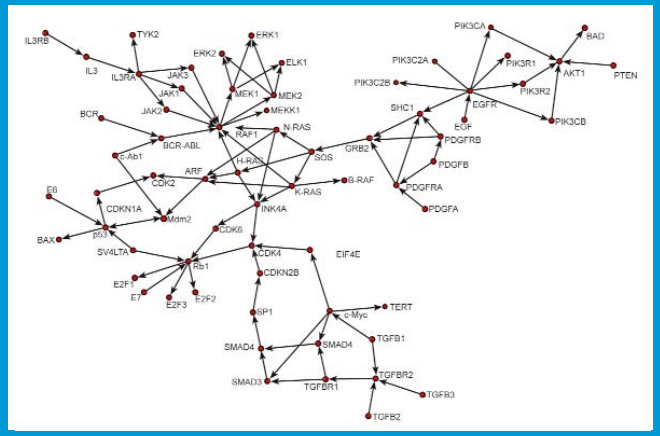
Our major goal is an understanding of how GRN network topology influences the dynamic behaviour of the network. In particular, we aim to identify specific interactions and, more importantly, patterns of interactions, which modulate the system dynamics in a predictable manner.

Lab members

Research Assistants:
Amanda Barnett
Daniel Bradley

PhD Students:
Simon Carter
Ben Skellett

Honours Students:
Tien Boon Phar



Such patterns of interactions will be potential targets for therapeutic intervention in conditions such as cancer or the differentiation of stem cells. To this end we will continue to develop the theory of GRNs and analysis of networks dynamics, while working more closely with laboratory biologists at the IMB.

Research Projects

- Development and analysis of computational models of networks
- Network models based on biological data

Internal Duties

Member, APRS and IMB Scholarship Selection committee
Member, ACB Research Committee

Key Publications Since 2000

Hallinan, J. (2004). Cluster analysis of the p53 genetic regulatory network: Topology and biology. *2004 IEEE Symposium on Computational Intelligence in Bioinformatics and Computational Biology.* San Diego 7-8 October, 2004.

Hallinan, J. (2004), Gene duplication and hierarchical modularity in intracellular interaction networks, *Biosystems*, 74:51-62.

Hallinan, J. & Wiles, J. (2004). Evolving genetic regulatory networks using an artificial genome. In Chen, Y.-P. (ed.) *2nd Asia-Pacific Bioinformatics Conference (APBC2004),* Dunedin, New Zealand. Conferences in Research and Practice in Information Technology, Australian Computer Society, Inc. Vol. 29:291 - 296.

Hallinan, J. (2003). Self-organization leads to hierarchical modularity in an internet community. *Proceedings of 7th International Conference on Knowledge-Based Intelligent Information and Engineering Systems(KES2003)* 3, 4 & 5 September 2003 University of Oxford, United Kingdom. Lecture Notes in AI 2773 ed. by V. Palade, R. J. Howlett & L. C. Jain. Springer-Verlag: Berlin.

Wiles, J., Schulz, R., Bolland, S., Tonkes, B. & Hallinan, J. (2001). Selection procedures for module discovery: Exploring evolutionary algorithms for cognitive science. Proceedings of the *Twenty-Third Annual Conference of the Cognitive Science Society* , 1 - 4 August, 2001, Edinburgh, Scotland. Moore, J. & Stenning, K. (eds). Lawrence Erlbaum Associates: Mahwah, N. J. pp. 1124 - 1129.

Jennifer Hallinan

RNA-BASED GENE REGULATION IN EUKARYOTIC DEVELOPMENT

John Mattick

Only 1.2% of the human genome codes for proteins. The vast majority of the human genome and that of other complex organisms consists of vast tracts of sequences within and between genes that are widely thought of as evolutionary debris, or junk. However most of these sequences are in fact transcribed into RNA that is not translated into protein. Therefore the human genome is either replete with useless transcription, or these nonprotein-coding RNAs are fulfilling some unexpected function.

Many of these transcripts are processed to smaller RNAs, called microRNAs, that control many aspects of development. MicroRNAs also regulate a variety of developmental processes in plants, and regulatory RNAs are clearly involved in chromosome dynamics and epigenetic modification in all multicellular organisms. Most if not all complex genetic phenomena in the eukaryotes appear to be connected to RNA signalling. In addition, a significant proportion of the mammalian genome appears to be under evolutionary selection, both positive and negative, including thousands of ultra-conserved sequences, which have remained essentially unchanged throughout mammalian evolution.

We are testing the hypothesis that the noncoding sequences actually constitute a hidden digital regulatory system that uses RNA signals to direct and coordinate complex suites of gene expression during our growth and development. We have shown that regulatory signals scale nonlinearly with genome size and that simple organisms have reached a complexity limit based on analog (protein) controls alone, implying that the more complex eukaryotes must have breached this limit, presumably by converting to a digital regulatory system based on RNA.

If this is correct, our current conceptions of the genomic information content and programming of complex organisms will have to be radically reassessed, with implications for many aspects of biology and biotechnology.

Lab members

Senior Research Officer:
Igor Makunin

Research officers:
Michael Gagen, Evgenj Glazov

Senior Research Assistant:
Kelin Ru

PhD Students:
Khairina Tajul Arifin, Stefan Stanley, Michael Pheasant, Cas Simons, Tim Mercer

MPhil Student:
Stuart Stephens

MSc Student:
Fiona Macrae

Honours Student:
Michael Lai

Research Projects:

- Comparative genomic analysis of positive and negative evolutionary selection in the human, mammalian and vertebrate genomes
- Bioinformatic analysis of RNA-regulatory networks by intra- and intergenomic sequence analyses
- Analysis of ultraconserved elements and other unusual features in the mammalian genome
- Analysis of patterns of conservation around alternative splice sites
- Analysis of the evolution and expression of noncoding RNAs during mammalian differentiation and development
- Dynamic regulation of RNA:RNA and RNA:DNA complexes using chromosome tiling arrays
- Proteomic analysis of proteins interacting with different forms of RNA signalling complexes
- Computational modelling of gene regulatory networks in differentiation and development
- Analyses of the relationship between regulation and nodal communication in the programming of selfassembling complex systems

Key Publications Since 2000

Mattick, J.S. (2001) Noncoding RNAs: the architects of eukaryotic complexity. *EMBO Reports* 2: 986-991.

Mattick, J.S. (2003) Challenging the dogma: the hidden layer of non-protein-coding RNAs in complex organisms. *Bioessays* 25:930-939.

Mattick, J.S. (2004) RNA regulation: a new genetics? *Nature Reviews Genetics* 5:316-323.

Bejerano, G., Stephen, S., Pheasant, M., Makunin, I, Kent, W.J., Mattick, J.S. and Haussler, D. (2004) Ultra-conserved elements in the human genome. *Science* 304:1321-1325.

Gagen, M.J. and Mattick, J.S. (2005) Accelerating networks. *Science* 307:856-858.

John Mattick

Research

We use advanced computational and database methods to investigate similarities and differences among genomes and the proteins they encode. Our goal is to make rigorous quantitative inferences about how genomes, gene families, regulatory networks and cellular functions have evolved and diversified.

Of particular interest to the group is lateral or horizontal gene transfer – the movement of genetic information across not with in genealogical lineages. Evidence suggests, that in bacteria at least, this occurs naturally at a rate far exceeding our expectations. While remaining controversial, the evidence in support of this observation is steadily growing, with far reaching consequences in the fields of environmental science, agriculture and medicine.

Research Projects

- Automated inference of vertical and lateral gene transmission in prokaryotic genomes
- Hybrid Markov-plus-linkage-based approach for highthroughput recognition of protein-sequence clusters
- Understanding the mammalian cell as a complex system of regulatory and molecular interaction networks.
- Automated recognition of maximally representative clusters of protein sequences
- Word-oriented objective function for scoring and ranking multiple sequence alignments
- Application of pattern discovery to alignment-free inference of molecular phylogenetic trees
- Bayesian and maximum likelihood phylogenetic analyses of protein sequence data under branchlength bias and model violation

External Duties

Member, Advisory Board, Bioinformatics Institute, University of Auckland

Member, Merit Allocation Committee, Australian Partnership in Advanced Computing (APAC)

Research Leader, Coordinated bioinformatics GRID computing, Bioinformatics Support Project, APAC

Member, Expert Task Force, National Bioinformatics Strategy, Commonwealth Department of Industry, Tourism and Resources

Lab members

Senior Research Officer:
Nicholas Hamilton

Research Officers:
Robert Beiko, Francis Clark, Joseph Pánek, Simon Wong

Research Assistant:
Timothy Harlow

Research Webmaster:
Lynn Fink

Database Administrators:
John Opitz, Oliver Cairncross

Casual Programmers:
Gerald Hartig, Chikako Ragan

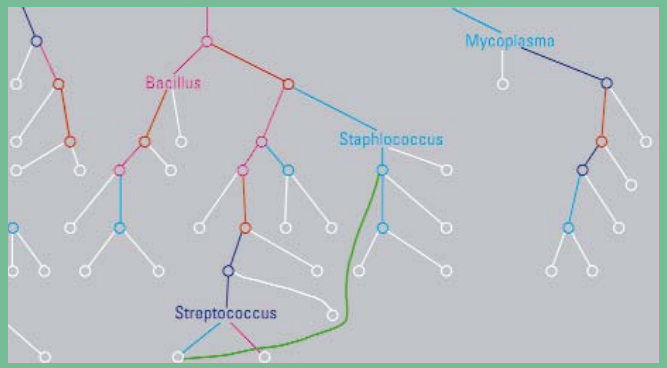
Postgraduate trainee:
Adrian Miranda

International interns:
Rafael Jiminez, Samuel Thoraval

Personal Assistant:
Lanna Wong

PhD Students:
Mohamed Rafi, Alex Garcia, Michael Höhl, Cheong Xin Chan

Undergraduate Student:
Robert McLeay



Member, Management Committee for DETYA Lectureships in Bioinformatics and Data Mining in Biotechnology

Internal Duties

Member, Advisory Board, ARC Centre in Bioinformatics
Head, IMB Division of Genomics and Computational Biology

Key Publications Since 2000

Garcia Castro A, Thoraval S, Garcia LJ, Ragan MA. 2005 Workflows in bioinformatics: meta-analysis and prototype implementation of a workflow generator. BMC *Bioinformatics*. 6:87.

Beiko RG, Chan CX, Ragan MA. (2005) A word-oriented approach to alignment validation. *Bioinformatics*. 21:2230-9.

Harlow TJ, Gogarten JP, Ragan MA. (2004) A hybrid clustering approach to recognition of protein families in 114 microbial genomes. BMC *Bioinformatics* 5:45.

Charlebois RL, Beiko RG, Ragan MA. . 2003 Microbial phylogenomics: Branching out. *Nature* 421:217.

She Q, Singh RK, Confalonieri F, Zivanovic Y, Allard G, Awayez MJ, Chan-Weiher CC, Clausen IG, Curtis BA, De Moors A, Erauso G, Fletcher C, Gordon PM, Heikamp-de Jong I, Jeffries AC, Kozera CJ, Medina N, Peng X, Thi-Ngoc HP, Redder P, Schenk ME, Theriault C, Tolstrup N, Charlebois RL, Doolittle WF, Duguet M, Gaasterland T, Garrett RA, Ragan MA, Sensen CW, Van der Oost J. (2001) The complete genome of the crenarchaeon Sulfolobus solfataricus P2. Proc *Natl Acad Sci* U S A. 98:7835-40.

Mark Ragan

Rohan Teasdale

Research

The application of computational biology techniques to cell biology is opening up new areas of scientific exploration.

Our group is developing new techniques to predict the function of novel proteins based on their sequence. We are also interested in identifying novel proteins implicated in membrane trafficking and the identification of the signals that proteins utilise for localisation to different regions of the cell.

This research has had a major impact on understanding the signals responsible for targeting membrane proteins to various subcellular regions within the cell.

This is based on our experimental characterisation and exploitation of localisation signals to develop computational approaches capable of accurately predicting the membrane organisation and localisation of novel proteins.

We have also applied a range of cellular and developmental techniques to characterise novel proteins localised to distinct regions of the cell including the Golgi, polarised cell surface membranes, nucleus, endosomes and proteins secreted into the extracellular environment.

As a result, we recently defined the protein composition of the human retromer complex and showed it was associated with mammalian endosomes.

Possessing the combination of cellular and bioinformatic skills allows our group more intuitive insights into the application of computational biology within cellular biology.

Research Projects

- Bioinformatic discovery of new genes and proteins
- Annotation of the membrane organisation of proteins associated with the mammalian secretory pathway.
- Subcellular localisation of membrane proteins
- Mouse Protein Localisation Database
- Algorithm development for prediction of protein features
- Characterisation of novel proteins involved in endosomal membrane trafficking: The Retromer Complex
- Towards renal regeneration

Lab members

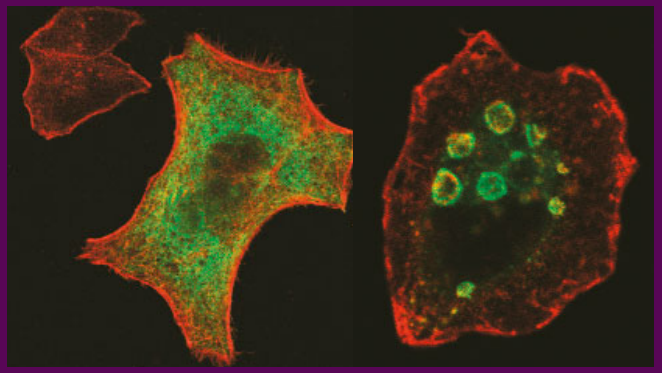
Senior Research Officer:
Zheng Yuan

Research Officers:
Lynn Fink, Donald Gardiner, Donna Mahony

Research Assistants:
Robert Luetterforst, Elizabeth O'Brien, Seetha Karunaratne, Melvena Teasdale, Shane Zhang

PhD Students:
Rajith Aturaliya, Melissa Davis, Markus Kerr, Kevin Miranda

MPhil Students:
Theingi Tun



Awards

NHMRC RD Wright Biomedical Career Development Fellowship

External Duties:

Member, Bioinformatics Australia steering committee

Member, Australian Genomic Information Centre (AGIC) Board.

Member, NHMRC Bioinformatics and Medical Genomics Working Group

Internal Duties:

Deputy Divisional Head Genomics and Computational Biology.

ARC Centre in Bioinformatics Research Committee.

Key Publications Since 2000

Teasdale,R.D., Loci, D., Karlsson,L. and Gleeson,P.A. (2001). A large family of endosomal localised proteins related to sorting nexin 1. *Biochem* J 358: 7-16

Miranda K.C., Khromykh T., Christy P., Le T.T., Gottardi C.J., Yap A.S., Stow J.L. and Teasdale,R.D. (2001) A dileucine motif targets E-cadherin to the basolateral cell surface in MDCK and LLC-PK1 cells. *J Biol. Chem.* 276:22565-22572

Yuan Z, Teasdale RD. (2002) Prediction of Golgi Type II membrane proteins based on their transmembrane domains. *Bioinformatics*. 18: 1109-1115.

The FANTOM Consortium and The RIKEN Genome Exploration Research Group Phase I & II Team (Teasdale RD) (2002) Analysis of the Mouse Transcriptome based upon Functional Annotation of 60,770 full length cDNAs *Nature*. 420: 563-73.

Grimmond, S., Miranda, K., Yuan, Z., Davis, M.J., Hume, D.A., Yagi, K., Tominaga, N., Bono, H., Hayashizaki, Y., Okazaki, Y., RIKEN GER Group Members and Teasdale, R.D. (2003) The mouse secretome. Functional classification of the proteins secreted into the extracellular environment. *Genome Res.*, 13(6B): 1350-9.

Rohan Teasdale

MODELLING AND VISUALISING REGULATORY NETWORKS

Kevin Burrage

Research

This group works on developing simulation and visualization methodologies for understanding the behaviour of genetic regulation. The simulation models take into account stochastic effects, while the visualisation focuses on 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 a new class of discrete stochastic methods based on Poisson processes that more accurately reflect the underlying cellular models.

The stochastic simulation algorithm (SSA) due to Gillespie has become a fundamental tool for simulating individual molecular reactions in the modelling of cellular behaviour and regulation. However, this method can be computationally quite demanding. In response we have introduced a new class of numerical methods, called Poisson Runge-Kutta methods, to generalise this approach.

A general formulation and order theory for this class of Poisson Runge-Kutta methods is given, and high order methods have been constructed. Numerical simulations illustrate the performance of these new simulations on some important cellular models.

Not only have investigated bi-stability and switching issues in the Genetic Regulatory networks of lambda phage using these approaches, we have also started to develop a three dimensional visualisation framework for simulating cellular models, both within a cell and for colony of cells.

Key Publications Since 2000

Burrage, K., Burrage, P.M. and (2004) Numerical methods for solutions of stochastic differential equations: an overview. *Proceedings the Royal Society of London.* Series 460:373-402.

Burrage, K. and Tian, T. (2004) Stochastic Runge-Kutta methods stochastic differential equations. *Numerical Mathematics* 44:21

Burrage, K., Tian, T. and Burrage, (2004) A multi-scaled approach for simulating chemical reaction systems. *Progress Biophysics and Molecular Biology* 85:217-234.

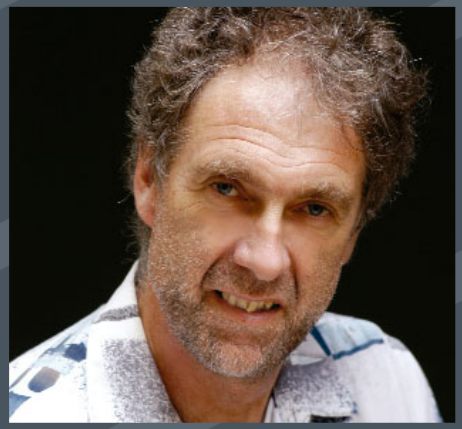
Hamilton, N., Burrage, K., Ragan, M.A. and Huber, T. (2004) Protein contact prediction using patterns of correlation. *Proteins: Structure, Function, and Bioinformatics* 56:679-684.

Tian, T. and Burrage, K. (2004) Binomial leap methods for simulating stochastic chemical kinetics. *Journal of Chemical Physics* 121:10356-10364.

Tian, T. and Burrage, K. (2004) Bistability and switching in the lysis/lysogeny genetic regulatory network of bacteriophage lambda. *Journal of Theoretical Biology* 227:229-237.

Turner, T.E., Schnell, S. and Burrage, K. (2004) Stochastic approaches for modelling in vivo reactions. *Computational Biology and Chemistry* 28:165-178.

Burrage, K. and Tian, T. (2004) Poisson Runge-Kutta methods for chemical reaction systems. *In:* Advances in Scientific Computing and Applications, (Y. Lu W. Sun and T. Tang Eds), Beijing and New York: Science Press, pp. 82-96.



Kevin Burrage

Research

My research in statistics is in the related fields of classification, cluster and discriminant analyses, 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.

A common theme of my research in these fields has been statistical computation, with particular attention being given to the computational aspects of the statistical methodology. This computational theme extends to my interests in the field of data mining. More recently, I have become actively involved in the field of bioinformatics with the focus on the statistical analysis of microarray gene expression data.

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 diagnosis tumours.

However, the complexity of tumours makes it is 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 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.

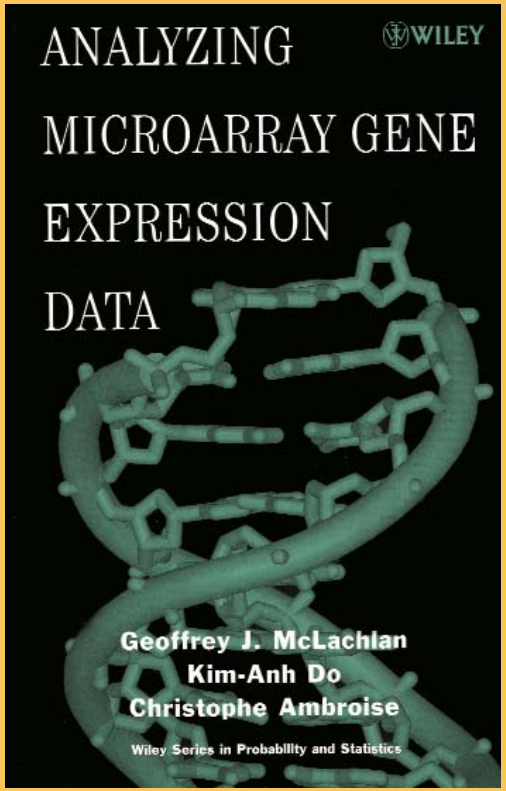
Research Projects

- Data mining and computational statistics
- Statistical analysis of microarray gene-expression data for the development of disease diagnostics.
- Develop diagnostic methods for cancer, using multiple molecular indices in conjunction with clinical factors.

Lab members

Research Officers:
Richard Bean
Liat Jones
Kui Wang

PhD Students:
Soong Chang
Justin Zhu
Katrina Monico



Key Publications Since 2000

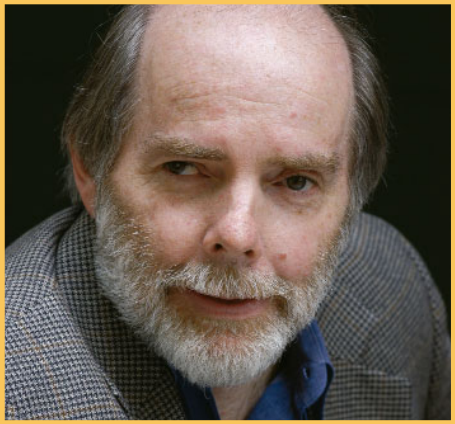
Ambroise, C. and McLachlan, G.J. (2002). Selection bias in gene extraction on the basis of microarray gene expression data. *Proceedings of the National Academy of Sciences USA* 99, 6562-6566.

McLachlan, G.J., Bean, R.W., and Peel, D. (2002). A mixture model-based approach to the clustering of microarray expression data. *Bioinformatics* 18, 413-422.

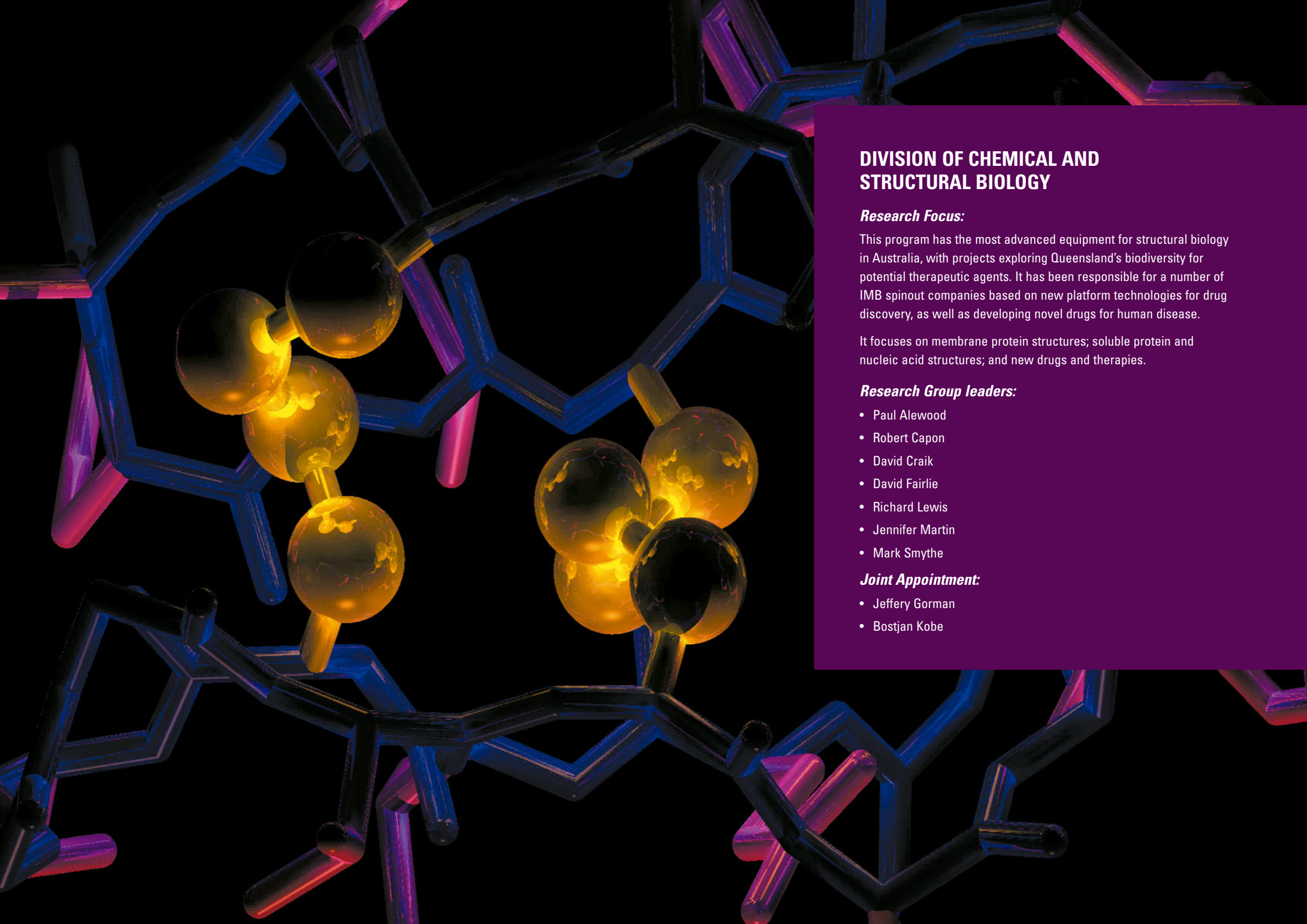
McLachlan, G.J., Do, K.-A., and Ambroise, C. (2004). Analyzing Microarray Gene Expression Data. Hoboken, New Jersey: Wiley.

McLachlan, G.J. and Khan, N. (2004). On a resampling approach for tests on the number of clusters with mixture model-based clustering of tissue samples. *Journal of Multivariate Analysis* 90, 90-105.

Ben-Tovim Jones, L., Ng, S.K., Ambroise, C., Monico, K., Khan, N., and McLachlan, G.J. (2005). Use of microarray data via model-based classification in the study and prediction of survival from lung cancer. In *Methods of Microarray Data Analysis IV* J.S. Shoemaker and S.M. Lin (Eds.). New York: Springer, pp. 163-173.



Geoffrey McLachlan



DIVISION OF CHEMICAL AND STRUCTURAL BIOLOGY

Research Focus:

This program has the most advanced equipment for structural biology in Australia, with projects exploring Queensland's biodiversity for potential therapeutic agents. It has been responsible for a number of IMB spinout 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
- Robert Capon
- David Craik
- David Fairlie
- Richard Lewis
- Jennifer Martin
- Mark Smythe

Joint Appointment:

- Jeffery Gorman
- Bostjan Kobe

BIOACTIVE MOLECULES, CHEMICAL PROTEIN SYNTHESIS AND PROTEOMICS

Paul Alewood

RESEARCH

The research interests of our group include the discovery and total synthesis of toxins from Australia"s venomous creatures, the chemical synthesis of proteins and bioactive peptides, development of new synthetic and analytical methods, and proteomics.

Special emphasis is placed on determining the structure-function relationships of natural and designed molecules. This has led to the development of three new classes of drugs addressing chronic pain and congestive heart failure.

Research projects

- New drugs from Australia's venomous creatures
- Discovery of new bioactives from bovine and human milk
- New-generation antibiotics from specific sources of Australian honey
- Fast chemistry to enable the synthesis of bioactive proteins.

Conferences/Workshops

Co-Founder of the Australian Peptide Society and Program coordinator of Biannual Symposia

Founder and chair of the Venoms to Drugs Symposia on Heron Island

Awards

Finalist, Eureka Prize 2004 (Interdisciplinary Scientific Research)

External Duties

Consultant, Xenome Ltd

Board Member, ACCMER

Current ARC International Reader

Internal Duties

Head, Division of Chemistry and Structural Biology, IMB

Member, IMB Executive Committee

Member, Queensland Bioscience Precinct Safety Committee

Lab members

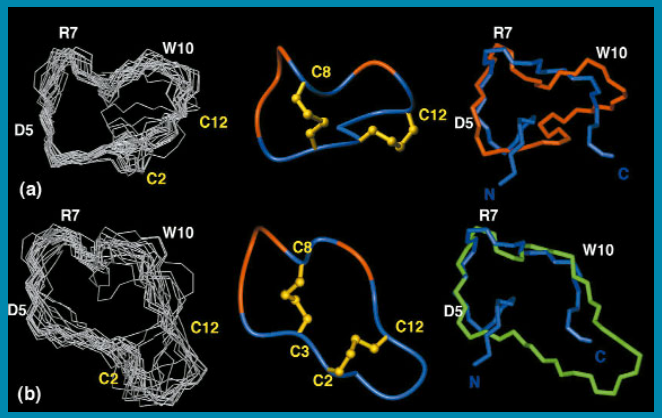
Senior Research Officers:
Paramjit Bansal, Peter Cassidy, John Holland

Research Officers:
Christopher Armishaw, Raj Gupta

Research Assistants:
Aaron Poth

PhD Students:
Gene Hopping, Lita Imperial, Jean Jin, Ryan O'Donnell, Natalie Steen

Visiting Researchers:
Ian Smith, Ed Nice



Key Publications Since 2000

RJ Lewis, D Adams, I.Sharpe, M Loughnan, T Bond, L Thomas, A. Jones, J-L Matheson, R Drinkwater, K Nielsen, DJ Craik and PF Alewood. (2000) Structure and Activity of novel omega-conotoxins from Conus catus. *J Biol Chem*, 275:35335-35344.

I Sharpe, J Gehrmann, M Loughnan, L Thomas, D Adams A Atkins, DJ Craik, D Adams PF Alewood and RJ Lewis, (2001) Two new classes of conopeptides inhibit the alpha1-adrenoceptor and the noradrenaline transporter *Nature Neuroscience*, 4:902-907.

DR Englebretsen, B Garnham, PF Alewood, (2002) Total Chemical Synthesis of the 101 Residue Protein Early Pregnancy Factor [Y(CH2S)28-29, 56-57, 76-77] by Sequential Thioether Chemical Ligation. *J Org Chem*, 67;5883-5890.

RC Hogg, G Hopping, DJ Adams, PF Alewood and D Bertand (2003) Alpha conotoxins PnIA and [A10L]PnIA stabilize different states of the alpha7 L247T nicotinic acetylcholine receptor. *J Biol Chem,* 278:26908-26914

John Holland, Hilton Deeth and Paul Alewood (2004) Proteomic analysis of kappa-casein micro-heterogeneity. *Proteomics*, 4:743-752.

Paul Alewood

Research

The Centre for Molecular Biodiversity (CMB) is a thematic biodiscovery research focus within the IMB, with a mission to explore and develop naturally occurring bioactive molecules from Australian plants, animals and microbes. Molecular products discovered by the CMB have application in the areas of human and animal health, and crop protection, and knowledge of these substances will advance Australia's national scientific and economic interests.

Research Projects

- Anticancer agents from Australian marine biodiversity:
- The discovery and development of novel broad spectrum antivirals.
- Novel antibiotics that target virulence determinants.
- Novel sodium ion channel modulators from Australian cephalopods.
- Australian Microbial Biodiscovery: Exploration of Bioactive Chemical Space
- Accelerated Anticancer Biodiscovery
- Novel marine-derived drug leads for the glycine and GABAA ion channel receptors

External Duties:

Member, Queensland Government Biodiversity Committee

Internal Duties

IMB Postgraduate Co-ordinator

Lab members

Senior Research Officer:
Mike Stewart

Research Officers:
Nick Trotter, Ertong Wang

Research Assistant:
Ben Mooney

PhD Students:
Ben Clark, Louise Dempster, Leith Fremlin, Ed Liu, Michelle McNally, Ranjala Ratnayake

Vacation and Undergraduate Scholars:
Chad Buxton, Tin Yan Chan, Lydia Hill, Cathy Wang, Mattew Smede, Myrtle Stibbe,

CSIRO Student Research Scheme:
Hannah Wood, Leanna Wang

Picture courtesy Dr Mark Norman

Key Publications Since 2000

Stewart, M., Capon, R. J., Lacey, E., Tennant, S. & Gill, J. H. (2005). Calbistrin E and two other new metabolites from an Australian isolate of *Penicillium striatisporum. J. Nat. Prod.* 68:581-584

Capon, R., Skene, C., Liu, E. H.-T., Lacey, E., Gill, J. H., Heiland, K. & Friedel, T. (2004)Nematocidal thiocyanatins from a southern Australian marine sponge, *Oceanapia* sp. *J. Nat. Prod.* 67:1277-1282.

Capon, R. J., Skene, C., Liu, E. H.-T., Lacey, E., Gill, J. H., Heiland, K. & Friedel, T. Esmodil: An acetylcholine mimic resurfaces in a southern Australian marine sponge *Raspalia (Raspailia)* sp. *Nat. Prod.* Res. 18, 305-309 (2004).

Capon, R. J., Skene, C., Stewart, M., Ford, J., O'Hair, R. A. J., Williams, L., Lacey, E., Gill, J. H., Heiland, K. & Friedel, T. Aspergillicins A-E: five novel depsipeptides from the marine-derived fungus *Aspergillus carneus. Org. & Biomol. Chem.* 1:1856-1862 (2003).

Capon, R. J., Skene, C., Vuong, D., Lacey, E., Gill, J. H., Heiland, K. & Friedel, T. (2002) Equilibrating isomers: bromoindoles and a seco-xanthine encountered during a study of nematocides from the southern Australian marine sponge *Hymeniacidon* sp. *J. Nat. Prod.* 65:368-370.

Rob Capon

Research

Our group uses Nuclear Magnetic Resonance 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.

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.

Research Projects

- Bioengineering of Circular Proteins
- Discovery of New Circular Proteins
- Structure activity studies of conotoxins
- Plant proteinase inhibitors

Awards

Australian and New Zealand Society for Magnetic Resonance 2004 Medal

Eureka Prize Finalist (with D Adams, P Alewood and R Lewis)

External Duties

Director, Kalthera Pty Ltd

Director, Cyclagen Pty Ltd

Member Editorial Board, Biopolymers (Peptide Science)

Member Editorial Board, Current Medicinal Chemistry

Pharmaceutical Sciences Section Editor, Handbook of Modern Magnetic Resonance

Guest Editor, Current Protein and Peptide Science (2004), Volume 5, Issue 5.

Internal Duties:

Member IMB Postgraduate Committee

Coordinator NMR Facility

Honours Supervisor, UQ Bachelor of Biotechnology

Honours Supervisor, UQ School of Molecular and Microbial Sciences

Lab members

Senior Research Officers:
Norelle Daly, Justine Hill, Ute Marx, Amanda Nourse

Research Officers:
Richard Clark, Masa Cemazar, Michelle Colgrave, Julie Dutton, Johan Rosengren, Horst Schirra, Manuela Trabi

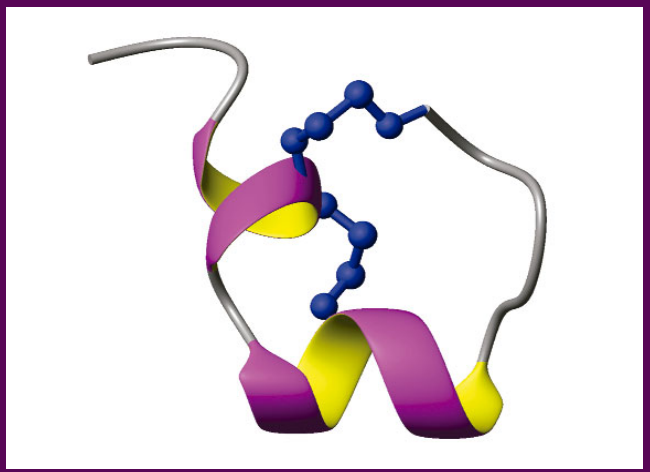
Research Assistants:
Rekha Bharathi, Fiona Foley

PhD Students:
Daniel Barry, Christian Gruber, David Ireland, Michael Korsinczky, Erica Lovelace, Emma Millard, Jason Mulvenna, Manuel Plan, Maria Quimo, Angela Salim, Lillian Sando, Ivana Saska, Shane Simonsen

Masters Student:
Philip Nguyencong

Honours Student:
Freda Jen, Tim Stephens

Undergraduate Students:
Bernie Patzold, Ernie Yulyaningsih, Damara McAndrew



Key Publications Since 2000

Jennings C, West J, Waine C, Craik D, Anderson M. (2001) Biosynthesis and insecticidal properties of plant cyclotides - the cyclic knotted proteins from *O. affinis*. PNAS 98:10614-10619.

Trabi M, Craik D J: Circular proteins – no end in sight. (2002) *TRENDS in Biochemical Sciences* 27:132-138. [Cover Feature]

Rosengren K J, Daly N L, Plan M R, Waine C, Craik D J: Twists, knots and rings in proteins: structural definition of the cyclotide framework. (2003) *Journal of Biological Chemistry* 278:8606-8616. [Cover feature]

Rosengren K J, Clark R J, Daly N L, Goransson U, Jones A, Craik D J. (2003) Microcin J25 has a Threaded Sidechain-to-Backbone Ring Structure and Not a Head-to-Tail Cyclized Backbone. *J. Amer. Chem. Society* 125:12464-12474.

Trabi M, Craik D J (2004) Tissue specific expression of head-to-tail cyclised mini-proteins in Viola species (Violaceae) and structure determination of the root cyclotide vhr 1. *The Plant Cell* 16:2204-2216.

David Craik

Research

We work at the interface of chemistry, biology and disease. Chemistry underpins all aspects of the molecular biosciences. Interactions between proteins and either small molecules, proteins, DNA or RNA determine the outcomes of all biological processes. We aim to use rational chemical intervention to mimic proteins, inhibit enzymes, or antagonize receptors that are pivotal in normal human physiology, aberrant in disease, or crucial mediators of infection.

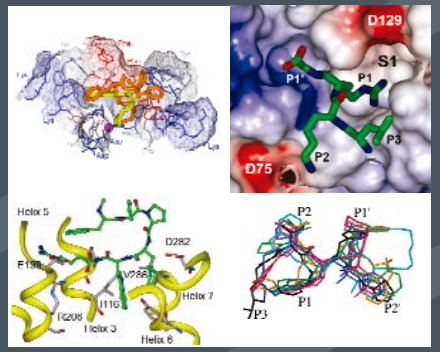
Compounds created by our group are used as biological probes to better understand the roles of vital proteins in life, ageing, and death. They are also developed into drug leads and development candidates for preclinical and clinical trials.

Chemistry researchers in our group develop expertise in computer-assisted molecular drug design, chemical synthesis methodologies, and molecular structure determination. Biology researchers in our group study enzymes and cellular receptors, use small molecules to interfere with protein-protein interactions, study structures of protein-ligand complexes, and investigate mechanisms of biological processes, disease development, and drug action.

Researchers gain interdisciplinary skills in diverse fields of biology, including enzymology, biochemistry, cell biology, immunology, pharmacology, oncology, parasitology, virology, and neurobiology.

Research Projects

- Fundamental chemical studies
- Drug design and discovery and disease
- Molecular recognition and protein surface mimics
- GPCRs, proteases and transcription factors



Lab members

Senior Research Officers:
John Abbenante, Bob Reid, Yogendra Singh, Martin Stoermer

Research Officers:
Huy Hoang, Giang Le, Andrew Lucke, Joel Tyndall, Philip Sharpe

Research Assistants:
Bernadine Flannigan, Tessa Nall, Renee Beyer, Jacky Suen

Students:
Nick Shepherd, Grant Barry, Dhiraj Hans, Praveen Madala, Tom Guthrie, Gavin Bryant, Renee Beyer Aarti Kishore Jacky Suen, Nicole Wheatley, Michelle Thomas, James Gardiner, Jade Blakeney, Chris Buhman, Dean Jennins

Key Publications Since 2000

Leung, D; Abbenante, G; Fairlie, DP. (2000) Protease Inhibitors: Current Status & Future Prospects, *J. Med. Chem.*, 43:305-341.

Fairlie, D. P.; Tyndall, J. D. A.; Reid, R. C.; Wong, A. K.; Abbenante, G.; Scanlon, M. J.; March, D. R.; Bergman, D. A.; Chai, C. L. L.; Burkett, B. A. (2000) Conformational Selection Of Inhibitors and Substrates By Proteolytic Enzymes : Implications for Drug Design and Polypeptide Processing, *J. Med. Chem.*, 43:1271-1281.

March, D. R.; Proctor, L. M.; Stoermer, M. J.; Sbaglia, R.; Abbenante, G.; Reid, R. C.; Wadi, K.; Paczkowski, N.; Tyndall, J. D. A.; Taylor, S. M.; Fairlie, D. P. (2004) Potent Cyclic Antagonists Of The Complement C5a Receptor On Human Polymorphonuclear Leukocytes. Relationships Between Structures and Activity. *Molecular Pharmacology,* 65:868-879.

Shepherd, N. E.; Hoang, H. N.; Abbenante, G.; Fairlie, D. P. (2005) Single Turn Alpha Helical Peptides With Exceptional Stability In Water. *J. Am. Chem. Soc.*, 127:2974-2983.

Singh, Y.; Stoermer, M. J.; Lucke, A.; Guthrie, T.; Fairlie, D. P. (2005) Structural Mimicry of Two Cytochrome b562 Interhelical Loops Using Macrocycles Constrained By Oxazoles and Thiazoles. *J. Am. Chem. Soc.*, 127, 6563-72.

Tyndall, J. D. A.; Pfeiffer, B.; Abbenante,G.; Fairlie, D. P. (2005) Over 100 Peptide-Activated G Protein-Coupled Receptors Recognize Ligands With Turn Structure. *Chemical Reviews,* 105:793-826.

David Fairlie

Research

My group's research focuses is on the discovery and characterization of conotoxins produced in the venom glands of cone snails (see Figure 1). These highly structures peptides act at ion channels, receptors and transporters found in the membranes of most cells. We are especially interest in those acting on the nervous system. Some of these peptides have clinical potential.

A major focus of the group is to develop research tools and potential therapeutics for chronic pain. This research involves assay-guided isolation of venom peptides, peptide synthesis, tissue pharmacology, radioligand binding and electrophysiological studies, peptide structure elucidation, receptor mutagenesis, modelling and docking. Our research received a major boost from the NHMRC with the award of a five-year Program Grant to develop new ways to understand and treat pain.

Several of the group's discoveries are being commercially developed. Currently, AMRAD is developing AM336 (omega-CVID) for chronic pain and Xenome Ltd is developing Xen2174 (an analogue of omega-MrIA). Other conotoxins we discovered may have potential in the treatment of cardiovascular disorders and benign prostatic hyperplasia.

Research Projects

- Discovery of new conopeptides useful in the treatment of pain
- Determining sites of conotoxin action at;
  - nicotinic acetylcholine receptor
  - calcium channels
  - sodium channels
  - the noradrenaline transporter
  - adrenoreceptor interaction
- Discovery of new bioactive venom peptides
- Identification of new anti-cancer agents from marine biodiversity
- Cone snail venom characterisation

Awards

Eureka Prize Finalist (with D. Adams, P. Alewood and D. Craik)

External Duties

Head of Pharmacology, Xenome Ltd

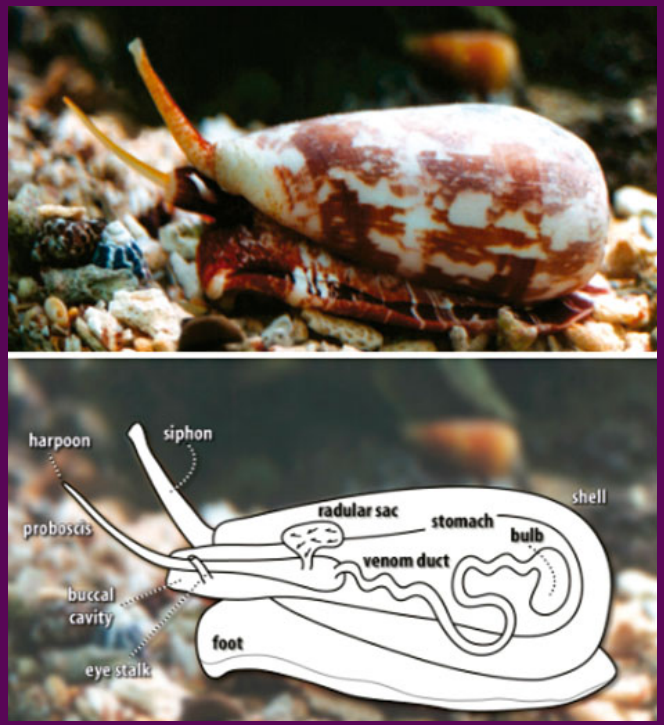
Lab members

Research Officers:
Brooke Purdue, Nicole Lawrence, Denise Adams, Marion Loughnan, Annette Nicke, Tina Schroeder, Iain Sharpe

Research Assistants:
Trudy Bond, Linda Thomas

PhD Students:
Trudy Bond, Sebastien Dutertre, Marion Loughnan, Jenny Ekberg, Fredrik Hellqvist, Christina Schroeder, Dimitra Temelcos, Takahiro Yasuda

Visiting Scholars:
Professor John Wood, University College, London



Key Publications Since 2000

Lewis RJ, Nielsen KJ, Craik DJ, Loughnan ML, Adams DA, Sharpe IA, Luchian T, Adams DJ, Bond T, Thomas L, Jones A, Matheson JL, Drinkwater R, Andrews PR, Alewood PF. (2000) Novel w-conotoxins from *Conus catus* discriminate among neuronal calcium channel subtypes. J. Biol. Chem. 275, 35335-35344.

Sharpe IA, Gehrmann J, Loughnan ML, Thomas L, Adams DA, Atkins A, Palant, E., Craik, DJ, Adams DF, Alewood PF, Lewis, RJ (2001) Two new classes of conopeptides inhibit the a1-adrenoceptor and noradrenaline transporter. *Nature Neurosci.* 4, 902-907.

Lewis RJ and Garcia ML (2003) Therapeutic potential of venom peptides. *Nature Reviews Drug Discovery* 2, 790-802.

Mould J., Yasuda T., Schroeder C.I., Beedle A.M., Clinton J. Doering C.J., Zamponi G.W., Adams D.J. and Lewis R.J. (2004) The a2d auxiliary subunit reduces affinity of w-conotoxins for recombinant N-type calcium channels *J. Biol. Chem.* 279, 34705-14

Daly N.L., Ekberg J.A., Thomas L., Adams D.J., Lewis R.J. and Craik D.J. (2004) Structures of μO-conotoxins from Conus marmoreus. Inhibitors of tetrodotoxin (TTX)- sensitive and TTX-resistant sodium channels in mammalian sensory neurons. *J. Biol. Chem.* 279, 25774-25782.

Richard Lewis

Research

We are interested in understanding the role of proteins in disease and developing novel compounds to modify the functions of disease-causing proteins. We use protein crystallography as the major biophysical approach to investigate protein structure and function, protein interactions, and as the foundation for inhibitor design.

A world class protein crystallography facility has been linked to a high throughput protein expression facility for protein structure determination. Together these facilities can be used to examine proteins of prime importance to human health. This research will underpin the future development of new medicines.

Research Projects

- Discovery and validation of new drug targets for chronic inflammatory disease
- Novel antibacterial and anti-virulence agents
- Protein folding and disease
- Development of adrenaline synthesis inhibitors
- Development of platform technologies for:
  - Drug discovery using X-ray crystallography
  - High through put crystallography

External Duties

Council member, National Science and Technology Centre (Questacon)

President, Society of Crystallographers in Australia and New Zealand

Member, National Scientific Advisory Committee to the Australian Synchrotron

Member, Protein Crystallography Beamline Advisory Panel, Australian Synchrotron

Co-organiser, The Protein Crystallisation Workshop 2004.

Member, Program Committee, 2005 International Union for Crystallography Congress.

Lab members

Senior Research Officer:
Shu-Hong Hu

Research Officers:
Nathan Cowieson, Niranjali Gamage, Christine Gee, Begona Heras, Gautier Robin

Research Assistants:
Casey Pfluger, Mareike Kurz

PhD Students:
Catherine Latham

Honours Student:
Rosemary Harrison

Undergraduate Students:
Nyssa Drinkwater, Natalie Saez

Visitors:
Prof Tom Alber, University of California Berkeley
Dr Munish Puri, Punjabi University
Ms Beth Wensley, University of Bath

Internal Duties

Member, University Research Committee, UQ.

Chair, Committee for UQ Women's Postdoctoral Fellowships and UQ Travel Awards

Chair, Committee for SRC Protein Expression Facility.

Consultations

X-ray crystallography, Progen Industries Limited, QLD 2004

Protein Structure, PanBio Limited, QLD 2004

Key Publications Since 2000

Martin JL, Begun J, McLeish MJ, Caine J, and Grunewald G (2001) "Getting the adrenaline going: crystal structure of the adrenaline-synthesizing enzyme PNMT" *Structure* 9, 977- 985

Edeling MA, Guddat LW, Fabianek RA, Thöny-Meyer L and Martin JL (2002) "Crystal structure of CcmG/DsbE at 1.14 Å resolution: high fidelity reducing activity in an indiscriminately oxidizing environment" *Structure* 10, 973-979

Gamage NU, Duggleby RG, Barnett AC, Tresillian M, Latham CF, Liyou NE, McManus ME and Martin JL (2003) "Structure of a human carcinogen converting enzyme, SULT1A1: structural and kinetic implications of substrate inhibition" *J Biol Chem* 278, 7655-7662

Heras B, Edeling MA, Schirra HJ, Raina S and Martin JL (2004) "Crystal structures of the DsbG disulfide isomerase reveals an unstable disulfide" *PNAS USA* 101, 8876-81

Aagaard A, Listwan P, Cowieson N, Huber T, Ravasi T, Wells C, Flanagan JU, Kellie S, Hume DA, Kobe B, Martin JL (2005) "An inflammatory role for the mammalian carboxypeptidase inhibitor latexin: relationship to cystatins and the tumour suppressor TIG1" *Structure* 13:309–317.

Jennifer Martin

Research

Our research focuses on advancing drug design and synthetic organic chemistry to discover novel biologically active molecules against numerous targets and for several therapeutic indications.

To this end, we have recently discovered conserved molecular recognition features that are enriched on macromolecular binding sites of proteins. We have also shown that many distinct folds share the same recognition features and that these are well buried in the interface and resemble protein hotspots. Such findings are currently being exploited in protein folding, further understanding protein evolution and the development of molecules to modulate protein function.

We have also identified the shared molecular recognition features of small molecule protein binding sites. These conserved features are found in diverse proteins and help explain how a common molecular substructure (privileged substructure) can to bind to unrelated proteins. Such common features are being used for the discovery of new privileged substructures.

Finally we wish to develop a new paradigm in drug discovery based on identifying molecules that match target classes. A target class, by our definition, is a series of proteins that share common molecular recognition features. We are using drug design tools to discover molecules that match these common recognition elements and have developed the required synthetic approaches to prepare arrays of such compounds.

We are applying such strategies to the discovery of small drug-like molecules that are modulating cytokines, GPCRs and kinases and we are focused on developing new preclinical candidates for obesity, asthma, cancer and microbial infections.

Research Projects:

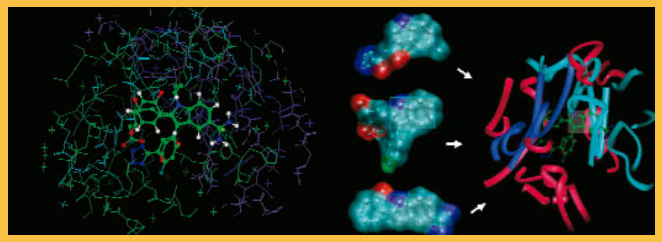
- New treatments for asthma
- Improving the efficiency of drug discovery; strategies for sampling biologically relevant chemistries.
- New treatments for microbial infections
- Developing new computational algorithms for efficient drug discoveries.

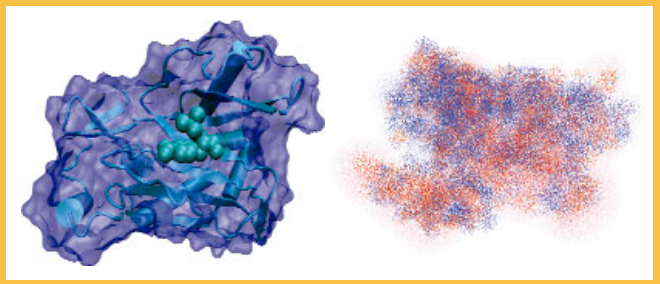
Lab members

Senior Research Officer:
Greg Bourne

Research assistants:
Justin Coughlan
Ngari Teakle
Jill Turner

PhD Students:
Gerald Hartig
Doug Horton
Andrew McDevitt





Key Publications Since 2000

Battersby, B.J., Bryant, D.E., Meutermans, W., Smythe, M.L., Trau, M., (2000) Chemical Libraries of unlimited size: Colloidal barcoding in combinatorial chemistry, *J. Am. Chem. Soc*, 122:2138-9.

Bourne, G.T., Golding, S.W., McGeary, R.P., Meutermans, W.D.F., Jones, A., Marshall, G.R., Alewood, P.F., and Smythe, M.L., (2001) The Development and Application of a Novel Safety- Catch Linker for BOC-Based Assembly of Libraries of Cyclic Peptides, *Journal of Organic Chemistry,* 66:7706-7713.

Horton, D.A., Bourne, G.T., 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., Smythe, M.L., (2003) Difficult Macrocyclisations: New Strategies for Synthesising Highly Strained Cyclic Tetrapeptides, *Organic Letters,* 5:2711-4.

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

Mark Smythe

RESEARCH

Research carried out by this new group will exploit the platform of contemporary protein chemistry and proteomics. This platform is broadly applicable to defining the chemical features of purified proteins, interactions between proteins at the molecular and cellular levels and the dynamics of the protein repertoires of cells in response to disease states and other stimuli.

Research topics of particular interest involve the interactions of viral proteins in assembled virus particles interactions between intracellular proteins and viral proteins during morphogenesis (virus particle formation) and interactions of viral proteins with cell membrane receptors during infection of cells.

Our research will be underpinned by our mass spectrometry expertise for the analysis of proteins and complemented by our excellent mass spectrometry infrastructure.

In addition to academic interest, our work has the potential to produce important leads for development of therapeutic agents to treat viral infections and other important medical conditions.

This group integrates the proteomics activities of CSIRO Livestock Industries through the establishment of a joint laboratory, as well as accommodating the proteomics needs of the SRC for Functional and Applied Genomics.

Research Projects:

- Interaction and structures of proteins in assembled virus particles
- Interactions of viral proteins with host cell proteins during infection and assembly.
- Regulation of signal-activated transcription factors by translational modifications and protein-protein interactions.

Lab members

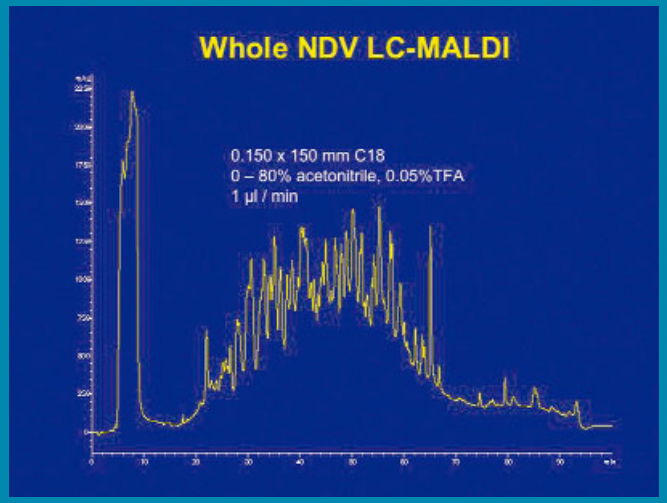
Research Officer:
Marcus Hastie

Professional Officer:
Alun Jones

Research Assistant:
Tristan Wallis

PhD Student:
Keyur Dave

Honours Student:
Au Yeung Sze Man



External Duties:

Member, Editorial Board, Molecular and Cellular Proteomics
Member, Editorial Board, Protein and Peptide Letters
Member, Organising Committee, Lorne Protein Conference
Grants assessor (national and international) peer review journals, research proposals, and examiner PhD awards.

Key Publications Since 2000

Lando, D., Peet, D. J., Whelan, D. A., Gorman, J. J. and Whitelaw, M. L. (2002) Asn Hydroxylation of the HIF Transactivation Domain: A Hypoxic Switch. *Science*. 295, 858-861.

Lando, D., Peet, D. J., Gorman, J. J., Whelan, D. A., Whitelaw, M. L. and Bruick, R. K. (2002) Identification of the asparagine hydroxylase responsible for regulating the transcriptional activity of HIF. *Genes and Development*. 16, 1466-1471.

Gorman, J.J., Wallis, T. P. and Pitt, J. J. (2002) Determination of Disulfide Bond Arrangements of Proteins by Mass Spectrometry. *Mass Spectrometry Reviews,* 21, 183-216.

Wallis, T. P., Huang, C.-Y., Nimkar S. B., Young P. R. and Gorman, J. J. (2004) Determination of the Disulfide Bond Arrangement of Dengue Virus NS1 Protein. *J. Biol. Chem.* 279, 20729-20741.

Purcell, A. W. and Gorman J. J. (2004) Immunoproteomics: Mass spectrometry based methods to study the targets of the immune response. *Molecular and Cellular Proteomics,* 3, 193-208.

Jeffrey Gorman

STRUCTURAL BIOLOGY OF PROTEIN – PROTEIN INTERACTIONS

Bostjan Kobe

Research

Our research focus on protein structure and function, with the emphasis on understanding the structural basis of interactions formed by these macromolecules. The primary technique used in the laboratory is X-ray crystallography, combined with a plethora of other molecular biology, biophysical and computational techniques. Our research vision is to apply structural biology in functional annotation of proteins (functional genomics).

Research Projects

- Specificity of signal transduction pathways
- Regulation of nuclear import
- Structural genomics of macrophage proteins

External Duties

Chair, Queensland Protein Group

Member of Editorial Board, Journal of Structural and Functional Genomics

Peer review

Grant applications:

- NHMRC,
- ARC,
- Wellcome Trust,
- Clive and Vera Ramaciotti Foundation,
- National Services and Engineering Research Council (Canada),
- Health Research Council (NZ),
- University of Adelaide

Synchrotron beam-time applications:

- Advanced Photon Source,
- Swiss Light Source

Journals (including):

- Science
- Nature Structural Biology
- EMBO Journal
- Structure,
- Journal of Molecular Biology
- Proceedings of the National Academy of Science USA

Lab members

Research Officers:
Jade Forwood, Pawel Listwan, Lynn Gregory-Pauron, Ross Brinkworth

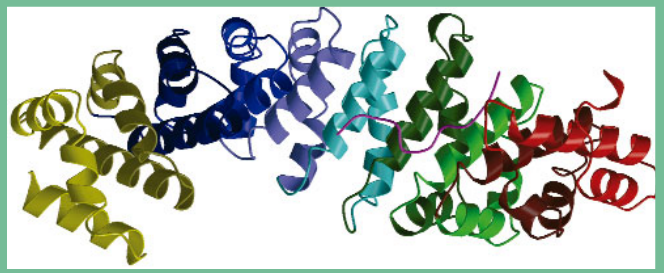
Research Assistant:
Trazel Teh

PhD Students:
Robert Serek, Sundy Yang, Thorsten Kampmann Anderson Wang, Dmitri Mouradov

MPhil Students:
James Clark, Carmel Walsh

Honours Student:
Ari Craven

Visiting Researcher:
Marcos R. Fontes



Internal Duties:

Member, Research Committee, School of Microbial and Molecular Sciences, UQ

Member, IT Committee, School of Microbial and Molecular Sciences, UQ

Member, Managing Committee, Protein Expression Facility, SRC for Functional and Applied Genomics

Key Publications Since 2000

Aagaard A, Listwan P, Cowieson N, Huber T, Ravasi T, Wells CA, Flanagan JU, Kellie S, Hume DA, Kobe B, Martin JL (2005) An inflammatory role for the mammalian carboxypeptidase inhibitor latexin: relationship to cystatins and the tumor suppressor TIG1. *Structure*. 13:309-17.

Lay, C.S., Wilson, K.A., Kobe, B., Kemp, B.E., Drummer, H.E. & Poumbourios, P. (2004) Expression and biochemical analysis of the entire HIV-2 gp41 ectodomain: determinants of stability map to N- and C-terminal sequences outside the 6-helix bundle core *FEBS Letters* 567:183-188.

Huber, T & Kobe, B. (2004) Comment on 'Protein isoelectric point as a predictor for increased crystallization screening efficiency' *Bioinformatics* 20:2169-2170.

Fontes MR, Teh T, Toth G, John A, Pavo I, Jans DA, Kobe B. (2003) Role of flanking sequences and phosphorylation in the recognition of the simian-virus-40 large T-antigen nuclear localization sequences by importin-alpha. *Biochem J.* 375:339-49.

Brinkworth RI, Breinl RA, Kobe B. (2003) Structural basis and prediction of substrate specificity in protein serine/threonine kinases. *Proc Natl Acad Sci U S A*. 100:74-9.

Bostjan Kobe

9.

Australian Collaborative Research

Further underlining the Institute's commitment to research excellence, IMB Group Leaders are core partners and participate in a Special Research Centre, several Cooperative Research Centres (CRC), a major National Research Facility, Australian Research Council (ARC) Centres of Excellence (COE) and an ARC Centre.

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 benefit to the country.

Involvement in these ventures reflects very highly on the participating researchers indicating the high 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 (SRC) provides and develops technologies enabling world-class research in the field of genomics. The SRC comprises an integrated network of core technologies including computational biology, structural biology, proteomics, animal transgenics service, as well as a microarray facility.

The past year has been one of consolidation for the SRC and for the IMB, host of the majority of SRC affiliated scientists.

A major highlight of 2004 was the installation of a TOF-TOF mass spectrometer, which greatly enhanced the throughput and sophistication of proteomic tools available to the SRC. This has led to a significant expansion in the number of research groups applying proteomic approaches to biological questions. In the area of functional genomics, the appointment of Andrew Perkins as well as successful funding applications and support from the IMB has enabled the establishment of a world-class zebrafish facility to complement our focus on the mouse as a vertebrate model organism.

The establishment of the Queensland Brain Institute (QBI) and the Australian Institute for Bioengineering and Nanotechnology (AIBN) has increased the depth of functional genomics research on the UQ campus and expanded demand for services provided by the SRC facilities. In the area of protein expression and structure determination, Dr. Linda Lua was appointed to head the Protein Expression Facility, bringing a wealth of experience in baculovirus expression in insect cells, and Dr. Ute Marx's arrival provided expertise to support a major initiative in NMR-based protein structure determination, complementing our existing strength in X-ray crystallography.

Continuing our active engagement with transcriptomics, SRC affiliates remained major players in the international FANTOM (Functional Annotation of Mouse) consortium, headed by Japanese colleagues at the RIKEN Genome Sciences Centre. The outcomes will be published in early 2005, and will provide the first comprehensive overview of the transcriptional landscape of the mammalian genome.

If 2003 was a year of transition, 2004 was a year in which the investments in facility development and personnel began to bear serious scientific fruit. The new resources and common location provide a powerful foundation for the SRC to fulfil its aim of providing all of the links in the pipeline from gene discovery to functional assignment and application. The future will see the coordinated application of these resources to provide meaningful description of biological systems such as mammalian cells, from the structure, location and function of individual proteins to the control networks that allow the system to respond to its environment in development, differentiation and disease.

Australian Phenomics Facility

This major national research facility enables Australian and international researchers to define the mammalian phenome: how the estimated 40,000 genes in the genome sequence of humans and other mammals regulate the phenotype or behaviour of cells, tissues and the body.

The completion of human and mouse genome sequences catalysed an international race to harness more efficient methods of disrupting gene function in the mammalian genome so as to illuminate phenotypic consequence and practical use for human and animal health, industry and environmental conservation.

The Australian Phenomics Facility builds upon and provides wide access to a new technology pioneered in Australia allowing high throughput analysis of all mammalian genes for their phenotypic effects by inducing mutations in mice, looking for specific changes to traits of medical importance and then isolating the genes responsible.

It includes researchers from John Curtin School of Medical Research, The Australian National University, Monash Institute of Reproduction and Development, Monash University, Dairy CRC, Garvan Institute, IMB, University of Queensland

The facility keeps Australia at the cutting edge of international efforts to advance human and animal health by defining the phenome. The facility is a leading facility of its kind, and in high demand nationally and internationally, generating international recognition, key intellectual property, new skills, and represents a prime opportunity to build new industries.

ARC Centre of Excellence in Biotechnology and Development

Solving human fertility disorders, fighting testicular cancer and controlling feral pests are the main targets of the Centre of Excellence in Biotechnology and Development (CBD).

The research team is focussing on decoding the complex genetic messages that drive the production of male germ cells (cells that form sperm cells) and to broadly apply the research to people, pets and pests.

The incidence of testicular cancer has doubled in the last 30 years while the rates of other cancers (eg ovarian, uterine and cervical) have remained constant. It is therefore imperative scientists find out more about the complex genetic processes involved in this cancer, as well as identifying any environmental factors that may be implicated in its occurrence.

IMB's Peter Koopman is searching for new genes involved in the development of male germ cells and establishing the function of these genes.

ARC Centre in Bioinformatics

The ARC Centre 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 modelling and visualisation environment to simulate its development and behaviour.

Although directed in the first instance toward understanding human health and development, the Centre's technologies and output are generally applicable to biotechnology, while building critical mass in advanced bioinformatics vital to Australia's international competitiveness in bio-based industries.

CRC Chronic Inflammatory Disease

The Cooperative Research Centre for Chronic Inflammatory Diseases (CRCCID) focuses on two diseases rheumatoid arthritis (RA) and chronic obstructive pulmonary disease (COPD). These are devastating chronic inflammatory diseases that afflict millions of people across the world leading to exceptional suffering, economic loss and premature death. Despite the importance of these diseases, which account for billions of dollars annually in health care costs around the world, there have been relatively few breakthroughs into their cause, treatment or cure, despite intensive global research.

The research activities of the CRC are focused on developing innovative therapies for RA and COPD inflammatory diseases through understanding their basic biology. To this end the CRC integrates basic biological research with more focussed work aimed at identifying novel targets for those diseases. The CRC has a major pharmaceutical company and a world leader in osteoarthritis as commercial supporting partners and works closely with them to identify and develop new potential therapies.

In 2004 the disease focus of the CRC expanded to include osteoarthritis (OA) as a result of a successful grant for supplementary funding. This has allowed the start of research projects that will enable development of new methods to treat debilitating joint disease and generate synthetic tissues to repair injured joints. Supplementary funding was also obtained to initiate a new program aimed at using bioinformatics and structural genomics to increase our understanding of the genes and proteins involved in chronic inflammatory diseases.

The Queensland node is based in Professor David Hume' lab at the IMB, and administered by IMB Affiliate Member Dr. Stuart Kellie. It makes up approximately 40% of the total CRC activity with a focus on therapeutic target gene identification and validation. The CRC seeks to identify genes that are regulated in inflammatory disease processes, and determine which of those genes is absolutely required for disease progression. From here, we will develop ways of screening for potential therapies that interfere with the function of the targeted gene. Further information can be obtained from the CRC's website (www.crccid.com)

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.

Costing Australasia at least $720 million p.a. through environmental, economic and social damage, the impact of invasive animal pests can only be reduced by a partnership between the public and private sectors. No individual land manager or agency carries the whole invasive pest animal problem but all are responsible for making a contribution and a commitment to the solution.

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.

NANO

The Nanostructural Analysis Network Organisation is an Australian Major National Research Facility and with the delivery and installation of the new Tecnai 300keV cryo electron-microscope and ancillary equipment the Queensland Node has developed into a unique facility in Australia.

In addition to infrastructural improvements NANO has completed the formation a commercialisation arm to provide a vehicle for rapid commercialisation of results as it characterises and manipulates matter and the atomic and molecular scale.

The interaction of NANO with the IMB is of paramount importance to understanding the structure and function of cellular complexes and how they combine to form a living cell.

Australian Genomic Research Facility

The Australian Genome Research Facility (AGRF), now in its seventh The building houses the AGRF, the GRDC/ARC Centre of Excellence in Plant Functional Genomics, the SARDI Molecular Marker Development Group and the CRC for Molecular Plant Breeding. The extensive co-location of nationally and internationally recognised organisations in the new Plant Genomics Centre creates a critical mass of agricultural researchers and breeders to rapidly translate new research findings into commercial practice.

The first service available for AGRF's Agriculture section was high throughput plant DNA purification, for clients in the local wheat and barley industry. Facilities for controlled plant growth and frost research came on line in June and November 2004, respectively.

The AGRF's Microarray section made the strategic decision to focus on custom arrays for species other than mouse and human. Our custom array service was very well utilised by researchers with access to cDNA libraries of their species of interest. An ongoing committment to the production of high quality arrays has seen the introduction of additional quality assurance (QA) steps. The Microarray section successfully introduced a training system where external researchers can come to the AGRF laboratory to gain hands-on experience in the use of microarrays.

Custom single nucleotide polymorphism (SNP) typing for fine mapping or candidate gene analysis as performed on the Sequenom MassARRAY grew considerably throughout 2004. It is now clear that, particularly for human genetic studies, a transition to genome wide SNP analysis from microsatellite markers is occurring with clients requesting the GeneChip System Affymetrix for these studies.

The Affymetrix platform can be utilised for both expression and SNP genotyping and completely complements existing platforms within the AGRF. It was essential that AGRF offer this platform to the scientific community and the uptake of the pilot service was excellent. Our focus remains on producing a quality output and therefore a significant amount of work was performed to develop all the essential QA steps.

As a result the AGRF was appointed the Authorised Service Provider for Affymetrix allowing us early access to technology updates. In addition, it is a platform widely used by other organisations to develop new genetic tools, affording AGRF the opportunity to expand into new markets.

Appointment of additional Research and Technology (RT) staff has greatly facilitated an enhanced interaction between the RT group and the service teams. The introduction of new technology requires a period of testing in the RT section before release as a service. This was clearly evident in the successful introduction of the Affymetrix expression and SNP array system.

The RT section also assisted with upgrading of existing service methodologies, implementing new technologies and conducting their own research in single cell genomics and DNA sequencing.

The team is examining opportunities for co-development of new technologies with the NANO MNRF, MiniFAB Victoria and other organisations working in the fields of nano and microtechnology. As analysis technology is rapidly superceded in genetics, and more advanced equipment is required in functional genomic analysis, the ability to integrate new nano-devices into testing regimes is essential for the AGRF to remain at the forefront of genomics services provision.

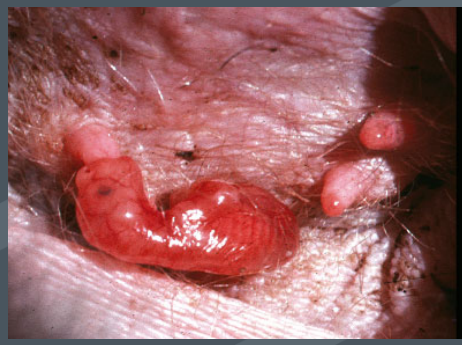
In December 2004 we saw the initiation of a flagship project of the AGRF, the sequencing of the genome of the Tammar wallaby *(Macropus eugenii)*. Our seed collaboration with the ARC Centre for Kangaroo Genomics had a massive leveraging effect with the unprecedented commitment by Professor Francis Collins to partner with a non-USA laboratory, AGRF, to achieve the sequence of this Australian marsupial.

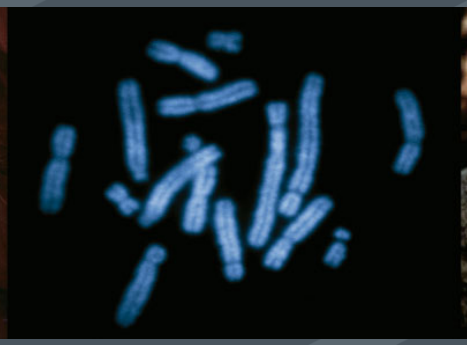
Approximately six million sequencing reads will be performed at AGRF and six million at the NIH funded laboratory, Baylor College of Medicine, Houston headed by expatriate Australian, Professor Richard Gibbs.

The State Government of Victoria recognised the scientific and commercial importance of generating the genome sequence of the Tammar and made a major commitment to the project with a grant of $4.5 million. The opportunity to enter into a major international collaboration with the National Human Genome Research Institute (part of NIH) was a significant drawcard. Applied Biosystems Australia have also contributed $500,000 in kind support.

The AGRF will have a major role in both the sequencing and bioinformatic analysis. As a result AGRF has been evaluating new highly automated sample processing methods in order to achieve the goals and timelines of the Wallaby Genome Project.

Opportunities exist to define critical regions for regulation of gene expression as well as developing strategies for sequencing genomes at lower levels of coverage. Professor Francis Collins emphasised the importance of the Tammar sequence in enhancing the understanding of the human genome as they are located at the "evolutionary sweet spot".





10.

Community Awareness and Engagement

This year the IMB introduced a range of programs and materials to build awareness among the general community about its research focus and achievements.

Angstrom Art Project

'Sweetbox', a delicious image illustrating the pollen from a pigeon pea flower, was just one of the spectacular images born from the research labs of the IMB and University of Queensland.

To celebrate its first anniversary, the IMB released ten images for sale as prints to raise awareness of the work of its scientists and contribute funds to IMB research.

Entitled the Angstrom Art Collection - an Angstrom being a very, very small unit of length (0.000,000,0001 of one metre) used most commonly when measuring the size of cells and proteins – it was the beautiful structures and images uncovered during research by IMB scientists into DNA and proteins, that provided the inspiration for this collection. The IMB aims to hold a national competition biannually and sell the prints to raise awareness of molecular bioscience research and provide some additional funds for labs and institutes across Australia.

Patron of the IMB Angstrom Art Project, Beverley Trivett of the John Trivett Foundation, is working to see further images adapted to gift cards and unique gift wrapping papers, available for sale everywhere.

"Unlike medical research, molecular bioscience is not considered 'sexy' by the general public. Not a lot of people understand it, but its future contribution to improving the health and quality of life of future generations will be staggering. The Angstrom Art Collection helps us bring the science closer to the people," she said.

The images, available for sale online at the IMB website, will be kept current so that people can constantly see examples of the great work being done at the IMB and contribute by purchasing an image to enjoy.

IMB Website www.imb.uq.edu.au

When a Google search is conducted using the key words 'molecular bioscience', the IMB website is top of the list. In fact the IMB site remains at the top of the list of around 467,000 pages worldwide, which means that the IMB site is the most visited site in this category. This is great news and will lead to more hits, more links and greater awareness of IMB research.

IMBoutput

Produced quarterly, the IMBoutput provides a concise and reader-friendly research update, which allows the general community to keep abreast of the outcomes and achievements of the Institute and to see that their investment in us is well placed.

Research Fact Sheets

Found on the IMB website under 'community information and involvement', the IMB's research fact sheets on cancer, cystic fibrosis and diabetes, provide information on the disease, IMB research into this area and some helpful links to further information. Further fact sheets will be produced in 2005.

Biotechnology 2020

Biotechnology Australia and the IMB hosted a free public forum in November 2004 to discuss the future impact of biotechnology on our society. The Biotechnology 2020 Forum highlighted applications and issues surrounding the use of biotechnology by our society, as well as enabled public participation through the use of Digi-vote technology.

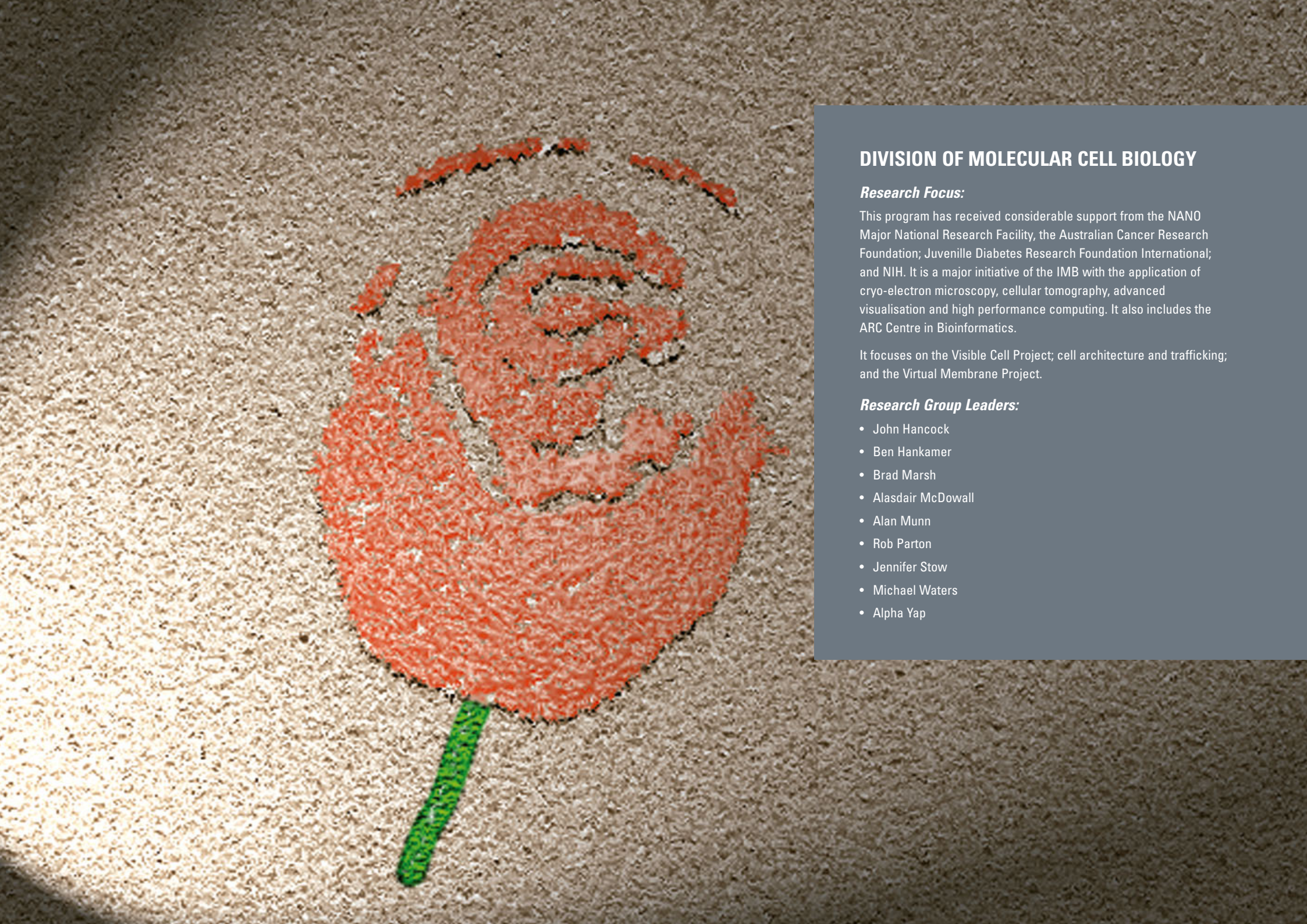
Chair of the Forum, IMB's Director of Ethics and Public Policy, Professor Wayne Hall, said execution of intelligent public policy for new and emerging biotechnologies required an informed and engaged public.

"The Forum was a great opportunity for the public to learn about new technologies only just beginning to appear on our horizon, consider possible pros and cons and offer some immediate feedback."

A top quality panel was assembled with experts in the areas of the products and developments, medical science, community concerns, developing countries perspectives and future concerns.

To increase audience interaction and provide the opportunity for people to 'voice their opinions' the forum used the Digi-Vote system, allowing the audience to vote on what they saw as benefits or risks, their priorities for biotechnology developments and what they felt might be useful or harmful applications of biotechnology.

There was also the added benefit for the panelists of receiving immediate feedback about community attitudes toward various applications of biotechnology, rather than reading survey results.



DIVISION OF MOLECULAR CELL BIOLOGY

Research Focus:

This program has received considerable support from the NANO Major National Research Facility, the Australian Cancer Research Foundation; Juvenille 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 in Bioinformatics.

It focuses on the Visible Cell Project; cell architecture and trafficking; and the Virtual Membrane Project.

Research Group Leaders:

- John Hancock
- Ben Hankamer
- Brad Marsh
- Alasdair McDowall
- Alan Munn
- Rob Parton
- Jennifer Stow
- Michael Waters
- Alpha Yap

Research

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 anti-cancer 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 signaling platforms.

We also remain interested in how confinement of signaling complexes onto a 2D surface in general and in plasma membrane microdomains 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 organization of the membrane alters in response to specific growth factors.

We also have a major interest in chacterising 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 microdomains.
- Electron microscopic visualisation and quantitative characterisation of surface microdomains to build up a high-resolution 2D map of the microdomains of the inner plasma membrane.
- Investigation of the dynamic regulation of microdomain localisation of Ras and Ras-interacting proteins in response to physiological stimuli.

Lab members

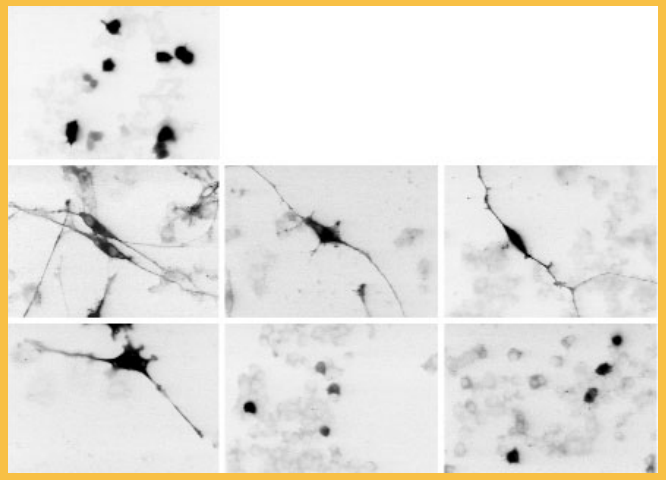
Research Officers:
Michael Hanzal-Bayer, Angus Harding, Michelle Hill, Sarah Plowman, Sandrine Roy

Research Assistants:
Annette Lane, Cornelia Muncke

Visiting Research Fellow:
Kim Yap-Weber

PhD Students:
Andrew Goodall, Chi-Yan Lau, Elizabeth Westbury

- Mechanism of Raf-1 activation, to characterise the multistep Raf-1 activation process spatially within the plane of the plasma membrane.
- Characterisation of the mechanism(s) whereby K-ras is transported to the plasma membrane and how Ras proteins engage different endocytic pathways.



Internal Duties

Division Head, Molecular Cell Biology

Key Publications Since 2000

Roy, S., Luetterforst, R., Harding, A., Apolloni, A., Etheridge, M., Stang, E., Rolls, B., Hancock, J. F. & Parton, R. G. (1999). Dominant-negative caveolin inhibits H-Ras function by disrupting cholesterol-rich plasma membrane domains. *Nature Cell Biol* 1: 98-105.

Prior, I. A., Harding, A., Yan, J., Sluimer, J., Parton, R. G. & Hancock, J. F. (2001). GTPdependent segregation of H-ras from lipid rafts is required for biological activity. *Nature Cell Biol* 3: 368-375.

Roy, S., Wyse, B., and Hancock, J.F. (2002) H-Ras signaling and K-Ras signaling is differentially dependent on endocytosis. *Mol Cell Biol.* 22: 5128-5140.

Prior, I.A, Muncke, C., Parton, R.G, and Hancock, J.F (2003) Direct visualization of Ras proteins in spatially distinct cell surface microdomains. *J Cell Biol,* 160: 165-170.

Hancock, JF (2003) Ras proteins: Different signals from different locations. *Nat Rev Mol Cell Biol.* 4: 373-385

John Hancock

MEMBRANE PROTEIN STRUCTURES

Benjamin Hankamer

Research

Our group is focused on developing a broad based platform for the structure determination of membrane proteins and macromolecular assemblies, based upon single particle analysis, electron and X-ray crystallography.

A strong research focus of the group involves developing 'pipelines' for the rapid and systematic structure determination of membrane proteins and soluble

macromolecular assemblies using computational (Single particle analysis) and crystallographic techniques.

To overcome the major rate-limiting step of membrane protein structure determination, high quality 2D and 3D crystal production, we are also developing a systematic template-assisted 2D monolayer crystallization approach.

Finally a selection of proteins involved in a range of important biological processes and biotechnology applications (eg.Biohydrogen) are also currently being investigated as part of the IMB's Visible Cell program.

In particular, molecular and structural biology studies of photosynthesis (in collaboration with Olaf Kruse, University of Bielefeld), are being conducted to develop algal mutants with improved photobiological H2 production capacities - an important step in the development of future solar powered H2 production systems.

Research Projects

- Single Particle Analysis
- Electron Crystallography

Internal Duties

Coordinator, IMB Monday Morning Meeting

Design, purchase, and testing of the new Tecnai F30 electron microscope

Assessor, NANO-Travel Access Program awards

Chair, PhD Confirmation Thesis Committee

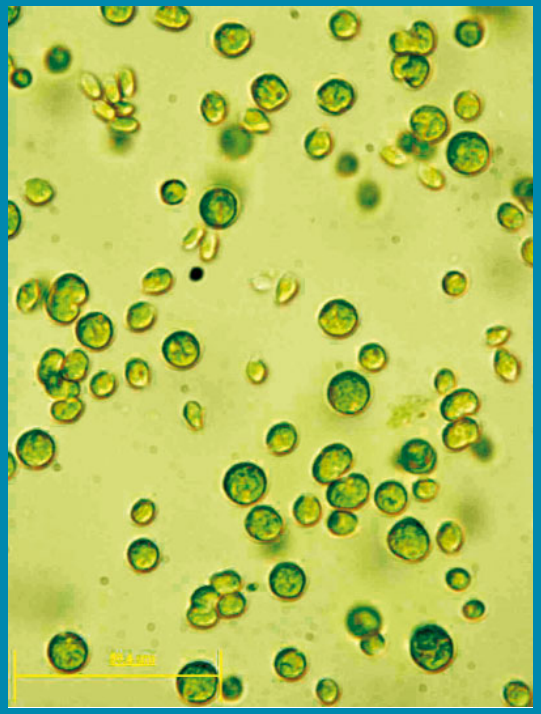
Lab members

Research Officers:
Jan Mussgnug
Jens Rupprecht

Research Assistants:
Rosalba Rothnagel
Michael Landsberg

PhD Student:
David Woolford

Honours Students:
Igor Kromin
Radosav Pantelic
Cameron Votan



Key Publications Since 2000

Hankamer B, Morris E, Nield J, Gerle C, Barber J. (2001) Three-Dimensional Structure of the Photosystem II Core Dimer of Higher Plants Determined by Electron Microscopy. *J Struct Biol* 135: 262-9.

Sennoga C, Hankamer B, Heron A, Seddon J, Barber J, Templer RH. Morphological Aspects of in cubo membrane protein crystallization. In: Templer RH, Leatherbarrow R, editors. *Biophysical Chemistry: Membranes and Proteins.* Cambridge: The Royal Society of Chemistry 2002. p. 221-236.

Hankamer BD, Elderkin SL, Buck M, Nield J. (2004) Organization of the AAA(+) adaptor protein PspA is an oligomeric ring. *J Biol Chem* 279: 8862-6.

Iwata M, Imamura H, Stambouli E, Ikeda C, Tamakoshi M, Nagata K, Makyio H, Hankamer B, Barber J, Yoshida M, Yokoyama K, Iwata S. (2004) Crystal structure of a central stalk subunit C and reversible association/dissociation of vacuole-type ATPase. *Proc Natl Acad Sci U S A* 101: 59-64.

Hankamer B, Barber J, Nield J. Electron microscopy of Photosystem II and its antenna system. In: Satoh K, Wydrzynski T, editors. Photosystem II: *The Water/Plastoquinone Oxido-Reductase in Photosynthesis:* Kluwer Academic Publishers; 2005.

Benjamin Hankamer

BETA CELL STRUCTURAL BIOLOGY/CELLULAR TOMOGRAPHY

Brad Marsh

Research

We are interested in how the hormone insulin is made in the pancreas and released into the bloodstream to regulate blood glucose and whole body metabolism at normal, healthy levels after consumption of a carbohydrate meal.

This work involves elucidating the basic cell biology and physiology of the pancreatic beta cell – the sole source of insulin in mammals. In humans, death of the beta cells, or their failure to make/release adequate amounts of insulin, results in the diseases known as Type 1 and Type 2 Diabetes, respectively.

We use three dimensional and high resolution (~5nm) structural cell biology methods to study the subcellular structures and mechanisms involved in insulin synthesis, processing and trafficking.

The majority of our studies are carried out using pancreatic islets of Langerhans isolated from adult mice.

3D reconstructions, also known as tomograms, generated from images of 300-400nm-thick sections have already provided us with important insights into how insulin is processed and packaged at the Golgi in islet beta cells prior to release into the bloodstream to regulate blood glucose levels.

As a result the next phase of our research focusses on the important mechanisms following insulin packaging into granules at the trans-Golgi.

In parallel with these rodent studies, we will adapt and optimise our preparative and 3D analytical methods for work with islets isolated from human donors.

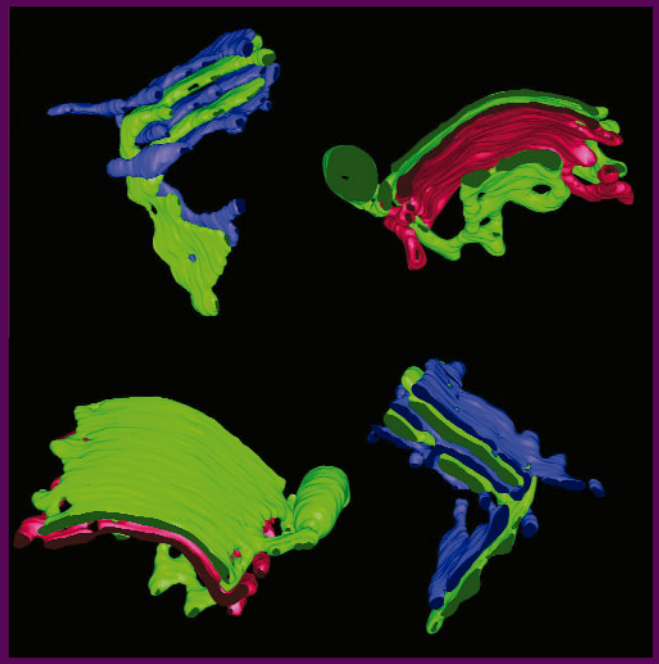
These studies will provide fundamental information about how insulin is packed and crystallised in islet beta cells under low, normal and stimulatory concentrations of glucose for different times.

By combining 3D cellular reconstruction and analysis with standard biochemical and molecular biological techniques, we ultimately hope to identify the sites and mechanical nature of the cellular defects that accompany states of impaired insulin synthesis, processing and secretion in Type 1 and Type 2 Diabetes.

Lab members

Research Assistants:
Adam Costin
Garry Morgan

Postgraduate Research Student:
Radosav Pantelic



Research Projects:

- 3D Structure Studies of the Pancreatic Beta Cell by High Resolution Electron Microscope (EM) Tomography
- 3D Structural Biology of the Human Islet
- The development and application of New Methods for Multi-Scale, 3D Imaging of the Islet of Langerhans by Correlative CLSM and EM
- Three-Dimensional Culture of Pancreatic Beta Cells
- The Visible Cell Atlas

Key Publications Since 2000

BJ Marsh, DN Mastronarde, KF Buttle, KE Howell and JR McIntosh. (2001) Organellar relationships in the Golgi region of the pancreatic beta cell line, HIT-T15, visualized by high resolution electron tomography. *Proc Natl Acad Sci USA.* 98:2399-2406.

BJ Marsh, DN Mastronarde, JR McIntosh and KE Howell. (2001) Structural evidence for multiple transport mechanisms through the Golgi complex in the pancreatic beta cell line, HIT-T15. *Biochem Soc Trans.* 29: 461-467.

BJ Marsh, N Volkmann, JR McIntosh and KE Howell. (2004) Direct continuities between cisternae at different levels of the Golgi complex in glucose stimulated mouse islet beta cells. *Proc Natl Acad Sci USA.* 101: 5565-5570.

BJ Marsh and KE Howell. (2002) Timeline: The mammalian Golgi — complex debates. *Nat Rev Mol Cell Biol.* 3:789-795.

S Mogelsvang, BJ Marsh, MS Ladinsky and KE Howell. (2004) Predicting function from structure: 3D structure studies of the mammalian Golgi complex. *Traffic.* 5: 338-345

Brad Marsh

CRYO-ELECTRON MICROSCOPY OF VITREOUS SECTIONS

Alasdair McDowall

Research

Science will always strive to question the in vivo structure and function of cellular complexes, where and how do the "building blocks" fit and work together in native cells and tissues?

One tool employed to answer this question is electron microscopy (EM). At IMB, EM is supported through UQ's Centre of Microscopy and Microanalysis (CMM), as a Major National Research Facility. This infrastructure complements the advanced techniques of cryo-electron microscopy, single particle 3D reconstruction, protein electron crystallography and cryo-electron tomography (CET).

Our specific interests investigate the architecture of cellular organelles and molecular complexes by rapid freezing, or vitrifying, of structures followed by ultra-thin sectioning and electron imaging of frozen hydrated specimens, (CEMOVIS).

Employing these techniques, fascinating detail from native ultrastructure of cells is posing new questions in biology with much remaining to be seen.

Our group is studying biological structures by cryosectioning vitreous bulk material for cryo-electron microscopy (cryo-EM). Considered the dream method by structural cell biologists, it involves vitrifying a native sample of cells or tissue by rapid cooling, cutting into ultra-thin <100nm sections and cryo-EM observation of the perfectly preserved details.

In collaboration with CMM, IMB's Brad Marsh and Professor Jacques Dubochet from the University of Lausanne we are using high pressure freezing and cryosectioning to investigate bulk structure systems of mammalian cells, bacteria and chloroplast organelles.

We are also using cryo-electron microscopy together with thin cryo-preparations to investigate plasma membrane protein packing arrangements in collaboration with the Parton group. Cryo-electron microscopy of vitreous sections (CEMOVIS) demonstrates its full potential when combined with computerized electron tomography for 3-D reconstruction.

The Nationally funded Tecnai 300keV cryo electron microscope was commissioned for operation in 2004. Final testing on the third party CCD cameras, software and cryo specimen holders and ancillary preparation tools will be completed in 2005.

Lab members

Research Officers:
Matthias Floetenmeyer
Jamie Riches

Research Assistants:
Eunice Grinan
Kay Hodge

Research Projects

- Electron microscopy of cellular organelles and complexes
- The Visible Cell Project

External Duties

Chair of National NANO Structural Biology Committee

Internal Duties

Deputy Director, Centre for Microscopy and Microanalysis, UQ

Member, Academic Board, UQ

Lecturer 3rd year BSc., Marcomolecular Design.

Key Publication

Ashraf Al-Amoudi, Jiin-Ju Chang, Amélie Leforestier, Alasdair McDowall, Laurée Michel Salamin, Lars P. O. Norlén, Karsten Richter, Nathalie Sartori Blanc, Daniel Studer and Jacques Dubochet. (2004) Cryo-electron microscopy of vitreous sections. *EMBO J.* 23: 3583-3588

Rojo,M., Emery, G., Marjomaki V., McDowall A., Parton R.G., and Gruenberg, J. (2000) Involvement of the transmembrane protein p23 in the organisation of the golgi apparatus. *J. Cell Science,* 113: 1043-1057

Bex, F., McDowall, A.W., Burny, A. and Gaynor, R. (1997) The human T-cell Leukemia Virus Type-I Transactivator Protein Tax colocalises in unique nuclear structures with NF-kB proteins. *J. Virology.* 71: 3484-3497

Weaver, A.J., McDowall, A.W., Oliver, D.B. and Deisenhofer, J. (1992) Electron Microscopy of Thin Sectioned Three-dimensional Crystals of SecA Protein from Escherichia coli: Structure in Projection at 40Å Resolution. *J. Structural Biology.* 109: 87-96

McDowall, A.W., Smith, J.M. and Dubochet, J. (1986) Cryoelectron Microscopy of Vitrified Chromosomes in Situ. *EMBO J.* 5: 1395-1403

Alasdair McDowall

ACTIN CYTOSKELETAL ORGANISATION, CYTOKINESIS, AND ENDOCYTIC MEMBRANE TRAFFIC

Alan Munn

Research

Endocytosis is the process by which cells take up cell surface molecules and particles and fluid from the environment. Material taken up by endocytosis can either return to the cell surface or, alternatively, be delivered to intracellular compartments.

Endocytosis is important for controlling the composition of the cell surface membrane, and is especially critical for the function of the immune and nervous systems. It also plays a role in controlling cell growth. It is also the major pathway used by infectious agents like viruses to gain entry to cells.

Although the basic process of endocytosis was first described in 1964, and in spite of exciting recent advances, many of the mechanisms remain unknown. Because of its well-characterised molecular genetics, the budding yeast *Saccharomyces cerevisiae* has become an excellent simple cell model for studying endocytosis using powerful molecular genetic, cell biological, and biochemical approaches.

Endocytosis has recently been shown to play a key role, not only in virus entry to cells, but also in virus exit from cells. Yeast is well suited to the type of high throughput screen now used extensively in the pharmaceutical industry for identifying lead compounds that have potential to be developed into therapeutics. We are using yeast to screen for anti-viral compounds – which is just one of the many biotechnology uses for yeast.

Research Projects

- Endocytosis in control of cell surfaces
- Control of cell growth and cell division
- Screening natural products for novel anti-viral drugs and drug target identification

External Duties

Member, Local Organising Committee, 23rd International Conference on Yeast Genetics and Molecular Biology (Melbourne, 2007).

Initiated the International Co-tutelle Agreement between The University of Queensland and The Universite Louis Pasteur, Strasbourg.

Lab members

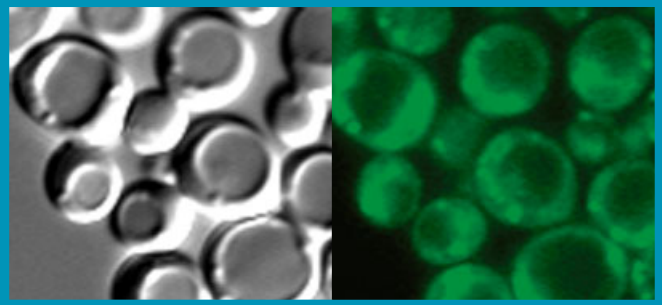
Research Officer:
Parimala Vajjhala

PhD Student:
Gang Ren

MSc Student:
Desmond Dorairajoo

Honours Students:
Shuxian (Julin) Wong
Jorge Zavaleta-Ahane

Undergraduate Students:
Hui Yi (Stephanie) To
Ai Lin (Jocelyn) Gan
Lydia Hill (with Rob Capon)



Internal Duties

Member, IMB Level 2 Safety Committee

Member, IMB IT Committee

Member, IMB PhD Student Supervisory Committees

Organiser, CSIRO-IMB Joint Postgraduate Research Project

Undergraduate teaching/lecturing, School of Biomedical Science, UQ

Key Publications Since 2000

Naqvi, S.N., Feng, Q., Boulton, V.J., Zahn, R., and Munn, A.L. (2001). Vrp1p Functions In Both Actomyosin-Ring Dependent and Hof1p-Dependent Pathways of Cytokinesis, *Traffic* 2: 189-201.

Zahn, R., Stevenson, B.J., Schröder-Köhne, S., Zanolari, B. Riezman, H., and Munn, A.L. (2001). End13p/Vps4p Is Required for Efficient Transport from Early to Late Endosomes in *Saccharomyces cerevisiae, J. Cell Sci.* 114: 1935-1947.

Thanabalu, T., and Munn, A.L. (2001). Functions of Vrp1p In Cytokinesis and Actin Patches are Distinct and Neither Requires a WH2/V Domain, *EMBO J.*, 20: 6979-6989.

Yeo, S.C.L., Xu, L., Ren, J., Boulton, V.J., Wagle, M.D., Liu, C., Ren, G., Wong, P., Zahn, R., Sasajala, P., Yang, H., Piper, R.C., Munn, A.L. (2003). Vps20p and Vta1p interact with Vps4p and function in multivesicular body sorting and endosomal transport in *Saccharomyces cerevisiae*. J. Cell Sci. 116: 3957-3970.

Zhang, S., Ren, J., Armstrong, J.S., Munn, A.L., Yang, H. (2004). Ncr1p, the yeast ortholog of mammalian Niemann Pick C1 protein, is dispensable for endocytic transport. *Traffic* 5: 1017-1030.

Alan Munn

Research

Our research interests focus on the organisation, dynamics, and functions of the plasma membrane. In particular, we are interested in the formation and function of caveolae, small pits, which cover the surface of many mammalian cells, and in a related domain termed a "lipid raft".

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.

We are using a number of systems in order to understand how caveolae form and their role in cellular function. In addition, our studies are providing new insights into the organisation and function of lipid raft domains.

Research Projects

- Caveolin functional studies
- Cavolae and caveolin-3 in muscle
- Caveolins in zebrafish
- Clathrin-independent endocytosis
- Caveolae formation and structure

External Duties:

Associate Editor:

- Traffic
- Molecular Biology of the Cell

Editorial board member, Faculty of 1000

Co-chairman; minisymposium American Society of Cell Biology Annual Meeting, Washington DC, USA

Co-chairman; symposium Australian Health and Medical Research conference, Sydney, Australia

Internal Duties

Deputy Director, Centre for Microscopy and Microanalysis

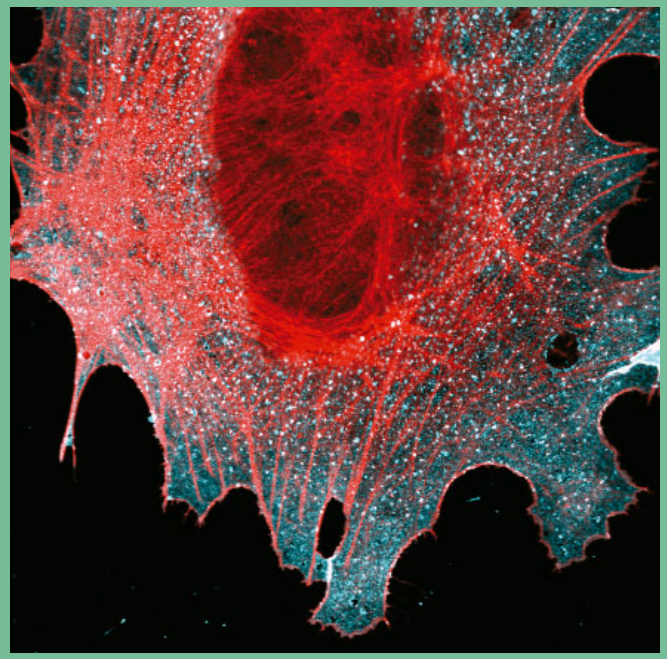
Lab members

Senior Research Officer:
Sally Martin

Research Officers:
Matthias Floetenmeyer, Margaret Lindsay, Michelle Hill, Piers Walser, Delia Hernandez-Deviez

Research Assistants:
Charles Ferguson, Annika Stark, Teresa Munchow

PhDStudents:
Matthew Kirkham, Isabel Morrow, Susan Nixon



Key Publications Since 2000

Pol, A., R. Luetterforst, M. Lindsay, S. Heino, E. Ikonen, and R.G. Parton. 2001. A caveolin dominant negative mutant associates with lipid bodies and induces intracellular cholesterol imbalance. *J Cell Biol.* 152:1057-70.

Pol, A., S. Martin, M.A. Fernandez, C. Ferguson, A. Carozzi, R. Luetterforst, C. Enrich, and R.G. Parton. 2004. Dynamic and regulated association of caveolin with lipid bodies: modulation of lipid body motility and function by a dominant negative mutant. *Mol Biol Cell.* 15:99-110.

Matsuo, H., J. Chevallier, N. Mayran, I. Le Blanc, C. Ferguson, J. Faure, N.S. Blanc, S. Matile, J. Dubochet, R. Sadoul, R.G. Parton, F. Vilbois, and J. Gruenberg. 2004. Role of LBPA and Alix in multivesicular liposome formation and endosome organization. *Science.* 303:531-4.

Miaczynska, M., S. Christoforidis, A. Giner, A. Shevchenko, S. Uttenweiler-Joseph, B. Habermann, M. Wilm, R.G. Parton, and M. Zerial. 2004. APPL proteins link Rab5 to nuclear signal transduction via an endosomal compartment. *Cell.* 116:445-456.

Kirkham, M., A. Fujita, R. Chadda, S.J. Nixon, T.V. Kurzchalia, D.K. Sharma, R.E. Pagano, J.F. Hancock, S. Mayor, and R.G. Parton. 2005. Ultrastructural identification of uncoated caveolin-independent early endocytic vehicles. *J. Cell Biology.* 168:465-76.

Robert Parton

Research

New and existing proteins are trafficked, or moved around, inside cells in order to deliver them to their destinations and to regulate their functions. The cellular machinery that governs protein trafficking is highly complex and involves many gene products in different cells. Deciphering the trafficking of key proteins is essential for understanding how they function in normal cells and in disease.

Our research group is focused on generating a detailed 'map' of protein trafficking in epithelial cells and macrophages using sophisticated imaging, biochemical, molecular and ultrastructural approaches.

In epithelial cells we study E-cadherin, an essential adhesion protein and a vital tumour suppressor. In macrophages our interest in trafficking is focussed on how these cells secrete proinflammatory cytokines, both as part of the normal immune response and in inflammatory disease.

In all, our studies seek to answer basic questions about protein trafficking and cell function that will provide important insights and suggest new therapeutic strategies in cancer and inflammatory disease.

Research Projects

- Sorting and polarized trafficking of E-cadherin in epithelial cells.
- Regulated endocytosis of E-cadherin for growth factor signaling, regulation of adhesion and in tumorigenesis.
- Post-Golgi trafficking; vesicle budding and protein transport in live cells.
- Secretory pathway in inflammatory macrophages.
- Trafficking and secretion of inflammatory cytokines in macrophages.

External Duties

Associate Editor, American Journal of Physiology: Cell Physiology
Member, Editorial Board, Traffic.

Internal Duties

Postgraduate coordinator (Academic) IMB
Member Postgraduate Studies Committee, UQ

Lab members

Senior Research Officer:
Fiona Wylie

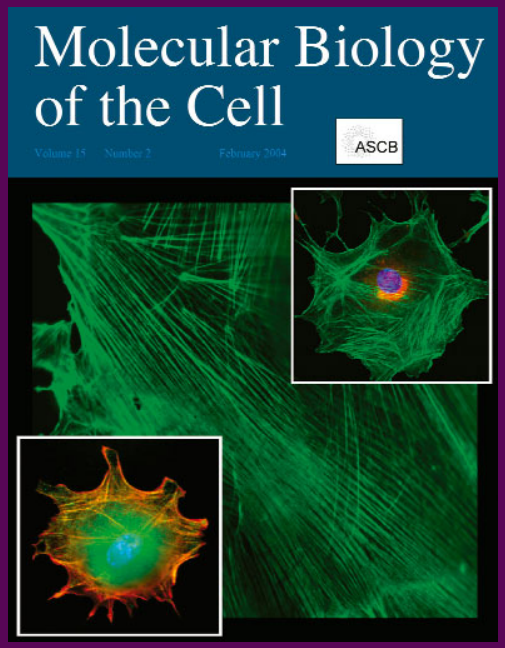
Research Officers:
Anthony Manderson, Rachael Murray

Research Assistants:
Darren Brown, Seetha Karunaratne, Tatiana Khromykh, Juliana Venturato

PhD Students:
Wang Bo, David Bryant, Shannon Joseph, Jason Kay, John Lock, Daniele Sangermani

Honours Student:
Stephanie Wood

Undergraduate student:
Luke Hammond



Key Publications Since 2000

Miranda, K.C., S.R. Joseph, A.S. Yap, R.T. Teasdale, and J.L. Stow. (2003). Contextual binding of p120ctn to E-cadherin at the basolateral plasma membrane in polarized epithelia. *J. Biol. Chem.* 278:43480-434488.

Pagan, J.K., F.G. Wylie, S. Joseph, C. Widberg, N.J. Bryant, D.E. James, and J.L. Stow. (2003). The t-SNARE Syntaxin 4 Is Regulated during Macrophage Activation to Function in Membrane Traffic and Cytokine Secretion. *Current Biology* 13:156-160.

Bryant, D.M., and J.L. Stow. (2004). The ins and outs of E-cadherin trafficking. *Trends Cell Biol.* 14:427-434.

Bryant, D., F. Wylie, and J.L. Stow. (2005). Regulation of endocytosis, nuclear translocation and signaling of FGFR1 by E-cadherin. *Mol. Biol. Cell.* 16(1):14-23.

Lock, J.G., and J.L. Stow. (2005). Rab11 in recycling endosomes regulates the sorting and basolateral transport of E-cadherin. *Mol. Biol. Cell* 16:1744-55.

Jennifer Stow

Research

The final height of an individual is determined by the actions of growth hormone during childhood and adolescence. In the adult, growth hormone is an important metabolic agent regulating body composition and strength, 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, from high resolution protein structures to genetically engineered animals. The centrepiece of these studies is the action of the growth hormone receptor, which determines the degree of the cell response to growth hormone, and which we cloned collaboratively with Genentech.

The surprising finding that the growth hormone receptor is located in the cell nucleus of dividing cells has led us to discover that nuclear localizing the receptor artificially can result in cancer. This is being actively pursued as a potential therapeutic target.

Research Projects

Growth Hormone and Cytokine Signalling

External Duties

NHMRC Peer Review Advisory Committees, Program Grant Committees.

Member, Executive, Growth Hormone Research Society.

Co-organizer, Second International GH and IGF Conference

Member, Editorial Board, Endocrinology

Internal Duties

Teaching : Coordinator for BIOM 3001, 14 lectures.

Faculty of Biological and Chemical Sciences Selection Committees

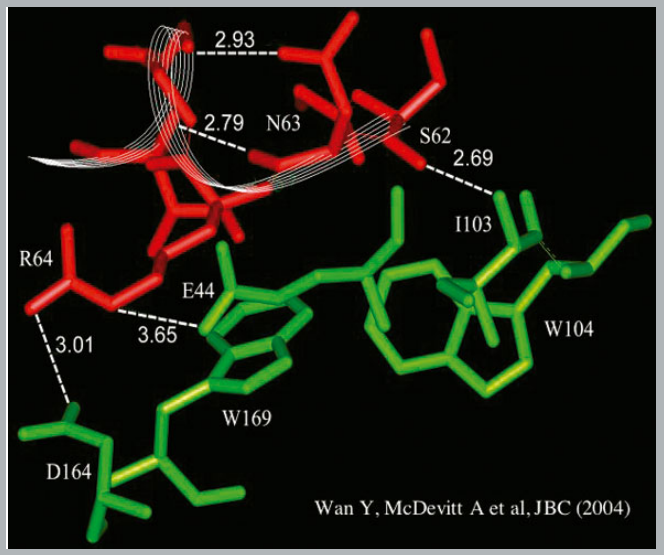
Lab members

Research Officers:
Richard Brown
Agnieszka Lichanska
Becky Conway-Campbell

Research Assistants:
Linda Kerr
Kathryn Fletcher
Elizabetta D'Aniello

PhD Students:
Rebecca Pelekanos
Jongwei Wooh
Hong Soon Chin

Honours Student:
Leela Buhmann



Key Publications Since 2000

Li H, Bartold PM, Young WG, Xiao Y, Waters MJ (2001) Growth hormone induces bone morphogenetic proteins and bone-related proteins in the developing rat periodontium. *J Bone Miner Res.* 16: 1068-76.

Wan Y, Zheng YZ, Harris JM, Brown R, Waters MJ (2003) Epitope map for a GH receptor agonist monoclonal antibody, MAb 263. *Molecular Endocrinology* 17: 2240-50

Shang CA and Waters MJ (2003) Constitutively Active Stat5 can replace the requirement for GH in adipogenesis of F442A *Molecular Endocrinology* 17: 2494-2508.

Wan, Y, McDevitt, A, Shen, B, Smythe, ML and Waters, MJ (2004) Increased Site 1 affinity improves biopotency of porcine growth hormone : Evidence against diffusion dependent receptor dimerization *J Biol Chem* 279: 44775-84

Rowland JE, Lichanska AM, Kerr LM, White M, D'Aniello E, Maher SL, Brown RJ, Teasdale R, Noakes PG and Waters MJ (2004) In vivo analysis of growth hormone receptor signalling domains and their associated transcripts. *Molecular Cell Biology* 25: 66-77

Mike Waters

Research

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.

Cell adhesion molecules, notably those of the cadherin family, mediate these interactions. Importantly, cadherin adhesion molecules are not simply glue. Rather they control the ability of cells to recognize one another, a process that is often lost in cancer and inflammation.

By understanding the basic biological mechanisms of cadherin-mediated cell recognition we hope to provide vital insights into the basis of developmental patterning and common human diseases.

Research Projects

- The molecular mechanism responsible for recruiting Arp2/3 to E-cadherin
- The molecular regulators of Arp2/3 activity at cadherin contacts (including WASP/WAVE proteins, cortactin and ena/VASP family proteins)
- The molecular basis of cadherin-activatied Rac and P13-kinase signalling.
- The morphogenetic consequensces of cadherin-activated cell signalling and cooperativity with the actin cytoskeleton

External Duties

Editorial Board, American J. Physiology (Cell Physiology)

Symposium Co-chair, Cellular Imaging, Combio 2004

Co-organizer, Special Interest Group meeting on Actin nucleation at adhesive contacts, 2004 American Society for Cell Biology

Internal Duties:

Honors committee, School for Biomedical Science, UQ

MB.BS. PhD Committee, UQ Medical School

Coordinator, ACRF/IMB Dynamic Imaging Facility for Cancer Biology

Lab members

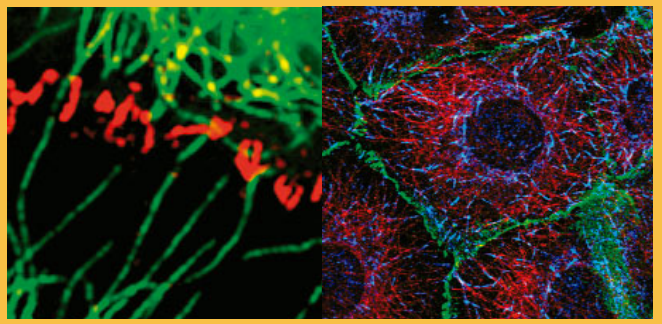
Research Officers:
Nicole den Elzen, Astrid Kraemer, Jian-Hong Pang, Annette Shewan

Research Assistants:
Terese Munchow, Suzie Verma

PhD Students:
Radiya Ali, Marita Goodwin, Falak Helwani, Madhavi Maddugoda, Andrew Paterson, Jeanie Scott, Samantha Stehbens

Honours Students:
Carmen Buttery, Stephen White

Undergraduate Student:
Rob McLachlan



Key Publications Since 2000

Kovacs, E.M., M. Goodwin, R.G. Ali, A.D. Paterson and A.S. Yap (2002a) Cadherindirected actin assembly: E-cadherin physically associates with the Arp 2/3 complex to direct actin assembly in nascent adhesive contacts. *Current Biology* 12, 379-382.

Kovacs*, E.M., R.G. Ali*, A. McCormack and A.S. Yap (2002b) E-cadherin ligation directly activates PI3-kinase and Rac GTPase signals to stabilize adhesion *J. Biol. Chem.* 277, 6708-6718 (*Equal contributions)

Goodwin, M., E.M. Kovacs, M.A. Thoreson, A.B. Reynolds, and A.S. Yap (2003) Mutation of the p120-catenin binding site abolishes the ability of E-cadherin to activate Rac but not PI3-kinase *J. Biol. Chem.* 278, 20533-20539.

Helwani, F.M.*, E.M. Kovacs*, A.D. Paterson, S. Verma, R.G. Ali, A.S. Fanning, S.A. Weed, and A.S. Yap (2004). Cortactin is necessary for E-cadherin-mediated contact formation and actin organization *J. Cell Biol.* 164, 899-910 (*Equal contributions)

Verma, S., A.M. Shewan, J.A. Scott, N.R. den Elzen, F.M. Helwani, H. Miki, T. Takenawa and A.S. Yap (2004). Arp 2/3 activity is necessary for efficient extension of cadherin adhesive contacts *J. Biol. Chem* 279, 34062-34070.

Alpha Yap

DIVISION OF MOLECULAR GENETICS AND DEVELOPMENT

Research Focus:

This program includes IMB's participation in the Cooperative Research Centre for Chronic Inflammatory Diseases; the Centre for 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:

- David Hume
- Peter Koopman
- Melissa Little
- George Muscat
- Andrew Perkins
- Rick Sturm
- Brandon Wainwright
- Carol Wicking

Joint Appointments:

- Stuart Kellie
- Joe Rothnagel

Research

The central issue being addressed in the Macrophage and Osteoclast Biology Research Group is the mechanism controlling the differentiation of macrophages and osteoclasts from their progenitor cells and the regulation of the function of these cells in health and diseases.

The group is a major node of the Cooperative Research Centre for Chronic Inflammatory Diseases, which focuses on identifying targets for the development of drugs to treat diseases such as osteoarthritis, rheumatoid arthritis and chronic obstructive lung disease.

We are interested in the signalling pathways that permit macrophages and osteoclasts to respond to agents such as growth factors (macrophage colony-stimulating factor, CSF-1; RANK ligand) and microbial products such as lipopolysaccharide and microbial DNA. To assess the function of individual gene products we utilise a combination of transfection analysis and transgenics using new technologies developed in the group, including macrophage and osteoclast-specific transgenes.

Using a systems biology approach we are trying to gain an overview of how macrophages and osteoclasts function and predict their response to external agents including candidate drugs.

Research Projects

- Gene expression in macrophages and osteoclasts
- Studies on macrophage inflammatory proteins
- Cellular responses to foreign DNA
- Macrophage involvement in inflammation and metastatic disease
- Macrophage differentiation and regulation of the CSF-1 receptor gene.
- Transcriptional networks in macrophages
- Identification of inhibitors for prostaglandin D2 synthase
- RANKL gene regulation in T cells
- The role of bone surface macrophages on bone remodelling and repair
- Artificial bone substrates
- PTH regulation of Syndecan-4 in bone metabolism

External Duties

Node Head, CRC for Chronic Inflammatory Diseases.

Senior Scientist, RIKEN Genome Sciences Centre, Yokohama, Japan

Board Member, Centre for Immunology and Cancer Research, University of Queensland, Princess Alexandra Hospital

Lab members

Senior Research Fellow:
Ian Cassady

Senior Research Officers:
Roy Himes, Ian Ross, Kate Stacey, Matthew Sweet

Research Officers:
Barbara Fletcher, Kate Irvine, Dmitry Ovchinnikov, Allison Pettit, Liza-Jane Raggatt, Jack Flanagan, Tim Ravasi, Tedjo Sasmono, Christine Wells, Jodie Robinson

Administrative Officer:
Julie Osborne

Lab Manager:
Greg Young

Research Assistants:
Ming Chang, Jane Lattin, Kristian Brion, Allan Burrows, Wendy van Zuylen, Kylie Alexander, Jasmyn Dunn, Tara Roberts, Stephen Cronau, Geoffrey Faulkner, Greg Kelly, Jane Mooney, Angela Trieu

Dabatase manager (CRC):
Xiang Liu

PhD Students:
Guy Barry, Myrna Constantin, Tamarind Hamwood, Katherine Irvine, Nicholas Meadows, Vera Ripoll, Tara Roberts, Kate Schroder, Brendan Tse, Christine Wells, Andy Wu

Honours Students:
Elke Seppanen, Adi Haji Idris

Member, Scientific Advisory Board, US Biodefence Initiative Anthrax Program, University of Chicago.

Member, Scientific Advisory Board, Progen Ltd

Chair, Interview panels for Queensland Cancer Fund Grants

Member, Editorial Board, Journal of Interferon and Cytokine Research.

Member, Review Panel, Journal of Molecular and Cellular Biology

Associate Editor, Journal of Immunology.

Section Editor, Journal of Leukocyte Biology

Associate Editor, Journal Structural and Functional Genomics

Editor, BioMed Central - Immunology

Internal Duties

Director, ARC Special Research Centre for Functional and Applied Genomics.

Director, Transgenic Animals Service Queensland.

Key Publications Since 2000

Riken Genome Exploration Phase II Group and FANTOM Consortium (2001) (Hume, D.A. acknowledged as major contributor and project organiser amongst 90 authors). Functional annotation of a collection of mouse full length cDNAs. *Nature*. 409: 685-690

Ravasi, T., Wells, C.A., Forrest, A.,Walsh, N., Underhill, D.M., Wainwright, B.J., Aderem, A., Grimmond, S., Hume, D.A. (2002). Generation of diversity in the innate immune system. Macrophage heterogeneity arises from gene-autonomous transcription probability of individual inducible genes. *J. Immunol.* 168: 44-50

Okazaki, Y. et al. The FANTOM Consortium and the RIKEN Genome Exploration Research groups Phase 1 and 2 Team (Hume, D.A. cited a member of the core authorship and planning team). (2002). Analysis of the mouse transcriptome based upon functional annotation of 60,770 full length cDNAs. *Nature*, 420: 563-573

Sasmono, R.T., Oceandy, D., Pollard, J., Tong, W., Himes, S.R., Hume, D.A. (2003). Definition of the mononuclear phagocyte system of the mouse using a macrophage colony-stimulating factor receptor (CSF-1R)-green fluorescent protein transgene. *Blood*. 101: 1155-1163

Roberts TL, Sweet MJ, Hume DA, Stacey KJ. (2005) Cutting edge: species-specific TLR9-mediated recognition of CpG and non-CpG phosphorothioate-modified oligonucleotides. *J Immunol*. 174: 605-8.

David Hume

MOLECULAR GENETICS OF MAMMALIAN DEVELOPMENT

Peter Koopman

Research

We are studying the genes that control the formation of various organs during the development of a mammalian embryo. In particular we are striving to understand the events that regulate the development of the embryo as a male or a female, and the laying down of an intact and functional network of blood vessels.

Aside from the basic science of understanding the molecular and cellular events underpinning these processes, this work is increasingly being applied to medical and biotechnological outcomes, namely the understanding and management of human disorders of sexual development and fertility, gender ratio manipulation in pest and livestock species, and novel routes to transgenesis.

Research Projects

- Sex Determination and Gonadal Development
- Sox Gene Function and Evolution
- Molecular Genetics of Vascular Development
- Development of Male Germ Cells

External Duties

Editorial Board, Developmental Dynamics (American Association of Anatomists, USA)

Editorial Board, Mouse Knockout and Mutation Database (Current Trends Publications, Elsevier Science, London; www.biomednet.com/db/mkmd)

Highlight Advisory Panel, Nature Reviews Genetics (Nature publications, UK)

Specialist Advisor, HUGO Gene Nomenclature Committee

Specialist Reader, Australian Research Council Discovery-Projects grant scheme

Organizer, Australian Developmental Biology Workshop

Member, Organizing Committee, Lorne Genome Conference.

Internal Duties

Convenor, Brisbane Developmental Biology Seminar Series

Executive, Program in Developmental Biology, UQ

Executive, Angstrom Art

IMB Seminar co-ordinator, Division of Genetics and Developmental Biology

Lab members

Senior Research Officers:
Josephine Bowles, Catherine Browne

Research Officers:
Annemiek Beverdam, Hirofumi Mizusaki, Shuji Takada, Neville Young, Dagmar Wilhelm, Megan Wilson

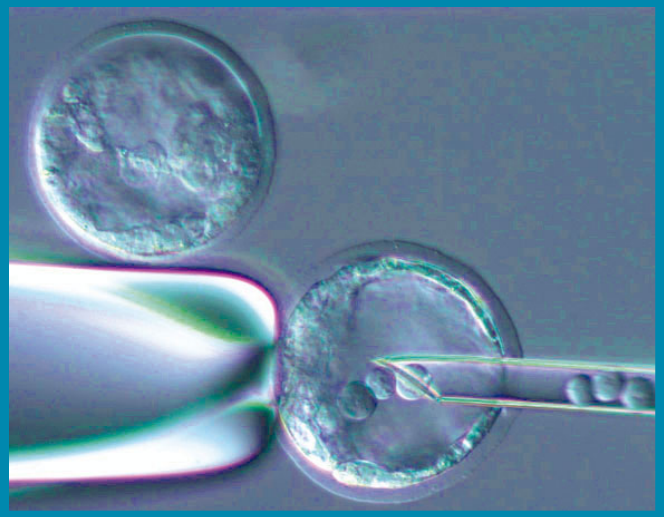
Research Assistants:
Alexander Combes, Tara Davidson, Deon Knight, Andrew Jackson, Alisa Poh, Desmond Tutt

Administration Assistant:
Lindsay Fowles

PhD Students:
Meredith Downes, Katherine Ewen, Fred Martinson, Juan-Carlos Polanco, James Smith, Stephen Bradford

Honours Students:
Angela Jeanes, Sonjia Layton

Visiting Scholars:
Anne Lagendijk, Netherlands
Christopher Smith, Queen's University, Canada



Key Publications Since 2000

Pennisi, D., Gardner, J., Chambers, J., Hosking, B., Peters, J., Muscat, G.E., Abbott, C. & Koopman, P.A. (2000), Mutations in Sox18 underlie cardiovascular and hair follicle defects in ragged mice, *Nature Genetics,* 24:434-437.

Koopman, P.A. (2001), "The genetics and biology of vertebrate sex determination", *Cell*, 105, pp.843-847.

Schepers, GE, Teasdale, RD and Koopman, P (2002). Twenty pairs of Sox: Extent, homology and nomenclature of the mouse and human Sox transcription factor gene families. *Developmental Cell* 3: 167–170.

Schepers, G, Wilson, M, Wilhelm, D and Koopman, P (2003). SOX8 is expressed during testis differentiation in mice and synergizes with SF1 to activate the Amh promoter *in vitro. J. Biol. Chem.* 278: 28101–28108.

Aitken, R.J., Koopman, P.& Lewis, S.E.M. (2004), Seeds of concern, *Nature*, 432:48-52. (Journal cover)

Peter Koopman

Research

The central theme of this laboratory is the molecular basis of the development of the kidney.

Each of us has a pair of kidneys that function to excrete waste products in the form of urine. The kidneys do this by filtering our entire blood volume around 30 times per day through tiny filters called nephrons. Yet only around 2 litres of fluid is lost, in the form of urine, from the body due to the enormous capacity of the kidney to reabsorb water, ions and nutrients.

The kidneys therefore also 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.

Loss of renal function is not compatible with life. Hence, chronic renal failure (CRF) is a devastating disease and an expensive one to treat. It is estimated that 60,000

Australians between 12 and 74 yrs have CRF. Each year, approx. 4000 Australian adults will be diagnosed with CRF, costing the health system greater than one billion dollars.

The most common cause of end stage renal failure (ESRF) is glomerulonephritis. The current steady rise in ESRF rates is primarily due to an increase in the number of people with Type II Diabetes.

The long term aim of the work is to develop novel cellular therapies for chronic renal disease. A greater understanding of the processes involved in normal kidney development will underpin such developments and hence unravelling the molecules directing kidney development is the focus of our laboratory.

Research Projects

- Characterizing the role of Crim1, a modulator of the TGFB superfamily, in kidney development
- Is there a Renal Stem Cell and Might it be used to Treat Renal Disease? Towards new therapies for renal disease.
- An atlas of gene expression for the developing urinary and genital tract.

Awards:

2004: Gottschalk Medal in Medical Sciences from the Australian Academy of Science, Listed, The Bulletin Smart 100 Awards

Lab members

Research Officers:
Gemma Martinez, David Pennisi, Fiona Rae, Mattieu Taveau, Lorine Wilkinson, Kyra Woods, Parimala Vajjhala, Gabriel Kolle

Research Assistants:
Kevin Gillinder, Bree Rumballe

Administrative officer:
Miranda Free

PhD Students:
Shannon Armstrong, Grant Challen, Genevieve Kinna

Honours Students:
Michael Lusis, Heng Hock Seow

External Duties:

Board member Lorne Genome Inc

Chair, Organising Committee, Lorne Genome Conference

Director Board, Nephrogenix

Board member Federation Australian Scientific and Technological Societies

Graduate Australian Institute Company Directors

Scenario Planning Workshop, Renal Regeneration Symposium & RRC Strategic Planning Retreat

Member, Pfizer Fellowship Award Selection Committee

Internal Duties:

Member, Project Control Group Australian Institute for Bioengineering and Nanotechnology

Undergraduate lecturing

Member PhD Student Thesis Committees

UQ Representative, Scientific Management and Advisory Board, Australian Stem Cell Centre

Key Publications Since 2000

Sim, E. U-H., Smith, A., Szilagi, E., Ioannou, P., Lindsay, M. and Little, M.H. (2002) Expression of Wnt-4 can be regulated by the Wilms' tumour suppressor gene, WT1. *Oncogene* 21: 2948-2960

Wilkinson, L., Kolle, G., Wen, D., Piper, M., Scott, J. and Little M.H. (2003) CRIM1 regulates the rate of processing and delivery of BMPs to the cell surface. *J. Biol. Chem* 278: 34181-8

Gross I, Morrison DJ, Hyink DP, Georgas K, English MA, Mericskay M, Hosono S, Sassoon D, Wilson PD, Little M, Licht JD. (2003) The receptor tyrosine kinase regulator sprouty1 is a target of the tumor suppressor WT1 and important for kidney development. *J. Biol Chem* 278: 41420-30

Rae, F., Martinez, G., Gillinder, K., Smith, A., Shooter, G., Forrest, A.R., Grimmond, S.M. and Little, M.H. (2004) The Wilm's tumour suppressor gene, WT1, represses the mevalonate pathway of cholesterol synthesis. *Oncogene* 23: 3067-79.

Challen, GA, Martinez, G, Davis, M, Teasdale, R, Grimmond, S and Little, MH. (2004) Identifying the molecular phenotype of renal progenitor cells. *J Am Soc Nephrol.* 15: 2344-5

Commercial

Patent:
Methods for maintaining cells in an undifferentiated state,
Application no: 2004906889, 1 December 2004

Melissa Little

NUCLEAR HORMONE RECEPTORS AND GENE REGULATION

George Muscat

Research

My research interests focus on the molecular regulation of fat, carbohydrate, and energy metabolism in skeletal muscle by nuclear hormone receptors (NHRs). NHRs are hormone controlled regulatory proteins that mediate the physiological control of gene expression. Specifically, we aim to understand the role of skeletal muscle in cardiovascular disease (CVD), obesity and diabetes.

CVD is the western world's most serious public health threat, accounting for more than 16 million deaths annually. It is the leading cause of death and disability in Australia and the United States, accounting for nearly 40% of all deaths. Major independent risk factors for cardiovascular disease include dyslipidemia (associated with anomolous levels of the lipid triad), hypertension, chronic inflammation, obesity, sedentary lifestyle, diabetes and smoking.

These are recognised by the world health organisation as being in the top ten global health problems. These risk factors are directly influenced by diet, metabolism and lifestyle. In this framework, skeletal muscle, a major mass peripheral tissue, must be considered an important therapeutic target tissue in the battle against cardiovascular and metabolic disease. Lean muscle accounts for >40% of the total body mass, and 50% of energy expenditure. This results in significant homeostatic interrelationships between the muscular system, and other body systems. Muscle mediates physical activity, is the primary site of glucose and fat metabolism, and more recently implicated in cholesterol efflux. Muscle has a very high rate of metabolism, and even at rest uses much more energy than adipose tissue. Consequently, this tissue has a significant role in obesity, the blood lipid profile, insulin sensitivity, and cardiovascular health.

Research Projects

- Skeletal Muscle and Nuclear Hormone Receptors: implications for cardiovascular disease
- The functional role of NR4A
- Understanding the role of Peroxisome Proliferator-Activated Receptors (PPAR) in skeletal muscle energy and lipid homeostasis.
- Elucidating the role of the NR4A subgroup [Nur 77, NOR-1] in skeletal muscle lipolysis, and energy expenditure.
- Examining the role of the NR1D subgroup [Rev-erb alpha and beta] in lipid absorption, and myokine expression

Lab members

Senior Research Officers:
Gary Leong, Uwe Dressel

Research Officers:
Brett Hosking, Pat Lau, Megan Maxwell, Aaron Smith, Les Burke, Senali Abayratna Wansa

Research Assistants:
Mary Wang, Rachel Burow, Shayama Wijedasa

PhD Students:
Tamara Allen, Jyotsna Pippal, Sathiya Ramakrishnan, Michael Pearon

- Examining the link between skeletal muscle myokine expression, energy expenditure, and inflammation
- Elucidating the function of RORalpha in skeletal muscle lipid homeostasis.
- Genetic programs induced by the oxy-cholesterol dependent nuclear receptor, LXR, in skeletal muscle: regulation of cholesterol metabolism
- Regulation of gene expression and mammalian differentiation by tissue specific transcription factors (e.g Sox 18) and chromatin remodelling factors (e.g protein arginine methyl transferases).
- Understanding the role of Sox18 in fat metabolism

External Duties

Chair, NHMRC Grant Review Panel (Endocrinology and Reproduction)

Journal Editor:
- Journal Biological Chemistry
- Nuclear Receptor

Convenor, UQ Office of Research and Postgraduate Studies NHMRC Project Grant Information Sessions

Internal Duties:

Member, IMB Executive
Division Head, Molecular Genetics & Development
Confirmation and PhD thesis committees
Chair of Examiners, Molecular Genetics & Development PhD students

Key Publications Since 2000

Megan A. Maxwell, Mark E. Cleasby, Angus Harding, Annika Stark, Greg J. Cooney, and George E.O. Muscat (2005) Nur77 regulates lipolysis in skeletal muscle cells: evidence for crosstalk between the beta-adrenergic and an orphan nuclear hormone receptor pathway. *J. Biol. Chem.* 280: 12573-84.

Uwe Dressel, Tamara L. Allen, Jyotsna B. Pippal, Paul R. Rohde, Patrick Lau, and George E.O. Muscat (2003) Peroxisome Proliferator Activated Receptors Regulate Lipid And Carbohydrate Utilization In Skeletal Muscle Cells: PPAR b/d agonist, GW501516, regulates the expression of genes involved in lipid catabolism and energy uncoupling in skeletal muscle cells. *Molecular Endocrinology* 17: 2477-2493.

Pier Lorenzo Puri, Simona Iezzi, Peter Stiegler, Tung-Ti Chen, R. Louis Schiltz , George E.O. Muscat , Antonio Giordano , Larry Kedes , Jean Y.J.Wang , and Vittorio Sartorelli (2001) Class I Histone Deacetylases Sequentially Interact with MyoD and pRb During Skeletal Myogenesis. *Molecular Cell* 8: 885-97.

Shen Liang Chen, Dennis H Dowhan, Brett M. Hosking and George E.O. Muscat (2000). The steroid receptor coactivator, GRIP-1, is necessary for MEF-2C dependent gene expression and skeletal muscle differentiation. *Genes and Development* 14: 1209-1229.

Pennisi, D, Gardner, J, Chambers, D, Hosking, B, Peters, J, George EO Muscat, Abbott, C and Koopman, P.(2000) Sox 18 mutations underlie cardiovascular and hair follicle dysfunction in Ragged mice. *Nature genetics* 24: 434-437.

George Muscat

Research

Our group is interested in the molecular regulation of stem cell generation and behavior.

We are primarily focused on how mesoderm is formed and programmed to produce stem cells capable of making or repairing the blood system and kidneys, two organs with embryological and genetic links. We are primarily concerned with transcriptional hierarchies and how transcription factors work within biochemical and genetic pathways.

The 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 are specifically interested in the transcriptional regulation of alternate mesodermal stem cell fate decisions. We want to understand how certain classes of zinc finger transcription factors work biochemically and also at a global genomic level. We are interested in delineating dynamic transcriptional networks and transcription factor interactions. Consequently there are three overlapping streams of work.

How do we direct embryonic stem (ES) cells into adult type stem cells with blood and kidney potential? 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 fluorescence and FACS.

We also investigate transcription regulation of erythropoiesis and particularly globin gene regulation. Mutations in the globin genes are the most common genetic mutations worldwide. These mutations are responsible for thalassaemia and sickle cell disease with cause serious morbidity and mortality around the world. We are particularly interested in trying to decipher the complex process of haemoglobin switching at a molecular level with long term hope of designing drugs which target key regulators of this process to reactivate fetal haemoglobin in adults. This strategy has the potential to revolutionize the management of haemoglobinopthies from a supportive to a curative approach.

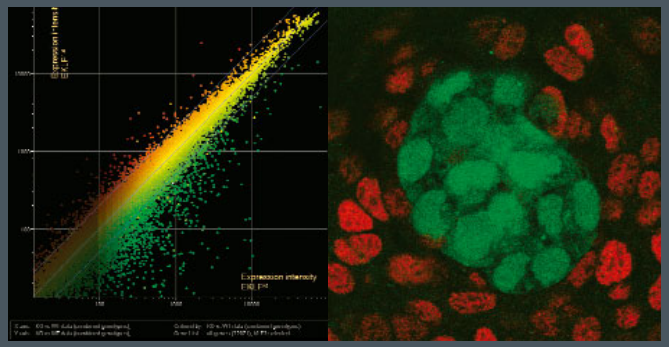
Lab members

Research Officers:
Janelle Keys, Les Burke, Robert Rea, Denise Hodge,

Research Assistants:
Belinda Hartmann, Anita Steptoe, Ashley Rossiter, Susie Green, Adrian Carter, Deanne Whitworth

PhD Students:
Stephen Bruce, Simon Wilkins, Simon Cridland, Melissa Gardiner

Honours Students:
Michael Tallach, Kathleen Robinson, Naomi Wakefield



Finally zebrafish are used as a model for dissection of some of the earliest events in embryo patterning, which underpin 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.

Research Projects:

- Embryonic stem cell differentiation
- Globin gene regulation
- Zebrafish mesoderm patterning and blood programming

External Duties

Member, Organising Committee, 2006 Australasian Zebrafish Meeting

Internal Duties

Manager, Zebrafish Facility, IMB

Key Publications Since 2000

Perkins AC, Peterson K, Stamatoyannopoulos G, Witkowska HE, Orkin SH (2000) Fetal expression of a human A _globin transgene rescues globin chain imbalance but not hemolysis in EKLF null mouse embryos. *Blood* 95:1827-1833.

Coghill E, Eccleston S, Brown C, Fox V, Cerutti L, Jane S, Cunningham J, and Perkins AC. (2001) Erythroid Kruppel-like factor (EKLF) co-ordinates erythroid cell proliferation and haemoglobinisation in cell lines derived from EKLF-/- mice. *Blood* 97:1861-1868.

Huber T, Perkins AC, Deconinck A, Chan F-Y, Mead PE, and Zon LI (2001) Neptune, a Kruppel-like transcription factor that participates in primitive erythropoiesis in *Xenopus. Curr. Biology*, 11:1456-1461.

Papathanasiou P, Perkins AC, Cobb BS, Ferrini R, Sridharan R, Hoyne GF, Nelms KA, Smale ST and Goodnow CC (2003) Widespread failure of hematolymphoid differentiation caused by a recessive niche-filling allele of the Ikaros transcription factor. *Immunity* 19;131-144

Gordon CT, Fox VJ, Najdovska S, and Perkins AC (2005) C/EBP_ and C/EBP_ bind the CCAAT-box in the human _-globin promoter and modulate the activity of the CACC-box binding protein, EKLF. *Biochim Biophys Acta* Apr 12; [Epub ahead of print]

Andrew Perkins

MELANOCYTE BIOLOGY AND PIGMENTATION GENETICS

Richard Sturm

Research

The pigmentary system is dependent on the production of the light absorbing biopolymer, melanin, and is responsible for skin, hair and eye colour. Melanocytes within human skin are situated on the basal layer between the dermis and epidermis and have a number of dendritic processes that interdigitate with the surrounding keratinocytes. The characterisation of proteins responsible for the pigmentation pathway has provided the basis to the biochemical understanding of some of the mouse coat colour and human albinism conditions.

Darker forms of melanin protect the skin from solar radiation exposure, however melanocytes are also the cell-type from which malignant melanoma can originate.

We are studying the human pigmentation system to understand the genetic basis of cellular differentiation, tissue-specific gene expression and cellular transformation induced by solar UV light. Primary melanocyte and melanoblast precursor cells have been cultured from human skin and the pigmentation, growth and differentiation characteristics of each cell-type are being investigated.

The major goal of our research efforts is to understand the genetic basis of human pigmentation and to assess the phenotypic association of these physical traits with skin UV-sensitivity and skin cancer promotion.

Research Projects

- Interaction of genes for skin, hair and eye colour in skin cancer risk phenotypes
- Parallel genetic and cellular analysis of melanogenesis
- Human melanoblasts in culture and regulation by growth factors
- Eye colour as a genetic trait

External Duties

Member, NHMRC Grant Review Panel, Oncology 1B

Associate Editor:

- Pigment Cell Research
- Melanoma Research

Lab members

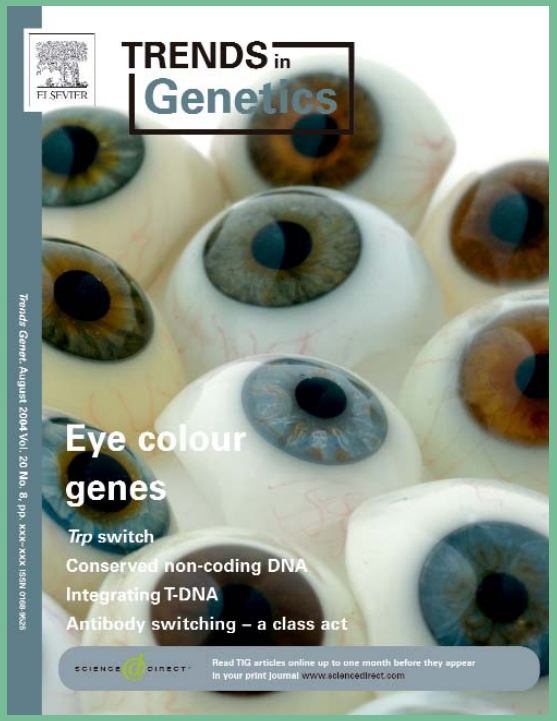
Research Officers:
Richard Newton, Anthony Cook

Research Assistants:
Wei Chen, Darren Smit, Alick Lau

PhD Students 2004:
Anthony Cook, Brooke Gardiner, Helene Johanson, Luke Kirkwood, Don Roberts, Tim Bladen

Honours Students:
Kimberley Beaumont

Undergraduate:
Ryan Galea, Christian Van Nieuwenhuysen



Internal Duties

Institutional Biosafety Committee, UQ

Member, Organising Committee and Session Chair Lorne Genome Conference

Key Publications Since 2000

Duffy, D.L., Box, N.F., Chen, W., Palmer, J.S., Montgomery, G.W., James, M.R., Hayward, N.K., Martin, N.G.& Sturm, R.A. (2004) Interactive effects of MC1R and OCA2 on melanoma risk phenotypes", Human Molecular Genetics, 13 (4), pp.447-461.

Sturm, R.A.& Frudakis, T.N. (2004) Eye colour: portals into pigmentation genes and ancestry", 20 (7), pp.327-332.

Box, N.F., Duffey, D.L., Chen, W., Stark, M., Martin, N.G., Sturm, R.A. and Hayward, N.K. (2001) MC1R genotype modifies risk of melanoma in families segregating CDKN2A mutations" Am J Hum Genet, 69, pp. 765-773.

N.F. Box, D.L. Duffy, R.E. Irving, A. Russell, W. Chen, L.R. Griffiths, P.G.

Parsons, A.C. Green and R.A. Sturm. (2001) Melanocortin-1 receptor genotype is a risk factor for basal and squamous cell carcinoma. J. Investigative Dermatology, 116: 224-229.

J.S. Palmer, D.L. Duffy, N.F. Box, J.F. Aitken, L.E. O'Gorman, A.C. Green, N.K. Hayward, N.G. Martin, R.A. Sturm. (2000) MC1R polymorphisms and risk of melanoma: Is the association explained solely by pigmentation phenotype? Am J Hum Genet. 66: 176-186.

Richard Sturm

RESEARCH

Our research group is focused on elucidating molecular pathology of human genetic disease, primarily through the analysis of the single gene disorder, cystic fibrosis and through the discovery of patched, the gene responsible for both the inherited and sporadic forms of basal cell carcinoma of the skin.

Cystic fibrosis (CF) is the most common inherited lethal disorder in caucasian populations affecting the lung and digestive system. CF patients have a chronic infection with the bacterial pathogen Pseudomonas aeruginosa.

Accordingly we examine the role of the cystic fibrosis gene (and modifier genes) in responding to inflammation and bacterial infection in the lung.

Through cloning the gene mutated in inherited skin cancer we identified the tumour suppressor gene patched.

Analysis of patient material has indicated a role for this gene and its signalling pathway in many tumour types.

Our laboratory applies genetic information from patient analysis to further our understanding of the patched pathway. A powerful approach to the analysis of human genetic disease is the use of model systems, such as the mouse.

Recently the patched/hedgehog pathway has been implicated in the development of the adult lung, and small cell lung cancer. This continues the theme of the relationship between regeneration and cancer and we are currently looking at the role of hedgehog in embryonic lung development, the influence on the stem cell compartment of the lung and its exact role when the airway becomes injured. This will lead us to a better understanding of how cell based therapies might be used to treat lung diseases as well as provide valuable insights into the mechanism of lung cancer.

Consequently, many of our studies are directed at understanding gene function in murine systems.

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

Lab members

Senior Research Officer:
Brendan McMorran

Research Officers:
Christelle Adolphe. Elaine Costelloe,Tammy Ellis, Wendy Ingram

Research Assistants:
Melissa Bourboulas, Emily Riley, Ailsa McCormack

PhD Students:
Azita Ahadizadeh, Susan Gillies, Karen McCue, Jim Palmer, Rehan Hetherington

Honours Students:
Uda Ho, Thu Tran

Research Projects

- Structure/function of the patched tumour suppressor gene
- The cellular origin of basal cell carcinoma and common brain tumours.
- Regulation of the inflammatory response by CFTR
- Origin of the cystic fibrosis inflammatory response
- Novel mouse modifier genes affecting lung development and inflammation the role of the patched/hedgehog pathway in lung development/lung cancer

External Duties:

Member, Scientific Advisory Board, John Curtin School of Medical Research

Member, Queensland Institute of Medical Research Council

Board Member, Australian Phenome Facility

Board Member, Australian Genome Research Facility

Member, NH&MRC Grant Review Panel

Key Publications Since 2000

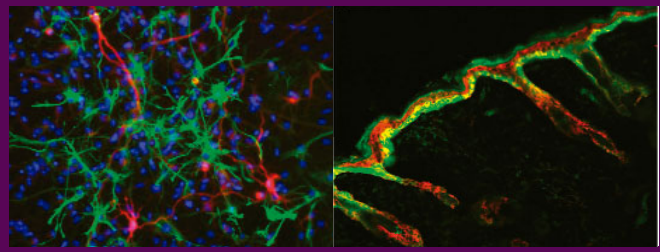
Taylor M, Liu L, Raffel C, Hui C-C., Mainprize, T, Agatep R, Chiappa S, Zhang, X. Gao L, Lowrance A, Goldstein , Scherer S, Dura W, Wainwright B, Rutka J and Hogg D. (2002) Mutations of Suppressor of Fused predispose to medulloblastoma through alterations in Hedgehog and WNT signaling. *Nature Genetics,* 3; 306-310.

Oceandy, D., McMorran, B.J., Smith, S.N., Alton, E.W.F.W., Hume, D.A., Wainwright, B.J. (2002) Gene complementation of airway epithelium in the cystic fibrosis mouse is necessary and sufficient to correct the pathogen clearance and inflammatory abnormalities. *Human Molecular Genetics*. 11: 1059-1067.

McGregor L, Makela V, Darling SM, Chalepakis G, Roberts C, Smart N, Rutland P, Prescott N, Bentley E, Roberts E., Mueller R, Philip N, Nelson J, Francannet C, Perez-Aytes A, Megarbane, A, Kerr B, Wainwright B, Woolf A, Winter R and Scambler PJ. (2003) Fraser syndrome and a murine blebbed phenotype caused by mutations in a novel protein related to extracellular matrix proteins with BMP interacting domains. *Nature Genetics*, 34: 203-8.

Ellis T, Smyth I, Riley E, Bowles J, Adolphe C, Rothnagel JA, Wicking C, Wainwright B.J. (2003) Overexpression of Sonic Hedgehog suppresses embryonic hair follicle morphogenesis. *Dev Biol* 263: 203-15.

Adolphe C, Narang M, Ellis T, Wicking C, Kaur P, Wainwright B. (2004) An in vivo comparative study of sonic, desert and Indian hedgehog reveals that hedgehog pathway activity regulates epidermal stem cell homeostasis. *Development* 131: 5009-19.



Brandon Wainwright

Research

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, supporting the conservation of molecular processes governing the development of these structures.

We are involved in isolation of novel genes involved in embryonic development of the limb and face, as well as more fully characterizing the role of these and other known genes in embryogenesis and disease.

In particular, a microarray screen based on the abnormal limbs of mice mutant for the Gli3 transcription factor, which mediates the Sonic Hedgehog signal, has resulted in the identification of a number of both known and novel genes regulated by Gli3 in the developing limb. We have shown that several of these genes are also regulated by Gli3 and Shh in a number of other developing organs, particularly the face.

We are currently undertaking functional and cell based studies of a number of novel genes, as well as previously characterised genes which to date had not been linked to hedgehog signalling in the context of limb and face development.

Research Projects

- Regulation of the hedgehog pathway by intracellular trafficking and sterol levels
- Microarray analysis in a mouse model of limb development
- Identification of genes involved in craniofacial development

Internal Duties

Member, UQ Medical Research Ethics Committee

Member, UQ Research Only Academic Promotions Committee

External Duties

Member, Organising Committee, Lorne Genome Conference

Lab members

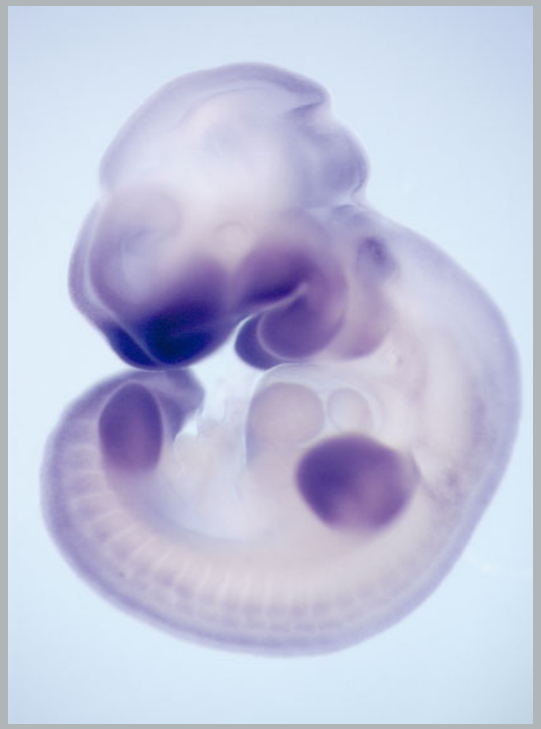
Senior Reserach Officer:
Fiona Simpson

Research Officer:
Edwina McGlinn

Research Assistant:
Timothy Evans (part-time)

PhD Students:
Timothy Evans (part-time), Jennifer Bennetts, Natalie Butterfield, Liam Town

Honours Student:
Salvatore Fiorenza



Key Publications Since 2000

Fowles, L.F., Bennetts, J.S., Berkman, J.L., Williams, E., Koopman, P., Teasdale, R.D. and Wicking, C. (2003) Genomic screen for genes involved in mammalian craniofacial development. *Genesis* 35: 73-87.

Evans, T.M., Ferguson, C., Wainwright, B.J., Parton, R.G. and Wicking, C. (2003) Rab23, a negative regulator of hedgehog signaling, localizes to the plasma membrane and the endocytic pathway. *Traffic* 4: 1-16.

Lalonde, J.P., Lim, R., Ingley, E., Tilbrook, P.A., Thompson, M.J., McCulloch, R., Beaumont, J.G., Wicking, C., Eyre, H.J., Sutherland, G.R., Howe, K., Solomon, E., Williams, J.H. and Klinken, S.P. (2004) HLS5, a novel RBCC familt member isolated from a hemopoietic lineage switch, is a candidate tumour suppressor. *J. Biol. Chem.* 279: 8181-8189.

Adolphe, C., Narang, M., Ellis, T., Wicking, C., Kaur, P. and Wainwright, B.J. (2004) An in vivo comparative study of Sonic, Desert and Indian Hedgehog reveals that Hedgehog pathway activity regulates epidermal stem cell maintenance. *Development* 131: 5009-5019.

Simpson, F., Martin, S., Evans, T., Kerr, M., James, D.E., Parton, R.G., Teasdale, R.D. and Wicking, C. (2005) A novel Hook-related protein family and the characterization of Hook-related protein 1. *Traffic* 6: 442-58.

Carol Wicking

Research

The aim of my lab within the CRC for Chronic Inflammatory Diseases is to identify genes that are aberrantly expressed during chronic inflammation, to identify the function of unknown genes, and to set up assays for the analysis of these genes in vitro and in vivo. Once these genes have been fully validated as targets in chronic inflammatory diseases they are integrated into the drug development pipeline of our industrial partners. To do this we work closely with other members of Prof. Hume's group, with collaborators in University of Melbourne and Monash University, and with two industrial partners: one a major pharmaceutical company and the other a world leader in osteoarthritis. The long-term aim is to generate inhibitors of these genes for therapeutic use. Due to the confidential nature of the CRC interaction with industrial partners, this work remains unpublished.

My basic research interests are focused on intracellular signalling and pathological consequences of aberrant signalling molecule function. My laboratory investigates the cell and molecular biology of tyrosine phosphatases and their relationships with kinases in the regulation of cells involved in cancer and inflammation.

Research Projects

- Identification of therapeutic targets for chronic inflammation
- Generation of target validation platforms for functional Analysis of Macrophage Genes
- Tyrosine Phosphatases in Macrophage Function

External Duties

Deputy CEO, CRC for Chronic Inflammatory Diseases

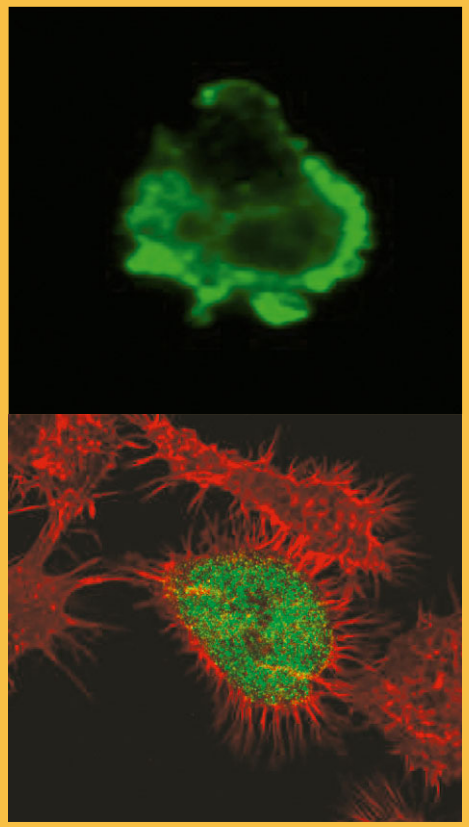
Cooperative Research Centre for
Chronic Inflammatory Diseases

Lab members

Research Assistants:
Jane Lattin
Wendy van Zuylen
Allan Burrows

PhD Students:
Richa Dave

Honours Students:
Cynthia Teo
Melissa Chen



Key Publications Since 2000

Aagaard A, Listwan P, Cowieson, N, Huber,T, Ravasi T, Wells C, Flanagan,JU, Kellie S, Hume, DA, Kobe,B, Martin JL. (2005) An inflammatory role for the mammalian carboxypeptidase inhibitor latexin: relationship with cysteine protease inhibitors and the tumor suppressor TIG1. *Structure* 13:309-317.

Scaife S, Brown R, Kellie S, Thomas AMC, Salmon M, Buckley CD. (2004) Detection of differentially expressed genes in synovial fibroblasts by Restriction Fragment Differential Display. *Rheumatology* 43:1346-52.

Kellie S, Craggs G, Bird, IN, Jones, GE. (2004). The tyrosine phosphatase DEP-1 induces cytoskeletal rearrangements, aberrant cell-substratum interactions and a reduction in cell proliferation. *J Cell Sci* 117: 609-618.

Craggs G, Kellie S. (2001) A functional nuclear localization sequence in the C-terminal domain of SHP-1. *J Biol. Chem* 276:23719-23725.

Craggs G, Finan P, Lawson DL, Wingfield J, Perera,T., Totty NF, Kellie S (2001) A nuclear SH3 domain-binding protein that co-localizes with mRNA splicing factors and intermediate filament-containing perinuclear networks. *J Biol Chem* 276:30552-30560.

Stuart Kellie

MOLECULAR ANALYSIS OF CUTANEOUS SYSTEMS

Joe Rothnagel

Research

Molecular genetics and molecular cell biology using the mammalian epidermis as the model system. Keratinocytes are the major cell type of the epidermis and have evolved to make terrestrial life possible. In laying down their lives, they provide a barrier that protects the organism from harmful UV radiation and from viral, fungal and bacterial invasions as well as preventing desiccation. Keratinocytes express a unique subset of proteins depending on their state of development, differentiation or proliferation. These characteristics make the skin a valuable resource for obtaining expression sequences. In addition, the accessibility of skin makes it the model system of choice for testing gene expression constructs that could be used in gene therapy applications.

Research Projects

- Tissue Specific Promoters
- Alternative Splicing of Key Transcripts

Lab members

Research officers:
Xue-Qing Wang
Lexie Friend

PhD Students:
Jonathan Beesley
Amy McCart
Wolfgang Hofmeister

External Duties

Director and Chief Scientific Officer, GeneDimmer Pty Ltd.

Board member, The Australasian Society of Dermatological Research.

Member, Organizing Committee, 2004 Lorne Genome Conference

Internal Duties

Chair, School of Molecular and Microbial Sciences Animal Welfare Committee

Key Publications Since 2000

Journals:

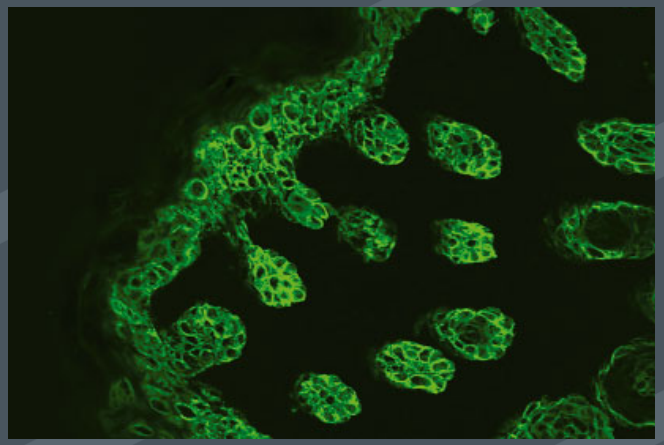
Wang XQ, Rothnagel JA. (2004) 5'-untranslated regions with multiple upstream AUG codons can support low-level translation via leaky scanning and reinitiation. *Nucleic Acids Res.* 32:1382-91.

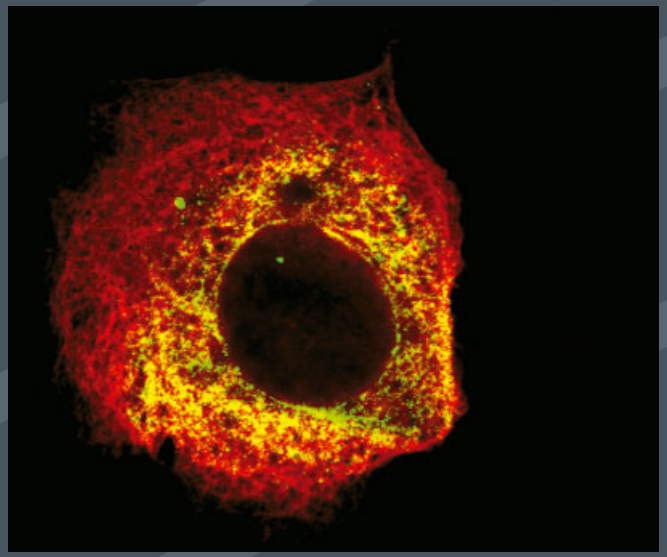
McCart AE, Mahony D, Rothnagel JA. (2003) Alternatively spliced products of the human kinesin light chain 1 (KNS2) gene. *Traffic.* 4:576-80.

Riley NE, Li J, Worrall S, Rothnagel JA, Swagell C, van Leeuwen FW, French SW. (2002) The Mallory body as an aggresome: in vitro studies. *Exp Mol Pathol.* 72:17-23.

Wang XQ, Rothnagel JA. (2001) Post-transcriptional regulation of the gli1 oncogene by the expression of alternative 5' untranslated regions. *J Biol Chem.* 276:1311-6.

Ellis T, Smyth I, Riley E, Bowles J, Adolphe C, Rothnagel JA, Wicking C, Wainwright BJ. (2003) Overexpression of Sonic Hedgehog suppresses embryonic hair follicle morphogenesis. *Dev Biol.* 263:203-15.





Joe Rothnagel

IMB OFFICE OF PUBLIC POLICY AND ETHICS (OPPE)

Research Focus:

OPPE undertakes research and analysis of the new ethics and public policy issues raised by biotechnology. It investigates the ethical and policy implications of biotechnology and genetics aiming to enhance public awareness and discussion of the issues concerning the application of biotechnology.

Research Group Leader:

Wayne Hall

Research

The Office of Public Policy and Ethics undertakes research on the ethical and policy implications of biotechnology and genetics with a particular focus on the potential uses of new biotechnologies to substantially reduce the burden of human disease.

The overarching aim of OPPE's endeavors is to provide even-handed analyses of contested issues in the public arena that are tangles of empirical and ethical issues at the intersection of biology and history.

The Office undertakes analyses of ethical issues raised by research on the genetics of addiction to nicotine and other drugs, pharmacogenetic research on the treatment of nicotine addiction and mental disorders such as depression; the use of vaccines against nicotine and cocaine to treat and prevent these forms of addiction; and the implications for public health policy of research on the genetics of tobacco use and dependence.

The Office is also assessing the implications for cancer treatment and prevention of public understanding of media coverage of research on the genetics of common forms of cancer, such as colorectal cancer, and new types of treatment for cancer, such as cancer vaccines and genetically targeted drugs.

Finally our interest in transgenesis is to do with the ethical objections raised by critics of the genetic modification of plants, animals and humans.

Research Projects

- Ethical and policy issues of life extension yechnology
- Disease control priority project: illicit drug use
- Epidemiological and economic modelling of a nicotine vaccine
- Ethical dimensions of debates about genetically modified foods
- Ethical issues raised by data linkage in health research
- Genes and criminal behaviour: a review
- The genetics of nicotine dependence: a review
- Governance of human genetic biobanks
- What it means to be in a family study of a complex disorder
- Using genetics to understand and increase smoking cessation

Lab members

Senior Research Officer:
Jayne Lucke

Research Assistant:
Bree Ryan

Specialist Librarian:
Sarah Yeates

PhD Students:
Lucy Carter, Jennifer Fleming, Kate Morley, David Turnbull, Katie Wilson

MPhil Students:
Angela Wallace

Undergraduate Research Student:
Jacqueline Murdoch

Undergraduate Student:
Amy Orlandi, Jessica Doerner

External Duties

Vice President, Alcohol and other Drugs Council of Australia

Chair, Research and Development Committee of the National Prescribing Service

Australasian Regional Editor, Addiction

Editorial Advisory Board, Addiction Abstracts

Editorial Board, Australian and New Zealand Journal of Psychiatry

Key Publications Since 2000

Hall WD. The prospects for immunotherapy in smoking cessation. The Lancet 2002; 360:1089-1091.

Morley KI, Hall WD. Using pharmacogenetics and pharmacogenomics in the treatment of psychiatric disorders: some ethical and economic considerations. Journal of Molecular Medicine 2004; 82:21-30.

Hall WD. The Australian policy debate about human embryonic stem cell research. Health Law Review 2004; 12:27-33.

Hall WD, Carter L. Ethical issues in using a cocaine vaccine to treat and prevent cocaine abuse and dependence. Journal of Medical Ethics 2004; 30:337-40.

Hall WD, Morley KI, Lucke JC. The prediction of disease risk in genomic medicine. EMBO Reports 2004; 5:S22-6.

Wayne Hall

7.

Postgraduate Research

GRADUATE PROGRAM

It has been another strong year for the IMB Graduate Program, with the number of IMB-enrolled Research Higher Degree (RHD) students passing 100 for the first time. Moreover, all 10 of IMB's first cohort of students have successfully completed their PhD degrees.

We welcomed our first Co-tutelle student, Mr Ren (Albert) Gang, who commenced his PhD studies with Dr Alan Munn as part of the Co-tutelle Scheme between France and Australia. This scheme was recently established at the University of Queensland (UQ) and IMB is delighted to host one of the first participants.

A number of policies and procedures associated with our students were addressed over the course of 2004. IMB's Special Projects Officer, Patricia McCauley, oversaw the completion and implementation of the IMB Graduate Handbook, containing information relevant to all aspects of Higher Degree candidature. She was also responsible for drafting institute-wide policies formalising the IMB Executive's decisions on matters such as:

- the IMB scholarship scheme,
- the postgraduate student relocation allowance, and
- the requirement for all students to present a completion seminar within six months of submission.

The Completion Seminars are presented at the newly established Divisional Forums. These forums are an ideal venue for PhD confirmation seminars and also fulfill the UQ Graduate School's new requirement for students to present their confirmation seminar to an open informed audience.

This year also saw the establishment of the CSIRO/IMB Joint Scholarship Scheme. The primary purpose of these scholarships is to recruit and support outstanding candidates to be jointly supervised by both organisations, so promoting research collaborations between QBP-based CSIRO Divisions and the IMB. Three IMB/CSIRO Livestock Industries scholarships and one IMB/CSIRO Plant Industry scholarship were offered for 2005 studies.

A record number of Honours students (34) undertook their projects at IMB. Most of our Honours students are enrolled through the BACS faculty but this year we also had two students enrolled through the Faculty of Engineering, Physical Sciences and Architecture, as their degrees were based within information technology. This type of interdisciplinary training is high priority for the Institute and we hope this trend continues.

The 2003 Amgen Award for the most outstanding Honours student at the IMB was presented to Ms Genevieve Kinna. Genevieve has continued her studies at the IMB, enrolling in a PhD with her Honours supervisor, Melissa Little.

IMB also continued the Undergraduate Research Scholarship Scheme (URSS), giving 22 third year students the opportunity to work in a laboratory for eight hours per week during semester. As a result two of our 2003 URSS students, Miss Thu Tran and Mr Salvatore Fiorenza, traveled to Melbourne to take part in the Genes CRC Presentation Day for its Undergraduate Research Opportunities Program (UROP).

Additionally, several third year students completed mini-research projects as part of the "Introduction to Research" module of their degree while Advanced Studies students completed research as part of their customised program.

International students from India, Germany and Sweden also joined IMB for several months as occupational trainees, undertaking overseas research placements as part of the their degree requirements. We also hosted over a dozen year 11 and 12 students from schools throughout Queensland to undertake a brief period of work experience within research laboratories. Placements were made after either direct contact by schools and students or via involvement in the CSIRO's Students Research Scheme.

The strength and vitality of the IMB student cohort was demonstrated by the busy program of social events and information sessions organised by our student society, SIMBA. Mid-year elections heralded the arrival of a new committee responsible for continuing the excellence established by previous executives.

The SIMBA-run information sessions were complemented by the Graduate Program's regular series of workshops designed to assist students in overall career development. These included IMBcom's "Introduction to Bio-Business" Workshop and the three-day "Bio-entrepreneurs Retreat" at Alexandra Headlands.

In addition Wayne Hall and the Office of Public Policy and Ethics conducted a workshop for the first years, discussing the topic "Pre-implantation Genetic Diagnosis: Boutique Medicine? Reproductive Right?" Associate Prof John MacMillan, a practicing clinical geneticist and visiting researcher with OPPE, facilitated informed and lively debates. IMB also ran the inaugural Bioinformatics Workshop. Conducted over five days and coordinated by Dr Mark Crowe, it highlighted the IMB's resources available across the disciplines.

Finally, 2004 has also been a time of change, with the appointment of a new Postgraduate Coordinator, Rob Capon. Our inaugural Postgraduate Coordinator, Jennifer Stow relinquished this position at the start of 2004, after over four years of dedicated work within the program. Jenny played an active part of the IMB's graduate community, prior to the program's inception, and was fundamental to the development of the IMB Graduate Program in the year 2000. Her dedication, commitment and wisdom have left a wonderful legacy and although no longer Coordinator, Jenny still sits as the IMB representative on the UQ Postgraduate Committee of the Academic Board.

Professor Capon, who is Director of IMB's Centre for Molecular Biodiversity was a natural choice as successor, as he held the position of Postgraduate Coordinator for the Faculty of Science at the University of Melbourne prior to joining the IMB in 2003. He has embraced the position with enthusiasm and the program is already benefiting greatly from his experience and leadership.

FAST FACTS

- **11** Australian Postgraduate Awards/University of Queensland Postgraduate Research Scholarships (8 accepted)
- **10** IMB scholarships
- **4** IMB students, Christelle Adolphe, Christopher Armishaw, Gabriel Kolle, Johan Rosengren were recognised in 2004 Dean's List for Outstanding Research Higher Degrees Theses.
- **3** National Health and Medical Research Council Dora Lush Scholarships
- **3** International Postgraduate Research Scholarships (all with accompanying stipend)
- **3** CSIRO Livestock Industries/IMB Joint Scholarships
- **1** CSIRO Plant Industry/IMB Joint Scholarship

IMB POSTGRADUATE DEGREES AWARDED IN 2004

Name	*Program*	*Thesis Topic*	*Supervisor*
Heidi Widberg	PhD	The Role of Tomosyn in Insulin-Regulated Glut4 Trafficking	Prof David James
K Disnika Abayratna Wansa	PhD	Structure-Function Analysis of the Orphan Nuclear Hormone Receptors Nr4a1 And Nr4a3	Prof George Muscat
Darryl Irwin	PhD	High Throughput Genetic Analysis of Limited Numbers of Cells	Prof John Mattick
Anthony Cook	PhD	Models Of Human Neural Crest Cell Differentiation In Vitro	Dr Richard Sturm
Christine Wells	PhD	Transcriptional Analysis of Macrophage Signalling in Response to Lipopolysaccharide	Prof David Hume
Katharine Irvine	PhD	The Expressions and Functions of G3BPS in Macrophages	Prof David Hume
Kevin Miranda	PhD	Post-Golgi Trafficking in the Mammalian Secretory Pathway	Dr Rohan Teasdale
James Smith	PhD	The Molecular Genetics of Mammalian Sex Determination	Prof Peter Koopman
Nicholas Drinnan	PhD	Towards the Synthesis of Biologically Active Carbohydrates, and Carbohydrate Mimetics	Dr Tracie Ramsdale
Isabel Morrow	PhD	Protein-Lipid Interactions within the Cell	Prof Robert Parton
Becky Conway-Campbell	PhD	A Novel Role for the Nuclear Growth Hormone Receptor in Cellular Proliferation	Prof Michael Waters
Susan Nixon	PhD	Functional Characterisation and Developmental Expression of Caveolin	Prof Robert Parton
Andrew Paterson	PhD	Membrane Movements of E-Cadherin	Ass Prof Alpha Yap
Laurence Croft	PhD	Design of Information Systems In Computational Genomics	Prof John Mattick
Hasnawati Saleh	MSc	Gene Expression Profile of Osteoclast-Like Cells	Prof David Hume
Andrew Leech	PhD	Characterisation of *Psedomonas aeruginosa* CHPA	Prof John Mattick
Jennifer Bolton	PhD	Identification And Characterisation of Retinoic Acid-Responsive Genes Expressed During Early Mouse Development	Prof John Mattick
Edwina McGlinn	PhD	Identification Of Novel Gli3 Dependent Transcripts in the Developing Vertebate Limb	Dr Carol Wicking
Shu-Ching (Mary) Wang	PhD	Functional Role And Transcriptional Regulation of the Novel Sox18 Gene	Prof George Muscat
Lotten Ragnarsson	PhD	Conantokin Probes Of NMDA Receptors in Mammalian CNS: Implications For Alzheimer's Disease	Dr Richard Lewis

8.

Visiting Speakers

The IMB encourages an environment of collaborative learning and research.

Its Friday Seminar Series is attended by all IMB research staff and students and provides an opportunity for learning across a variety of research areas. The 2004 seminar series presented national and international speakers at the leading edge of molecular bioscience research. Thank you to our 2004 Series Sponsors Genesearch, SGI, Millipore and Millennium Science.

Friday 12 March

Universal signaling mechanisms in M.tuberculosis receptor Ser/Thr protein kinases

A seminar in Chemistry and Structural Biology
Prof Tom Alber
Department of Molecular and Cell Biology
University of California at Berkeley USA

Friday 19 March

Gene discovery, functional genomics and molecular breeding in pasture plants

A seminar in Genomics and Computational Biology
Prof German Spangenberg
Australian Centre of Plant Functional Genomics
University of Adelaide

Friday 26 March

Methylationm mysteries in malignancy

A seminar in Molecular Genetics and Development
Dr Susan Clarke
Garvan Institute of Medical Research
Sydney, Australia

Friday 2 April

Challenging centromere dogmas

A seminar in Molecular Genetics and Development
Prof K. H. Andy Choo
Murdoch Childrens Research Institute
Melbourne, Australia

Friday 16 April

Using free radicals to fight cancer, why Pacman should be chiral, and other short stories

A seminar in Chemistry and Structural Biology
Dr Mick Sherburn
Research School of Chemistry
Australian National University

Friday 23 April

Evolution, structure and function of the translocases for protein targeting to mitochondria.

A seminar in Molecular Cell Biology
Dr Trevor Lithgow
Biochemistry and Molecular Biology
University of Melbourne, Australia

Friday 30 April

New insights into K+ channel gating: crystal structure of an inward rectifier assembly

A seminar in Chemistry and Structural Biology
Dr Jacqui M Gulbis
Structural Biology Division
Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

Friday 7 May

Nanostructural bioengineering

A seminar in Chemistry and Structural Biology
Dr Anton P Middelberg
Department of Chemical Engineering
University of Cambridge, UK

Friday 14 May

Sequence information independent technologies for genetic analysis

A seminar in Genomics and Computational Biology
Dr Andrzej Kilian
Director of Genomics Research, CAMBIA

Friday 21 May

Antisense oligos and the dystrophin gene: making something from nothing

A seminar in Molecular Genetics and Development
Assoc Prof Steve Wilton
Experimental Molecular Medicine Unit
Australian Neuromuscular Research Institute
University of Western Australia

Friday 28 May

Using functional genomics tools to unravel the mechanism of cell wall assembly in cereals

A seminar in Chemistry and Structural Biology
Prof Tony Bacic
Australian Centre for Plant Functional Genomics,
University of Melbourne, Australia

Friday 4 June

Cloning genes, cloning cells, cloning people: where are the boundaries?

A seminar in Public Policy and Ethics
Prof Bob Williamson
The Murdoch Children's Research Institute
Melbourne, Australia

Friday 11 June

Roles of bHLH/PAS transcription factors in development and disease

A seminar in Molecular Genetics and Development
Assoc Prof Murray Whitelaw
Department of Biochemistry
University of Adelaide, Australia

Friday 18 June

From in vitro analyses of phagosomal actin to rational therapies against pathogenic mycobacteria.

A seminar in Molecular Cell Biology
Dr Gareth Griffiths
Cell Biology, European Molecular Biology Laboratory

Friday 30 July

Molecular control of cell motility in the drosophila ovary and in ovarian cancer

A seminar in Molecular Genetics and Development
Prof Denise J Montell
Department of Biological Chemistry
John Hopkins School of Medicine, Baltimore, USA

Friday 6 August

Paradigms to study the hierarchical levels of eukaryotic genome regulation and define genetic networks in development and disease

A seminar in Genomics and Computational Biology
Dr Hamish Scott
Genetics and Bioinformatics Division
The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia
Presented by Millenium Science

Friday 13 August

Metabolomics: a platform for identifying new metabolic pathways in parasitic protozoa

A seminar in Molecular Cell Biology
A/Prof Malcolm McConville
Department of Biochemistry and Molecular Biology, University of Melbourne, Australia

Friday 20 August

Ion channel structure and mechanism

Dr Michael Stowell,
University of Colorado, Boulder, USA

Friday 27 August

Beyond BRCA1 and BRCA2

Dr Georgia Chenevix-Trenchv
Cancer and Cell Biology, Queensland Institute of Medical Research Brisbane, Australia

Friday 3 September

The SERA gene family in Plasmodium: multiple criteria for assessing and improving inferred gene trees

Prof Terry Speed,
Division of Genetics and Bioinformatics
The Walter and Eliza Hall Institute of Medical Research, Melbourne, Australia

Friday 10 September

Molecular mechanisms of facial (beak) morphogenesis

Dr Joy Richman
Faculty of Dentistry, The University of British Columbia, Canada

Friday 17 September

Platypus venom; new structures and functions

Prof Philip W Kuchel
School of Molecular and Microbial Biosciences
University of Sydney, Australia

Friday 24 September

The history of our Genome: Comparative genomics of vertebrates

Dr Chris Ponting
MRC Functional Genetics Unit
University of Oxford, UK

Friday 1 October

Functions and applications of marine natural products

Prof Marcel Jaspars
Marine Natural Products Laboratory
University of Aberdeen, UK

Friday 8 October

Genes and Ingenuity: Genetic Research, Intellectual Property and Human Health

Prof David Weisbrot
Australian Law Reform Commission

Friday 15 October

Automated CryoElectron Microscopy at NRAMM

A/Prof Clint Potter
National Resource for Automated Molecular Microscopy
The Scripps Research Institute, USA

Friday 22 October

Gene discovery, functional genomics and molecular breeding in pasture plants

Prof German Spangenberg
Primary Industries Research, Victoria
Plant Biotechnology Centre, Australia

Friday 29 October

Is continual production of neurons required for normal brain function?

Prof Perry Bartlett
The Queensland Brain Institute
The University of Queensland, Australia
Presented by Sigma Aldrich

Friday 5 November

A Seminar on taking discovery from the lab bench to the marketplace

Dr John Holaday
Founder of EntreMed, Inc., MaxCyte, Inc., Co-founder of Medicis Pharmaceutical Corp. Medicis (MRX, NYSE). Member of the Board of Directors of CytImmune Sciences, BSI Proteomics, Rexahn and LabBook.

14.

IMB 2004 Publications

Division of Genomics and Computational Biology

1. Baum, B.R., and Ragan, M.A. (2004) The MRP method. In Supertrees. Bininda-Emonds, O.R.P. (ed). Amsterdam: Kluwer Academic.
2. Bejerano, G., Pheasant, M., Makunin, I., Stephen, S., Kent, W.J., Mattick, J.S., and Haussler, D. (2004) Ultraconserved elements in the human genome. *Science* **304:** 1321-1325.
3. Charlebois, R.L., Beiko, R.G., and Ragan, M.A. (2004) Genome phylogenies (invited chapter). In *Organelles, genomes and eukaryotes phylogeny: an evolutionary synthesis in the age of genomics.* Hirt, R. and Horner, D. (eds). London: Systematics Association, pp. submitted 9/2002.
4. Gilson, P.R., Vergara, C.E., Kjer-Nielsen, L., Teasdale, R.D., Bacic, A., and Gleeson, P.A. (2004) Identification of a Golgi-localised GRIP domain protein from Arabidopsis thaliana. *Planta* **219:** 1050-1056.
5. Hallinan, J. (2004) Game Theory. In *Encyclopedia of Nonlinear Science.* Vol. Fitzroy Dearborn. Scott, A. (ed). London: Fitzroy Dearborn, pp. in press.
6. Hallinan, J. (2004) Gene duplication and hierarchical modularity in intracellular interaction networks. *Biosystems* **74:** 51-62.
7. Hallinan, J., and Wiles, J. (2004) Evolving genetic regulatory networks using an artificial genome. In *2nd Asia-Pacific Bioinformatics Conference (APBC2004). Conferences in Research and Practice in Information Technology.* Vol. 29. Chen, Y.-P. (ed.) Dunedin, New Zealand: Australian Computer Society, Inc.
8. Hamilton, N., Burrage, K., Ragan, M.A., and Huber, T. (2004) Protein contact prediction using patterns of correlation. *Proteins* **56:** 679-684.
9. Harlow, T.J., Gogarten, J.P., and Ragan, M.A. (2004) A hybrid clustering approach to recognition of protein families in 114 microbial genomes. *BMC Bioinformatics* **5:** 45-59.
10. Huang, B., Ru, K., Yuan, Z., Whitchurch, C.B., and Mattick, J.S. (2004) tonB3 is required for normal twitching motility and extracellular assembly of type IV pili. *Journal of Bacteriology* **186:** 4387-4389.
11. Mattick, J. (2004) RNA regulation: a new genetics? *Nature Reviews Genetics* **5:** 316-323.
12. Mattick, J.S. (2004) The hidden genetic program of complex organisms. *Scientific American* **291:** 30-37.
13. Mattick, J.S. (2004) The regulatory architecture of the human genome. *Asia-Pacific Journal of Clinical Nutrition* **13:** S14.
14. Mattick, J.S. (2004) RNA regulation: a new genetics? *Nat Rev Genet* **5:** 316-323.
15. McLachlan, G.J., and Chang, S.U. (2004) Mixture modelling for cluster analysis. *Stat Methods Med Res* **13:** 347-361.
16. Merino-Trigo, A., Kerr, M.C., Houghton, F., Lindberg, A., Mitchell, C., Teasdale, R.D., and Gleeson, P.A. (2004) Sorting nexin 5 is localized to a subdomain of the early endosomes and is recruited to the plasma membrane following EGF stimulation. *J Cell Sci* **117:** 6413-6424.
17. Ng, S.K., and McLachlan, G.J. (2004) Using the EM algorithm to train neural networks: misconceptions and a new algorithm for multiclass classification. *IEEE Trans Neural Netw* **15:** 738-749.
18. Ng, S.K., McLachlan, G.J., Yau, K.K., and Lee, A.H. (2004) Modelling the distribution of ischaemic stroke-specific survival time using an EM-based mixture approach with random effects adjustment. *Stat Med* **23:** 2729-2744.
19. Pekkarinen, M., Lom, J., Murphy, C.A., Ragan, M.A., and Dykova, I. (2004) Phylogenetic position and ultrastructure of two Dermocystidium species (Ichthyosporea) from the common perch (Perca fluviatilis). *Acta Protozoologica* **42:** 287-307.
20. Poudel, S.K., and Barker, S.C. (2004) Infestation of people with lice in Kathmandu and Pokhara, Nepal. *Medical and Veterinary Entomology* **18:** 212-212.
21. Shao, R., Aoki, Y., Mitani, H., Tabuchi, N., Barker, S.C., and Fukunaga, M. (2004) The mitochondrial genomes of soft ticks have an arrangement of genes that has remained unchanged for over 400 million years. *Insect Molecular Biology* **13:** 219-224.
22. Shao, R., Barker, S.C., Mitani, H., Aoki, Y., and Fukunaga, M. (2004) Evolution of Duplicate Control Regions in the Mitochondrial Genomes of Metazoa: A Case Study with Australasian Ixodes Ticks. *Molecular Biochemistry and Parasitology: [*Epub ahead of print].
23. Whitchurch, C.B., Leech, A.J., Young, M.D., Kennedy, D., Sargent, J.L., Bertrand, J.J., Semmler, A.B., Mellick, A.S., Martin, P.R., Alm, R.A., Hobbs, M., Beatson, S.A., Huang, B., Nguyen, L., Commolli, J.C., Engel, J.N., Darzins, A., and Mattick, J.S. (2004) Characterization of a complex chemosensory signal transduction system which controls twitching motility in Pseudomonas aeruginosa. *Molecular Microbiology* **52:** 873-893.
24. Yuan, Z., Mattick, J.S., and Teasdale, R.D. (2004) SVMtm: support vector machines to predict transmembrane segments. *Journal of Computational Chemistry* **25:** 632-636.

Division of Molecular Genetics and Development

25. Adolphe, C., Narang, M., Ellis, T., Wicking, C., Kaur, P., and Wainwright, B. (2004) An in vivo comparative study of sonic, desert and Indian hedgehog reveals that hedgehog pathway activity regulates epidermal stem cell homeostasis. *Development* **131:** 5009-5019.
26. Aitken, R.J., Koopman, P., and Lewis, S.E. (2004) Seeds of concern. *Nature* **432:** 48-52.
27. Bullejos, M., and Koopman, P. (2004) Germ cells enter meiosis in a rostro-caudal wave during development of the mouse ovary. *Molecular Reproduction and Development* **68:** 422-428.

28. Challen, G.A., Martinez, G., Davis, M.J., Teasdale, R.D., Grimmond, S., and Little, M. (2004) Identifying the molecular phenotype of renal progenitor cells. *JASN* **15:** 2344-2357.

29. Dong, C., Wilhelm, D., and Koopman, P. (2004) Sox genes and cancer. *Cytogenetics and Genome Research* **105:** 442-447.

30. Duffy, D.L., Box, N.F., Chen, W., Palmer, J.S., Montgomery, G.W., James, M.R., Hayward, N.K., Martin, N.G., and Sturm, R.A. (2004) Interactive effects of MC1R and OCA2 on melanoma risk phenotypes. *Human Molecular Genetics* **13:** 447-461.

31. Gangnuss, S., Cowin, A.J., Daehn, I.S., Hatzirodos, N., Rothnagel, J.A., Varelias, A., and Rayner, T.E. (2004) Regulation of MAPK activation, AP-1 transcription factor expression and keratinocyte differentiation in wounded fetal skin. *Journal of Investigative Dermatology* **122:** 791-804.

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33. Hosking, B.M., Wang, S.-C.M., Downes, M., Koopman, P., and Muscat, G. (2004) The VCAM-1 gene that encodes the vascular cell adhesion molecule is a target of the Sry-related high mobility group box gene, Sox18. *The Journal of Biological Chemistry* **279:** 5314-5322.

34. Kasukawa, T., Katayama, S., Kawaji, H., Suzuki, H., Hume, D.A., and Hayashizaki, Y. (2004) Construction of representative transcript and protein sets of human, mouse, and rat as a platform for their transcriptome and proteome analysis. *Genomics* **84:** 913-921.

35. Koopman, P., Schepers, G., Brenner, S., and Venkatesh, B. (2004) Origin and diversity of the SOX transcription factor gene family: genome-wide analysis in Fugu rubripes. *Gene* **328:** 177-186.

36. Lalonde, J.-P., Lim, R., Ingley, E., Tilbrook, P.A., Thompson, M.J., McCulloch, R., Beaumont, J.G., Wicking, C., Eyre, H.J., Sutherland, G.R., Howe, K., Solomon, E., Williams, J.H., and Klinken, S.P. (2004) HLS5, a novel RBCC (ring finger, B box, coiled-coil) family member isolated from a hemopoietic lineage switch, is a candidate tumor suppressor. *Journal of Biological Chemistry* **279:** 8181-8189.

37. Listwan, P., and Rothnagel, J.A. (2004) Keratin bundling proteins. *Methods Cell Biol* **78:** 817-827.

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42. Ravasi, T., Hsu, K., Goyette, J., Schroder, K., Yang, Z., Rahimi, F., Miranda, L.P., Alewood, P.F., Hume, D.A., and Geczy, C. (2004) Probing the S100 protein family through genomic and functional analysis. *Genomics* **84:** 10-22.

43. Schroder, K., Hertzog, P.J., Ravasi, T., and Hume, D.A. (2004) Interferon-gamma: an overview of signals, mechanisms and functions. *J Leukoc Biol* **75:** 163-189.

44. Schroeder, C.I., Smythe, M.L., and Lewis, R.J. (2004) Development of small molecules that mimic the binding of omega-conotoxins at the N-type voltage-gated calcium channel. *Molecular Diversity* **8:** 127-134.

45. Smith, J.M., Bowles, J., Wilson, M., and Koopman, P. (2004) HMG box transcription factor gene Hbp1 is expressed in germ cells of the developing mouse testis. *Developmental Dynamics* **230:** 366-370.

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47. Smith, J.M., and Koopman, P.A. (2004) The ins and outs of transcriptional control: nucleocytoplasmic shuttling in development and disease. *Trends in Genetics* **20:** 4-8.

48. Smyth, I., Ellis, T., Hetherington, R., Riley, E., Narang, M., Mahony, D., Wicking, C., Rothnagel, J.A., and Wainwright, B.J. (2004) Krt6a-Cre transgenic mice direct LoxP-mediated recombination to the companion cell layer of the hair follicle and following induction by retinoic acid to the interfollicular epidermis. *Journal of Investigative Dermatology* **122:** 232-234.

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51. Taylor, M.D., Zhang, X., Liu, L., Hui, C.C., Mainprize, T.G., Scherer, S.W., Wainwright, B., Hogg, D., and Rutka, J.T. (2004) Failure of a medulloblastoma-derived mutant of SUFU to suppress WNT signaling. *Oncogene* **23:** 4577-4583.

52. Trajkovic, V., Sweet, M.J., and Xu, D. (2004) T1/ST2--an IL-1 receptor-like modulator of immune responses. *Cytokine Growth Factor Rev* **15:** 87-95.

53. Valizadeh, M., Schenk, G., Nash, K., Oddie, G.W., Guddat, L.W., Hume, D.A., de Jersey, J., Burke Jr, T.R., and Hamilton, S. (2004) Phosphotyrosyl peptides and analogues as substrates and inhibitors of purple acid phosphatases. *Archives of Biochemistry and Biophysics* **424:** 154-162.

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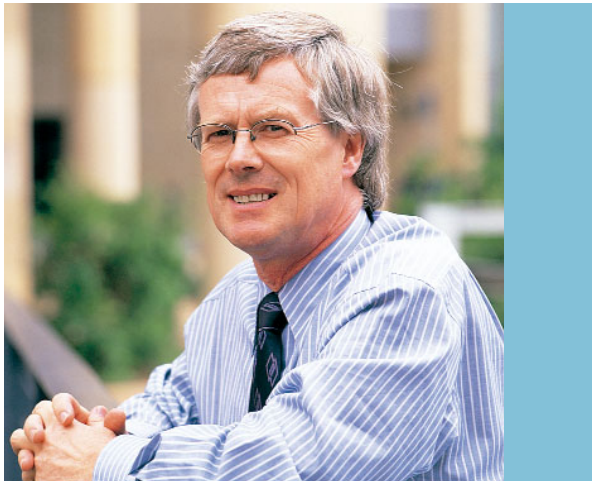
11.

IMB Research Support

Systems, communication and administration



IMB Deputy Director (Systems and Administration), Ian Taylor

In June 2004, the IMB celebrated the first anniversary of its move to the Queensland Bioscience Precinct and I believe it is safe to say that our 385 research staff and students are now settled and concentrating on what they do best – research.

Just over 60 staff form the 'support team' for our researchers in a range of areas including administration and finance; animal house; central sterilising; graduate coordination; information technology; laboratory management; marketing and communication; technical services; building maintenance; and QBP reception.

I thank these staff for a job well done and for keeping the wheels turning at the IMB, literally 24 hours a day, 365 days a year.

EQUIPMENT AND FACILITIES

This year, the IMB established three new research support facilities, including:

Australian Cancer Research Foundation Dynamic Imaging Facility for Cancer Biology

A significant grant from the ACRF enabled the purchase of two Zeiss 510 Meta Confocal microscopes, each based on Zeiss Axiovert inverted microscope platforms. Each system has the capacity for spectroscopic detection and unmixing of fluorescent signals, allowing an unmatched capacity for investigators to probe multiple different molecules simultaneously. Both microscopes are equipped with fully automated stages to permit live cell and high-throughput imaging. This provides the capacity for us to study detailed molecular dynamics as well as perform large-scale screening. Professor Alpha Yap manages the facility.

Cyro EM

A Tecnai 300keV cryo electron microscope, funded by the Major National Research Facility fund, was commissioned for operation in 2004. Final testing on the third party CCD cameras, software and cryo specimen holders and ancillary preparation tools will be completed in 2005. Alasdair McDowall's Group (cell and molecular architecture) is studying biological structures by cryosectioning vitreous bulk material for cryo-electron microscopy (cryo-em). Considered the dream method of structural cell biologists, it involves vitrifying a native sample of cells or tissue by rapid cooling in liquid nitrogen, cutting into ultra-thin <100nm sections and cryo-em observation of the perfectly preserved details.

Zebrafish Facility

In 2004 the IMB established a zebrafish aquarium, housed within the IMB to facilitate an expanded research program in the genetics and cell biology of organogenesis. Establishment of the facility was possible due to the generous support of a University of Queensland Infrastructure Grant and is managed by Associate Professor Andrew Perkins.

Features of the facility include:

- Built by Ben Erin Aqua, a Brisbane based company. The design is based upon the Aquatic Habitats self-cleaning tank system, and is stocked with tanks from Aquatic Habitats®.
- Currently over 800 tanks are in use, with capacity to expand to over 2000 tanks as required, permitting a number of research groups to make use of the system simultaneously.
- An independent AQIS accredited Quarantine System, and a MaxHatchR fry feeding station. Fry are raised on a variety of foods including Golden Pearls®, paramecia, vinegar eels, and artemia.

Information Technology

IMB's computational and data-intensive research capacity was increased significantly in 2004. An IBM opteron-based linux cluster was installed and storage on the research systems was tripled. A further doubling of capacity is planned for early 2005. These resources have been heavily used by several research groups within the Institute.

EVENTS

The IMB coordinated and hosted eight research conferences and meetings in 2004 and assisted in the coordination of more than 170 events by external operators, eager to use the new facilities at the QBP.

The monthly rooftop BBQ following the Friday Seminar maintained its popularity among research staff and students as an opportunity to mingle with colleagues over a 'snag'.

A new concept, the *Tuesday Trade Off (TTO),* was introduced in 2004 in conjunction with CSIRO, to provide a forum for all staff within the QBP to gather for morning tea every Tuesday morning. Each TTO is sponsored by a commercial company who enjoy an audience of more than 100 'potential buyers' of their products and services. TTO sponsors for 2004 included: Edward Keller; Medos; Radiometer; John Morris Scientific; Pall Life Sciences; DKSH; and Thermo Electron Company.

VISITING DELEGATIONS AND VIPS

Throughout the year the IMB welcomed international delegations from Japan, the USA, Brazil, China, Taiwan and Korea. Delegations were briefed on IMB research and introduced to scientists in particular fields of interest. The IMB also hosted a number of visits and provided briefings and site tours for local, state and federal Government Ministers and media.

TECHNICAL SERVICES

As IMB facilities, equipment, labs and staff numbers grow, so does the role of technical services and asset management. In 2004, the 'workshop' team reported more than 2,600 maintenance jobs, representing a 24.5% increase from 2003. Just over 5000 electrical items were tested and tagged and the details of more than 1700 'non asset' electrical items were added to the database.

12. Financial Statement – Statement of Operating Income and Expenditure Year Ended 31 December 2004

INCOME:	Note	2000	2001	2002	2003	2004
University of Queensland (Operating Grant)	1	2,942,718	6,664,365	6,023,929	8,122,858	6,877,099
University of Queensland Research Grants		200,990	100,000	269,358	277,337	228,999
State Government		5,500,000	2,500,000	6,000,000	8,500,000	10,000,000
SRC Grant (Australian Research Council)		1,631,153	1,039,320	1,148,975	1,005,151	1,117,038
Australian Research Council	2	1,131,271	1,668,000	1,599,576	3,218,103	4,261,849
Australian Cancer Research Foundation		0	0	0	0	600,000
Australian Stem Cell Centre		0	0	0	0	306,219
Cancer Council South Australia		0	0	0	30,500	30,500
Clive and Vera Ramaciotti Foundation		43,545	9,545	0	0	0
CRC for Discovery of Genes for Common Human Diseases		220,958	232,415	122,469	48,946	0
CRC for Chronic Inflammatory Diseases		0	0	943,401	968,800	1,261,017
Dairy Australia		0	0	0	0	338,779
Department of Primary Industries		0	0	98,040	0	0
Diabetes Australia Research Trust		33,409	35,791	37,700	0	0
Department of Industry Science and Technology		166,400	0	0	0	0
Human Frontiers Science Program		127,242	0	0	146,291	138,057
Glaxo Welcome Australia		670,000	62,000	0	0	0
Government Employees Medical Research Fund		45,000	0	0	0	0
Juvenile Diabetes Foundation International		299,626	267,704	77,084	0	151,732
Mayne Bequest Foundation		60,000	0	0	0	0
The Merck Genome Research Institute		261,559	0	0	0	0
National Institute of Health (US)		0	0	1,391,005	1,049,548	1,475,684
National Health and Medical Research Council	2	2,938,586	5,359,112	4,306,397	6,761,404	6,438,350
National Heart Foundation		45,000	0	50,000	42,735	50,000
Novartis		0	0	0	641,790	0
Post Graduate Scholarships		28,209	15,882	38,214	73,467	91,968
QIMR		0	0	53,908	60,575	0
Queensland Cancer Fund		230,072	116,447	92,750	72,590	140,000
Sylvia and Charles Viertel Charitable Foundation		165,000	165,000	165,000	0	0
Wellcome Trust		28,011	23,829	0	204,763	180,706
Commercial Income		1,371,664	2,589,861	2,127,649	1,517,449	1,473,905
Cross-Institutional contributions to LIEF		0	0	0	122,500	192,800
University of Newcastle (re ARC Centre)		0	0	0	127,727	127,893
QBP recoveries		0	0	0	331,594	312,979
Shared Grants		0	0	0	105,845	128,764
Conference Income		0	0	0	55,275	25,501
QBPStore		0	0	0	0	44,021
Miscellaneous Income		415,591	272,136	19,593	392,822	355,652
TOTAL INCOME:		18,556,004	21,121,405	24,565,049	33,878,069	36,349,511
Funds brought forward from previous year	3	1,009,031	3,843,597	3,594,479	7,545,101	6,746,999
TOTAL FUNDS AVAILABLE		19,565,034	24,965,002	28,159,528	41,423,170	43,096,510
EXPENDITURE:						
Salaries – Research		6,549,841	7,809,255	9,066,745	12,238,779	16,195,354
– Administration		1,090,220	1,117,375	1,342,520	1,365,120	1,243,375
– Infrastructure		541,043	813,527	1,012,400	1,735,158	2,131,608
Research Services		2,635,745	6,034,723	4,865,433	6,938,972	7,667,863
Education Programs	4	317,726	378,436	500,939	484,360	418,784
Administration	5	937,703	550,574	452,021	519,046	383,224
Infrastructure	6	357,436	928,651	786,809	1,568,251	1,772,942
Capital Equipment	7	2,307,116	3,132,769	1,840,664	8,649,700	5,521,066
IMBcom		984,608	605,214	746,896	1,176,785	1,205,144
TOTAL EXPENDITURE:		15,721,437	21,370,523	20,614,427	34,676,171	36,539,360
Funds carried forward:	**8**	**3,843,597**	**3,594,479**	**7,545,101**	**6,746,999**	**6,557,150**

Explanatory Notes to Statement of Income and Expenditure Year Ended 31 December 2004

1 In-kind Contributions

Figure does not include the following salaries for joint appointments paid by other departments:

	Department	*Percentage*
K.Burrage	ACMC	80
T. Bailey	ACMC	80
P. Koopman	Biomedical Sciences	10
M.Waters	Biomedical Sciences	20
A.Yap	Biomedical Sciences	20
J. Hallinan	ITEE	20
G. McLachlan	Mathematics	80
A. McDowall	Microscopy & Microanalysis	80
S. Barker	Molecular & Microbial Sci.	80
D. Hume	Molecular & Microbial Sci.	20
J. Martin	Molecular & Microbial Sci.	10
S. Kellie	Molecular & Microbial Sci.	80
J.Rothnagel	Molecular & Microbial Sci.	80
B.Wainwright	Molecular & Microbial Sci.	20
B.Kobe	Molecular & Microbial Sci.	80
J. Stow	Molecular & Microbial Sci.	20
R.Parton	Biomedical Sciences/CMM	20
W. Hall	Social Behaviourial Sci.	20

2 Fellowship/Projects from Government Agencies

Australian Research Council

Projects	3,621,474
Fellowships	640,375
	4,261,849

National Health and Medical Research Council

Projects	5,234,457
Fellowships	1,203,893
	6,438,350

3 Funds brought Forward from 2003

University of Queensland Operating Grant	1,645,629
University of Queensland Research Grants	26,038
Post Graduate Scholarships	3,734
State Government	125,166
SRC Grant	374,734
Fellowships (as approved by funding bodies)	149,096
Overseas Grants funded mid year	1,709,903
Contract Research	1,270,789
Project Grants (as approved by funding bodies)	1,441,911
	6,746,999

4 Education Programs

Postgraduate scholarships	396,626
Postgraduate recruitment & training	22,158
Total Education Services	**418,784**

5 Administration

Annual Report	34,696
Marketing	62,094
Personnel Recruitment and Training	38,056
Visiting Scientists/Seminars	31,001
Fees	32,243
Entertaining	16,328
Photocopying	45,692
Postage and Freight	764
Printing & stationery	57,386
Telephone	77,634
Travel Expenses	(5,324)
Board Fees	53,231
Cost Recovery	(60,576)
Total Administration	383,224

6 Infrastructure

Building Maintenance	203,645
Rental -Storage	7,865
Safety Equipment	33,328
Laundry	8,415
Minor Equipment & Furniture	5,045
Equipment Maintenance	185,100
Animals	17,537
Computer Services	822,080
Glass washing and replacement	34,171
Reticulated gases, RO water & dry ice	144,662
Sundries	53,772
Stores	257,322
Total Infrastructure	**1,772,942**

7 Capital Equipment

Scientific Equipment	5,395,057
Minor Equipment	126,009
Total Capital Equipment	**5,521,066**

8 Funds carried forward to 2005

University of Queensland Operating Grant	835,636 #
University of Queensland Research Grants	30,718
Post Graduate Scholarships	15,059
State Government	774,052 #
SRC Grant	148,517
Fellowships (as approved by funding bodies)	182,521
Overseas Grants funded mid year	1,505,209
Contract Research	1,172,077
Project Grants (as approved by funding bodies)	1,893,362
	6,557,150

Of this, $1.1m is the carry forward on IMB Group Leader core accounts, $0.5m relates to oustanding 2004 equipment commitments.

13.

Glossary of terms

Some readers may be unfamiliar with some of the scientific terms used in this Annual Report. Please check below for a short explanation to some of the more common terms. More information about current issues in biotechnology can be downloaded from the Office of Public Policy and Ethics pages in the IMB website.

Alzheimer's disease A disease associated with the breakdown of nervous tissue in the brain, giving rise to a dementia in the patient.

Amino Acid Amino acids are the building blocks of proteins. The sixty-four codons of the genetic code allow the use of twenty different amino acids (the primary amino acids) in the synthesis of proteins.

Apoptosis The normal process of programmed cell death. Disruptions to this process often lead to cancers.

ARC Australian Research Council. The ARC plays a key role in the Australian Government's investment in the future prosperity and well-being of the Australian community. The ARC's mission is to advance Australia's capacity to undertake quality research that brings economic, social and cultural benefit to the Australian community.

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

Cancer Any malignant, cellular tumour. Cancers can be divided into two types carcinoma and sarcoma.

Carcinoma A malignant new growth made up of epithelial cells tending to infiltrate surrounding tissues and to give rise to metastases.

Chromosome A package of wound-up DNA in the nucleus of a cell. Humans have 23 pairs of chromosomes.

Combinatorial chemistry A technique for systematically assembling molecular building blocks in many combinations to create thousands of diverse compounds.

Computational biology The study of living systems using computation.

Cryo EM Cryo electron microscopy – an electron microscopy technique in which the sample is frozen rather than stained.

Cystic fibrosis A genetic disease with symptoms that usually appear shortly after birth. They include breathing difficulties and respiratory infections due to accumulation of sticky mucous problems with digestion and excessive loss of salt in sweat.

Diabetes A disorder characterised by excessive urine production. Commonly used when referring to diabetes mellitus (Type 1) a metabolic disorder in which there is inability to oxidise carbohydrates due to a disturbance of the normal insulin mechanism, producing hyperglycemia, glycosuria, polyuria. Also refers to non-insulin dependant diabetes (NIDD) an asymptomatic form of diabetes mellitus with onset after 40 years of age. Often brought on by a lifestyle of sedentary living with high intake of lipids in diet.

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

EM Electron microscope – a microscope that uses a beam of highly energetic electrons to examine objects on a very fine scale.

Functional Genomics The use of genetic technology to determine the function of newly discovered genes by determining their role in model organisms.

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

Gene Expression The actual production of the protein encoded by a gene.

Genome All DNA contained in an organism or cell.

Genomics The study of genes and their function.

Genotype Is the hereditary genetic constitute of an organism.

Inflammatory disease A disease characterized by inflammation. Examples studied at IMB include rheumatoid arthritis, chronic obstructive pulmonary disease.

National Institutes of Health (NIH) A large biomedical research organization that is part of the U.S. Public Health Service. NIH includes various institutes, centers and divisions including National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) which funds several groups in the IMB.

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

NHMRC National Health and Medical Research Council. A national organisation responsible for, among other things, fostering medical research and training and public health research and training throughout Australia.

Peptide Two or more amino acids joined by a peptide bond.

Pharmacogenomics The study of the interaction of an individual's genetic makeup and response to a drug.

Phenome The physical characteristics of an organism.

Protein A large molecule composed of one or more chains of amino acids in a specific order; the order is determined by the base sequence of nucleotides in the gene that codes for the protein. Proteins are required for the structure, function, and regulation of the body's cells, tissues, and organs; and each protein has unique functions. Examples are hormones, enzymes, and antibodies.

Proteomics The study of structure and function of all the proteins expressed in a cell.

Recombinant DNA Any new combinations of genes or gene parts spliced together to form a single DNA molecule.

RNA A chemical similar to a single strand of DNA. RNA delivers DNA's message to the site of protein synthesis.

Sarcoma A malignant tumour made up of a substance like the embryonic connective tissue.

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

X-ray Crystallography A technique of determining a molecule's three-dimensional structure by analysing the x-ray diffraction patterns of crystals made up of the molecule in question.