



# The Institute

# About the IMB



## ■ About the IMB

The Institute for Molecular Bioscience (IMB) is based at The University of Queensland. It incorporates the ARC Special Research Centre for Functional and Applied Genomics, and the headquarters and Brisbane division of the Australian Genome Research Facility, as well as significant components of the Advanced Computational Modelling Centre and the Centre for Microscopy and Microanalysis.

Recognised nationally and internationally, the IMB is one of Australia's leading research institutes and a major centre for molecular bioscience research. It links leading edge genomic discovery and bioinformatic facilities with state-of-the-art research to better understand human and animal biology, and to develop new pharmaceuticals, diagnostics, nanotechnologies and disease therapies.

Research at the IMB includes the genomic and genetic analysis of mammalian development and cell biology, as well as structural analysis of key proteins and the discovery of new chemicals that may interact with these proteins as the basis for new pharmaceutical development aimed at cancer, inflammatory and infectious diseases, and a range of common human diseases.

Exploring new scientific realms while integrating emerging fields and new discoveries ensures the IMB's position at the forefront of world bioscience research.

The IMB is a core partner in two new Australian Research Council Biotechnology Centres of Excellence (COE). These are the COE in Stem Cells and Tissue Repair and the COE in Biotechnology and Development. Additionally the IMB is centrally involved in two Cooperative Research Centres (CRC), the CRC for the Discovery of Genes for Common Human Diseases and the CRC for Chronic Inflammatory Diseases.

Creating operational synergies between research, industry and government, the IMB provides an integrated environment of excellence that capitalises on a spectrum of intellectual and physical resources, a multi-disciplinary approach and effective links between groups involved in discovery and those involved in developing practical applications.

The Institute's commercialisation arm, IMBcom Pty Ltd provides a dedicated vehicle for the commercialisation and development of IMB's research and technologies.

In early 2003, the IMB together with CSIRO, will relocate to the new \$105 million, state-of-the-art facility constructed at The University of Queensland. Approximately 800 scientists, research students and support staff from the IMB, CSIRO and Queensland Department of Primary Industries, will work in the new complex, making it one of the largest and most innovative biological research centres in the Southern Hemisphere.

## ■ Chair's Report

THE opening in 2003 of the \$105 million research complex that will house The University of Queensland's Institute for Molecular Bioscience (IMB) marks a significant milestone for the University and for biotechnology research.

The IMB facility forms the nucleus of a cluster of research institutes that will help establish UQ as an important player in international bioscience.

Importantly, it also will enhance the University's ability to contribute substantially to areas of research that promise to improve and prolong human life.

The IMB already is making important contributions to research on cancer, Alzheimer's disease, cystic fibrosis, schizophrenia, obesity, human genome structure and expression, bioinformatics, inflammatory diseases, drug design and bioethics.

Its new state-of-the-art premises, made possible with contributions from the State and Federal Governments, a large private donation and the University's own contribution, will help lift this work to even higher levels.

The IMB is joined in the new facility by the CSIRO in a move that will encourage collaborative partnerships and help ensure a gathering of top minds on this important work.

The IMB is one of Australia's leading research institutes and has contributed to The University of Queensland becoming one of the top three research universities in the nation.

There is a growing awareness in Australia of the importance of intellectual infrastructure in underwriting our future economic wellbeing. The links between research and a knowledge-based future economy are indisputable and necessary rather than merely hypothetical or optional.

Research-strong universities, such as UQ, will play a vital role in promoting this understanding and driving it towards practical outcomes.

The new IMB-CSIRO research complex brings our knowledge-based future into sharp focus. It is an exciting development that will place us at the cutting edge of discovery.



**Professor John Hay  
Vice-Chancellor, UQ**

# Co-director's Report



## ■ Professor Peter Andrews

The short history of IMB has been all about dreams. Some have been individual, some collective. Most have been scientific, some commercial. All have been ambitious, many breath-taking. Most will undoubtedly prove to be rewarding.

For me, there were three.

The first was the Centre for Drug Design and Development, commonly known as the 3D Centre. Pioneered by the same hardy (foolhardy?) band of researchers who had moved with me from the Victorian College of Pharmacy to Bond University in 1988, the 3D Centre's arrival at The University of Queensland in 1991 was not met with unanimous support. At my first meeting with the Faculty Executive all eleven of my proposals were rejected *nem con*. But others saw the potential, and our dreams of building a research centre that would not only conduct strong fundamental research, but also develop it in collaboration with industry, were strongly backed by the University, government and industry.

By 1995, we had fully equipped laboratories covering structural biology, molecular design, medicinal chemistry, protein chemistry and biochemical pharmacology, and had grown to a quorum of 60 researchers, all supported by earnings from grant agencies and industry.

The second was biobusiness. At the 3D Centre's 1995 annual retreat, I asked the Centre's staff and students whether any of them wanted to start a biotech company. To my surprise, eight people put up their hands. Today, all of them have founded or contributed substantially to the establishment of start-up companies.

Three of their companies, Xenome, Protagonist, and Alchemia, have employed a combined total of 100 staff, of whom almost half have come from IMB. In all, seven start-ups have emerged from the research of the 3D Centre, and many more IMB scientists are now working to achieve similar goals.



The engine driving these developments, IMBcom Pty Ltd, provides a new paradigm in technology transfer for Australian universities, with a team of specialists working side-by-side with scientists to identify and develop their intellectual property.

The third was IMB. The origins of that dream also date back to the mid-1990s, when John Mattick, then director of the Centre for Molecular and Cellular Biology (CMCB), was the after-dinner speaker at another of the 3D Centre's annual retreats. John's theme was the wealth of opportunity to be found at the interface of molecular biology and chemistry. In short, he argued that by combining 3D's culture of chemistry and commercialisation with CMCB's culture of biology and basic research, we could play a significant role in key aspects of medicine, agriculture, energy and the environment. It was a long bow, but that dream is now rapidly coming to fruition.

Through its interactions with CSIRO and others, IMB is already applying its knowledge well beyond its core business of human biology and pharmaceutical discovery. It is also thoroughly immersed in the business of nurturing fundamental research at the interface of chemistry, biology and computing – the place to be for the 21<sup>st</sup> century - whilst simultaneously translating that research into health and economic outcomes of benefit to the community.

The culmination of that dream, and the start of many more, will be IMB's move into the IMB/CSIRO Research Complex early in 2003. There is no doubt that the new complex will become a key international centre for molecular bioscience, fostering the discovery of new genes, proteins and drugs, the forging of new partnerships, and the building of new centres, companies and even institutes.

Many people have asked me how I could bear to leave at this point in the Institute's development. It's a good question, but I think it's the right time. For me, the next dream is to play a role in building Australia's biobusiness.

I can't yet say exactly what that role will be, but I am hopeful that it will continue to involve frequent and productive interactions with the remarkable people of IMB.

I look forward to sharing more dreams!

A handwritten signature in black ink, appearing to read 'Peter Andrews'.

Professor Peter Andrews

# Co-director's Report



## ■ Professor John Mattick AO

The Institute for Molecular Bioscience (IMB) continues to grow and to develop its intellectual and physical resources to address the key questions and opportunities in biomedical research and biotechnology:

- How genetic information is transduced through regulatory circuitry, macromolecular structures and chemistry, to form different cells and to organise these into complex organisms like humans?
- How variation in this information influences our characteristics and susceptibility to disease? and
- How this knowledge can be utilised to solve health and environmental problems and to create new products and industries?

There have been many important discoveries and highlights during 2002, which are listed elsewhere in this report. Among many important developments, IMB is a core partner in the Biotechnology Centre of Excellence for Stem Cells and Tissue Repair, through Associate Professor Melissa Little and in the Australian Research Council (ARC) Centre of Excellence in Biotechnology and Development, through Professor Peter Koopman. We also obtained significant additional funding for the Cooperative Research Centre (CRC) for Chronic Inflammatory Diseases, through Professor David Hume, and for the Australian Genome Research Facility, through Dr Sue Forrest, as well as a major grant from the US National Institutes of Health for a new program in kidney research, led by Associate Professor Melissa Little. IMB, through Professor Mark Ragan and IMBcom, was also awarded a \$3 million Shared University Research (SUR) Grant from IBM to help set up the computing infrastructure for our bioinformatics program.

We have been fortunate also to attract some outstanding new scientists to IMB to establish new research groups and to create new capabilities: Dr Ben Hankamer from Imperial College, London, who in conjunction with Dr Alasdair McDowall will



establish cryo-electron microscopy at IMB, a vital approach to bridging the present gap in our knowledge between protein structure and cell biology; Professor Jeff Gorman from CSIRO Melbourne, who will lead the joint IMB-CSIRO Proteomics Laboratory, a key facility for exploring gene expression and for identifying the components of macromolecular complexes, which will complement our existing microarray facilities; and Professor Rob Capon, from the University of Melbourne, who will establish a new Centre for Molecular Biodiversity to explore the world of natural chemistry as a platform for drug discovery and new drug design.

Turnover and renewal are healthy, as institutions acquire new people with new skills and fresh ideas. They also lose people who move on to new challenges. We are delighted that so many of our postdoctoral fellows and graduating PhD students have obtained positions in excellent research institutions and industries elsewhere in Australia and abroad. We also bid farewell to Professor David James, who joined us in 1993 and departed early in 2002 to become the Director of the Diabetes and Obesity Research Program at the Garvan Institute of Medical Research in Sydney. We thank David for his great contributions to our development, and wish him well in his new and important position.

The IMB's productivity is built on the talents and dedication of its people. We have outstanding group leaders, postdoctoral researchers and PhD students, as well as excellent administrative and support staff, which space precludes mentioning individually. However, I would like to particularly acknowledge and thank Dr Ian Taylor (Deputy-Director, Systems and Administration), Professor Mark Ragan (Program Leader, Genomics and Bioinformatics), Professor Brandon Wainwright (Program Leader, Developmental and Cell Biology), Professor Paul Alewood (Program Leader, Structural Biology and Chemistry), and Professor David Hume (Deputy-Director of the ARC Special Research Centre for Functional and Applied Genomics), and our other senior staff for their contributions to IMB's management and development during 2002. We are all indebted to the IMBcom team, headed by Professor Peter Andrews and Dr Peter Riddles, for their assistance in developing the commercial opportunities arising from our research, and for ensuring that we have once again met and in most cases exceeded the key performance indicators that underpin the Queensland Government's investments in the capital and operating costs of the Institute.

I congratulate the Director of IMB's Office of Public Policy and Ethics, Professor Wayne Hall AM, on his election to the Australian Academy of Social Sciences. I am also delighted to report that Professor Wainwright has been appointed Deputy-Director (Research) of the Institute from the beginning of 2003.

I thank the Vice Chancellor Professor John Hay, the Senior Deputy Vice Chancellor Professor Paul Greenfield, the Deputy Vice Chancellor (Research) Professor David Siddle and our other senior colleagues at the University of Queensland for their ongoing support of IMB. I also thank the Members of our Board and Scientific Advisory Board for their guidance, as well as the State and Federal Government for their financial support. We will move into our new facilities in the new IMB-CSIRO Research Complex early in 2003, and have already had many discussions with Dr Shaun Coffey and other colleagues at CSIRO and QDPI about developing joint programs and new collaborations to take advantage of what we intend will become one of the most dynamic research environments in Australia.

My final words are reserved for my friend and partner, Professor Peter Andrews, the Director of the Centre of Drug Design and Development, and the Co-Director of IMB. As explained in his report, Peter has resigned from the end of 2002 to pursue his interests in developing the biotechnology industry. Peter's contributions to the University, to the establishment of IMB, and to the development of pharmaceutical and biotechnology industries in Queensland and Australia generally have been immense. On behalf of all at IMB, and particularly myself, I thank Peter most sincerely. He will be sorely missed. The good news is that he will be close by.

Professor John Mattick AO

## ■ As at 31 December 2002



### **Chair**

Prof. John Hay  
Vice-Chancellor  
The University of Queensland



### **Deputy Vice-Chancellor**

Prof. Paul Greenfield  
Deputy Vice-Chancellor  
The University of Queensland



### **IMB representative**

Prof. John Mattick AO  
Co-director IMB  
Director AGRF  
Director ARC SRC for Functional and Applied Genomics





**IMBcom representative**

Prof. Peter Andrews  
Co-director IMB  
CEO IMBcom



**State Government representative**

Mr. Paul Fennelly  
Director-General  
Queensland Department of State Development



**State Government representative**

Mr. Scott Flavell  
Director-General  
Queensland Department of Innovation and Information Economy



**International Scientist**

Prof. Frank Gannon  
Executive Director  
European Molecular Biology Organization (EMBO)  
Germany



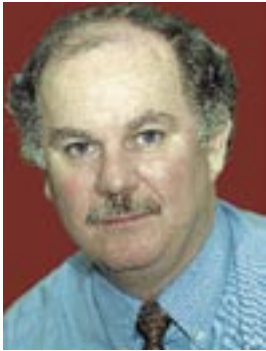
**Biotechnology Industry representative**

Dr Russell Howard  
CEO  
Maxygen Inc., USA



**Business Representative**

Ms Helen Lynch AM  
Non-Executive Director Southcorp Ltd., Coles Myer Ltd. and Westpac  
Banking Corp.  
Deputy Chair, OPSM Protector Ltd.  
Chair, Sydney Symphony Orchestra



**Executive Dean**

(rotating)

Prof. Mick McManus

Executive Dean

Faculty of Biological and Chemical Sciences

The University of Queensland



**Business representative**

Mr. Ross Rolfe

CEO

Stanwell Corp Ltd.



**Community representative**

Sir Sydney Schubert

Chair CRC Reef Research Centre

Former Co-ordinator General of Queensland Premier's Department

Former Chief Executive and Chair, Daikyo Australia

# IMBcom Pty Ltd

Peter Andrews, CEO  
Daniela Bellomo, Development Officer (in part)  
Catherine Benham, Administrative Assistant  
Ashley Bowen, General Manager,  
Commercialisation and Finance  
Kellie Broderick, Executive Assistant (on leave)  
Sam Cobb, Development Officer  
Kim Flanagan, Administrative Assistant  
(on leave)  
Wei-Lin (Maggie) Hsu, Commercial Intelligence Analyst  
(in part)  
Sam Modini, Team Secretary  
Christine Morrison, Manager, Business Support  
Katherine Nielsen, Manager, Intellectual Property &  
Business Analyst  
Peter Riddles, Deputy CEO  
Goslik Schepers, Biotechnology Analyst

In 2002 IMBcom continued to work with IMB scientists to identify and develop projects with commercial potential. These projects will result in spin-offs, alliances and licensing opportunities with industry partners and underpin the growth of a biotechnology industry in Queensland and Australia.

The past year saw IMBcom dedicated to working with IMB to develop collaborations with a number of partners in industry and government.

An alliance between computing giant IBM and IMB has resulted in the development of a joint research program which shares bioinformatics knowledge and tools, and will result in the establishment of a world class bioinformatics hub at the IMB. This collaboration will advance bioinformatic research, aimed at harnessing technology to create more effective treatments for disease.

A Memorandum of Understanding has also been signed between



Academica Sinica and the IMB.

The close collaboration between business and science enabled a number of commercial licenses to be established with a range of national and international biotechnology industry leaders.

Additionally two new spin off companies, Cyclagen and Nephrogenix, were incorporated to be further developed during 2003.

An IMBcom initiative saw staff working with IMB scientists on NHMRC Development, ARC Linkage and Biotechnology Innovation Fund (BIF) grant applications. As a result IMB scientists had a 100 percent success rate in round one of the ARC Linkage funding process and established exciting industry collaborations involving natural products and new therapies.

In August 2002 approximately 20 PhD students along with the IMBcom team ventured to the Sunshine Coast on a Biobusiness Retreat for a series of seminars and workshops on intellectual property and business development.



## SPIN-OUT COMPANIES

### Cyclagen Pty Ltd

Cyclagen was established to exploit the potential of gene technology to create new insecticidal proteins for crop protection. Cyclagen was awarded a Biotechnology Innovation Fund (BIF) grant of \$250,000 in August 2002 and as a result was incorporated in December 2002. Further sources of pre-seed funding are being investigated.

### Nephrogenix Pty Ltd

Nephrogenix Pty Ltd was established to commercialise the research of the Renal Regeneration Consortium comprising of researchers from IMB, UQ, Monash University, RMIT and Canberra Hospital. The consortium has obtained considerable funding to exploit recent advances in tissue engineering and growth factors, to develop novel therapeutics for patients with renal disease.

### Protagonist Pty Ltd

Protagonist is focused on the discovery of drug candidates for targets previously resistant to small molecule discovery, and on designing and constructing arrays of molecules that sample biologically relevant regions of chemical diversity. Protagonist was awarded its second BIF grant of \$198,000 in August 2002. It is now in the early stages of preparing for a second round of major fund raising.

### Nanomics Biosystems Pty Ltd

Nanomics Biosystems has a variety of high throughput screening technologies with applications in genomics, proteomics and combinatorial drug discovery. Nanomics was awarded a BIF grant of \$250,000 in March 2002. A management and technical team has been appointed to advance the technology development program.

### Mimetica Pty Ltd

Mimetica is in the business of making molecules using a new technology that mimics the shape and function of biologically important peptides. Mimetica secured \$1 million from Biostart, BIF and a follow-on venture capital investor. Mimetica has appointed a management and technical team to advance the technology development program.

### Promics Pty Ltd

Promics creates small molecules that reproduce or mimic secondary structural characteristics of proteins to make therapeutic compounds. It was awarded a BIF grant of \$216,800 in March 2002 and is progressing with development and clinical work on its lead compounds.

In addition IMBcom continued to support other IMB spin-off companies Kalthera and Xenome.



# Highlights

## 2002

Built on the scientific excellence and the unfailing dedication of its staff, IMB research is at the leading edge of the worldwide quest to better understand human and animal biology. This culture of excellence is recognised by awards, discoveries and scientific grants. Following is a snapshot of some of the many IMB highlights during 2002

### DISCOVERIES AND RESEARCH

#### Queensland team vital to genome discoveries

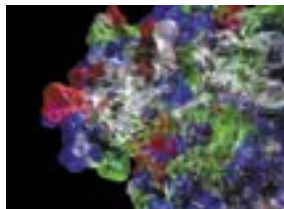
A team of researchers from the IMB led by Professor David Hume, Dr Rohan Teasdale, Dr Sean Grimmond, Dr Tim Ravasi, Mr Al Forest and Ms Christine Wells, played an integral role in the world-first mapping of the functional output of the mouse genome, or 'transcriptome', published in the prestigious science journal *Nature*.

#### Out muscling cholesterol

A new study by Dr George Muscat proved that muscle tissue plays a vital role in regulating cholesterol levels in the body with implications for diseases like atherosclerosis, cardiovascular disease, obesity, and diabetes.

#### 'Nicotine vaccine' not for teenagers

One of the world's leading bioethics and public policy experts, Professor Wayne Hall cautioned against using a potential 'nicotine vaccine' to prevent smoking in teenagers saying it should only be considered after extensive testing on adult smokers.



"Vector Jelly" by Gerald Hartig.  
First place in the 2002 Ångström  
Art "Expose Your Science"  
competition.

#### Queensland researchers leading their fields

The demonstrated research and development excellence of Queensland's IMB is a major driving force behind the State's rapidly expanding biotechnology industry, Professor Peter Andrews told guests at the Queensland Day breakfast.

#### New discovery may help prevent infections in Cystic Fibrosis

Professor John Mattick's research team has made a significant discovery with implications for the treatment of Cystic Fibrosis (CF). Published in the prestigious US journal *Science*, the scientists from the IMB and the Technical University of Denmark described a possible way of preventing a particular bacterial infection experienced by many CF patients.



John Mattick AO (Co-Director),  
Wayne Hall (Director OPPE)  
and Peter Andrews (Co-Director)

#### Human genetics goes to the people

Dr Rick Sturm and PhD student Helene Johanson commenced a genetic study to better understand human pigmentation disorders and improve the quality of life for South Pacific Islanders with albinism.

#### Cell structure under the microscope

Dr Ben Hankamer, a leading expert in protein structures has been lured to the IMB where he will use state-of-the-art cryo-electron microscopy facilities to continue his work with the potential to develop more efficient drugs.

#### Smart State welcomes bioinformatics brain

One of the world's foremost experts in genomics and bioinformatics, Professor Mike Waterman, spent quality time with scientists from the IMB mapping out a strategic plan for national biological research as part of his maiden visit to Queensland.

#### Alternative to heroin for trial

Professor Wayne Hall, a world leader in addiction studies, published a controversial paper in *Medical Journal Australia* calling for a trial using the legal drug hydromorphone in place of heroin.

### AWARDS

#### New Fellow on the block

The election of IMB's Director of Public Policy and Ethics Professor Wayne Hall AM as a Fellow of Academy of the Social Sciences in Australia recognised his world-leading research on addictions, ethics, biotechnology and public policy.

#### Amgen awards IMB student honours

Academic excellence was recognised when IMB student researcher Ms Emily McGhie was awarded the prestigious Amgen Australia prize for her work on the causes of changes in protein function.

#### IMB scientist wins national award

IMB's Professor Peter Koopman was awarded the prestigious 2002 Amersham Biosciences Medal ahead of other distinguished Australian researchers. The Medal was awarded by the Australian Society for Biochemistry and Molecular Biology for his outstanding contributions to understanding the genetic processes involved in the development and growth of mammals.



Peter Koopman receiving the  
Amersham Biosciences Medal

#### Student prize winner

IMB PhD student Mr Gabriel Kolle won the Australia New Zealand Society for Cellular and Developmental Biology Keith Dixon Prize in Developmental Biology at COMBIO conference.



### IMBer - an honourable fellow

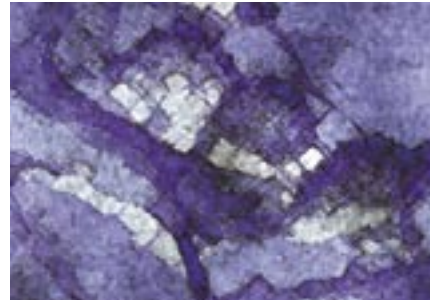
IMB Co-director Professor John Mattick AO was awarded a prestigious Honorary Fellowship of the Royal College of Pathologists of Australasia. This award recognised his research contributions made over the course of his career, and his early identification and unstinting promotion of the far reaching potential that genomic research has for the health of all Australians.

### Building project wins Queensland award

The \$105 million UQ/CSIRO Joint Building Project and new home of the IMB which has created new jobs and contributed millions of dollars to local industry was Highly Commended in the 2002 Local Content Awards.

### Sustained and outstanding research acknowledged

An outstanding research career investigating potential new drugs in the fight against diseases including cancer and chronic pain has been recognised with the awarding of the Adrien Albert Medal by the Royal Australian Chemical Institute to IMB's Professor Paul Alewood.



*"Cellular Monet" by Daniel Sangermani and Darren Brown. Runner-up in the 2002 Ångström Art "Expose Your Science" competition.*

### GRANTS

#### Brisbane Foundation to fight the causes of brain tumours

The fight against brain cancer was further boosted with the awarding of the John Trivett Research Fellowship bursary to Dr Tammy Ellis to continue her work in the IMB with UQ's School of Medicine.

#### Queensland's contribution to fertility

Helping solve human fertility disorders, fighting testicular cancer and controlling feral pests are just some of the benefits the new Centre of Excellence in Biotechnology and Development involving an IMB research team led by Professor Peter Koopman.

#### Boost for Queensland medical research

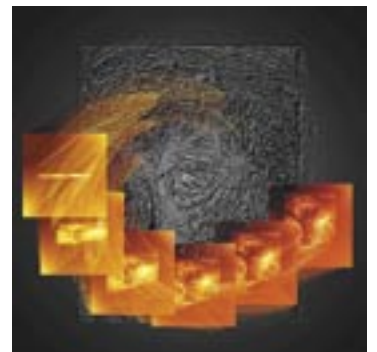
Queensland medical research received a massive boost with Associate Professor Melissa Little's chronic kidney disease research team, forming an integral part of the successful Biotechnology Centre of Excellence in Stem Cells and Tissue Repair.

#### IMB boosted by funding bonanza

With implications for drug design and development to combat many human ailments, IMB research received a welcome boost of approximately \$3.8 million in the latest round of Australian Research Council (ARC) Grants.

#### Grants help Australia's health

Professor Peter Koopman and Dr Josephine Bowles head up an IMB project to find and study the genes that control whether an embryo develops as a male or a female, which attracted \$720,000 funding from the National Health and Medical Research Council.



*"Confocal Continuum" by John Lock. Runner-up in the 2002 Ångström Art "Expose Your Science" competition.*



*Left to right: The Hon. Ian Macfarlane, Minister for Industry, Tourism and Resources, Co-Director Peter Andrews, Architect Mark Roehrs and Co-Director John Mattick on site inspecting the building's progress.*

### Six degrees of biological separation

IMB Computational Biologist Dr Jennifer Hallinan was awarded the prestigious Steinmetz Fellowship by the Santa Fe Institute in the United States for her work on complex networks. These networks are somewhat akin to the social phenomenon 'six degrees of separation', which is used as a model to understand the inner working of cells and assist in the development of drugs with fewer side effects to combat many human diseases.

### Science the winner in art competition

IMB swept the pool in the 2002 Angstrom Art 'Expose Your Science' competition. First prize was won by Mr Gerald Hartig for his image 'Vector Jelly' while Mr Daniel Sangermani and Darren Brown, and Mr John Lock took out the Runners Up prizes.

# Highlights

## US awards Australia's kidney research

Australian scientists led by Associate Professor Melissa Little won a multimillion-dollar US grant from the National Institutes for Health, for research into kidney disease that will be used to spearhead new therapies and treatments for kidney failure in the longer term, by capturing the latest developments in tissue engineering and regenerative medicine today.



Head of the NIH grant  
Melissa Little

## IBM and IMB to focus on bioinformatics research leading to new treatments for disease

International computer giant IBM and IMB announced a \$3 million Shared University Research Grant to advance bioinformatic research aimed at harnessing technology to create more effective treatments for disease.

## COMMERCIALISATION

### Further funding for biotech spin-off

The latest IMB biotech spin-off company, Mimetica, received a quarter of a million dollar boost to drive the investigation and development of new molecules which have the potential to impact on a wide variety of human diseases.

### Grant to boost commercialisation

Development of a new class of pharmaceuticals with applications in the fight against a wide range of human ailments by IMB spin-off company Protagonist, received a further boost with the announcement of a \$198,000 Biotechnology Innovation Fund (BIF) grant by the Federal Minister for Industry Tourism and Resources Ian MacFarlane.

### Biotech grant fights insects

Reduced insecticide use and increased crop productivity are just two of the potential benefits that may result from the new biotech venture Cyclagen, which was awarded a \$250,000 BIF grant.

## FACILITIES

### Genomic speed limit raised by new machines

The Australian Genome Research Facility (AGRF) boosted Australia's leading role in the worldwide genomics revolution with the unveiling of two new DNA sequencing machines by Senator George Brandis.

## Brisbane proteomics instrument an Australian first

The first proteinchip instrument in Australia was launched at IMB, giving scientists a powerful new tool in their fight against common human diseases such as cancer, Alzheimer's and diabetes.

## CONFERENCES

### World first in Brisbane

IMB secured a first to host the prestigious Intelligent Systems in Molecular Biology (ISMB) conference in 2003. This is the first time the conference has been held outside the United States or Europe

### Microarray meeting attracting megastars

Leading Australian scientists will drive the international development of the next wave of bioscientific discovery following the IMB-organised Australian Microarray Meeting, which met at Queensland's Couran Cove Resort.



The signing of the Shared University Research grant by representatives of IBM and IMB

### Workshopping development

IMB hosted some of Australia's leading scientists as they gathered to workshop the genetic basis of devastating diseases such as cancer and cystic fibrosis at the record Australian Developmental Biology Workshop.

### Venomous creatures doing their bit for research

Analysing the venoms of poisonous creatures to develop new drugs and pharmaceuticals is the life-time passion of many of the world's leading scientists who converged on Queensland's Heron Island for the Venoms to Drugs conference coordinated by IMB.





# Genomics and Bioinformatics

By bringing the power of mathematics, computer science and information technology to molecular biology and genomics, the IMB's Division of Genomics and Bioinformatics offers a more quantitative understanding of the complexities of living organisms.

## COMPARATIVE AND COMPUTATIONAL GENOMICS



### Group Leader

Mark Ragan

### Postdoctoral fellow

Josef Pánek

### PhD Students

Alex Garcia  
Michael Höhl

### Research Assistant

Timothy Harlow

### Honours Student

Brendan Tse

**W**e use advanced computer and database methods to investigate similarities and differences among genomes and the proteins they encode. Our goal is to make quantitative inferences about how genomes have come to have their observed contents of genes, how protein families have diversified, and how cellular function has evolved.

Automated inference of vertical and lateral gene transmission in microbial genomes

We are constructing an automated computer-based system to manage genomic data, identify protein families, generate structure-sensitive multiple sequence alignments, and infer and topologically compare phylogenetic trees.

Although motivated by a search for laterally transferred genes, the system will also yield comprehensive libraries of protein motifs and other information useful in applied areas of bioscience, including drug design and metabolic engineering.

Novel algorithmic methods in comparative genomics

Existing methods to identify protein families are often limited by high backgrounds of false positive matches. Markov clustering avoids many false positives, but does not provide topological information as a function of cluster membership threshold.

We have developed a scalable hybrid method that combines the selectivity of Markov clustering with the power of naive clustering.

Pattern-discovery methods offer many opportunities for relating structure, sequence, function and annotation among large datasets.

In collaboration with Dr Isidore Rigoutsos (IBM Thomas J. Watson Research Centre) we are exploring the application of pattern-based methods in high-throughput multiple sequence alignment, phylogenetics, and identification of lateral transfer.

Phylogenetic inference is NP-hard, i.e. as more sequences are added, we can eventually no longer be sure of finding an optimal solution.

An approach based on Bayesian statistics appears able to postpone this point of incomputability.

We have carried out extensive comparisons of classical and Bayesian methods using both synthetic (computer-generated) and real protein-sequence data.

Relational database structures for genomic data

The continuing flood of new sequence information, together with the appearance of new data types, make it increasingly important that we use advanced tools from information science to organise and query genomic data.

We have implemented microbial and the ENSEMBL human genome databases under Oracle, developed complex schema and learned to mount complex queries involving external software.



Photo courtesy of Don Thompson, The University of Queensland.

## EXPRESSION GENOMICS



### Group Leader

Sean Grimmond

### Research Officer

Tina MaGuire

### Research Assistants

Darrin Taylor

Rowena Cecil

Chris Johns

Milena Gorgona

Alistair Forrest

### Honours Student

Alex Combes

The central focus of our research is the study of the mammalian transcriptome to define the underlying genetics of biological processes such as kidney and blood vessel development. We are applying a combination of bioinformatics, microarray based technologies and functional genomics to define specific phenotypes of lead genes.

### Annotating the mammalian transcriptome

The IMB is a participant in the international Functional Annotation of Mouse (FANTOM) consortium. We took part in the functional annotation of 60,000 full-length cDNAs as part of the RIKEN Mouse Gene Encyclopedia project.

Detailed computational analyses have been carried out to define specific classes of genes, including the mammalian phospho-regulators, cell cycle related genes and all gene products secreted into the extracellular space (the secretome).

### Functional genomic screens of the proteome

In collaboration with the IMB's Rohan Teasdale, we have established the cell based microarray assays known as reverse transfection arrays.

A large project aimed at confirming the sub-cellular localization of the genes studied in the RIKEN protein-protein interaction screen is underway in collaboration with Dr Harukazu Suzuki.

Reverse transfection arrays are also being used to screen the roles of phosphoregulators and cell cycle genes.

### Searching for renal progenitors

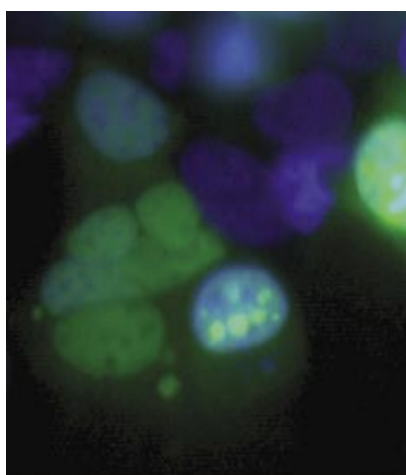
We have established informatic and molecular tools for defining the process of cell commitment to a renal fate during normal development.

The combination of transcriptome annotation and expression profiling is being used to identify novel renal progenitor cell markers and growth factors.

### Transcriptional programs in angiogenesis

Vasculature is essential for all tissue maintenance and repair.

The transcriptional programs driven by endogenous promoters of angiogenesis (hypoxia, VEGF family, bFGFs) are being recorded with microarrays with the hope of identifying key regulators of the process.





## BACTERIAL PATHOGENESIS AND RNA-BASED GENE REGULATION IN EUKARYOTIC DEVELOPMENT



### Group Leader

John Mattick

### Research Officers

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### Research Assistant

Kelin Ru

Our group takes a genomic approach to two important problems - the role of type IV pili in host colonization by *Pseudomonas aeruginosa* and other bacterial pathogens, and the role of noncoding RNA in the programming of differentiation and development in humans and other complex organisms.

*P. aeruginosa* is an important opportunistic pathogen which affects compromised individuals, such as those affected by cystic fibrosis, burns or immune-deficient conditions. Like other surface pathogens it uses external filaments called type IV pili to attach to and move across host surfaces by a process called twitching motility, which occurs via extension and retraction of the pili. We have identified most of the genes which control pili assembly and function, including those encoding a central chemosensory system integrating multiple signals to control twitching motility and other responses to environmental variables.

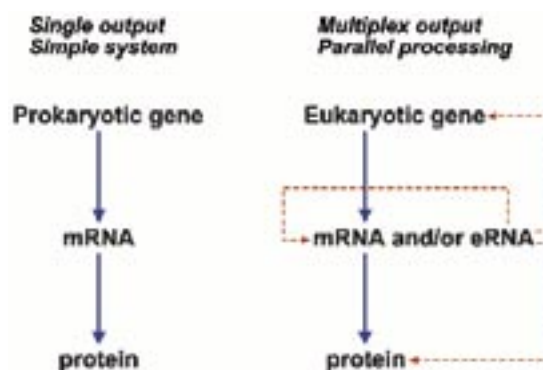
Twitching motility is also required for the formation of *P. aeruginosa* biofilms, which we have recently shown requires extracellular DNA, an unexpected finding that will have impact on the design of anti-infection strategies.

For a number of years our group has been developing an interest in one of the great mysteries of biology – what, if anything, is the function of the vast amount of introns and genomic sequences in the genes of the higher organisms that do not appear to have any function?

These sequences are often referred to as “junk DNA”. Many of these sequences are in fact expressed as noncoding RNAs, and account for around 98% of all genomic output in humans.

We have deduced that these sequences form a second highly parallel network that functions to integrate complex suites of gene expression and to control the programmed responses required for the autopoietic development of multicellular organisms.

We are using computational techniques to map these networks in meiosis, ribosomal biogenesis and alternative splicing, and developing new databases and microarray chips to examine the expression of noncoding RNAs in humans and mice during development and in different disease states. This work will become the main focus of our laboratory from 2003.



## COMPUTATIONAL CELL BIOLOGY



**Group Leader**  
Rohan Teasdale

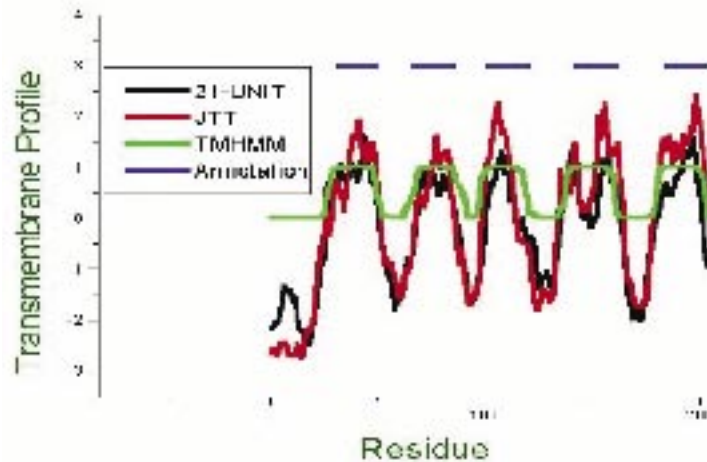
**Research Officer**  
Zheng Yuan

**PhD Students**  
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Cameron Flegg  
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**Honours Students**  
Rajith Aturaliya  
Elaine Thomas

The application of computational biology techniques allows for the prediction of the functional properties of novel proteins based on their sequence. The goal of our research group is to develop and apply such techniques to open up new avenues of scientific exploration within cell biology.



Our research group possesses the combination of cellular and bioinformatic skills allowing a more intuitive insight into the application of computational biology within cellular biology.

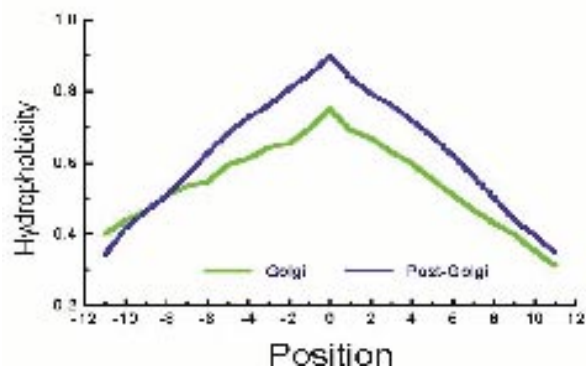
Our research has had a major impact on understanding the signals responsible for targeting membrane proteins to various subcellular regions within the cell.

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

Reverse transfection has allowed high throughput determination of various cellular properties.

We 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.





# Cellular and Developmental Biology

As the number of sequenced mammalian genomes increases, the challenge is the derivation of function. The Division of Cellular and Developmental Biology seeks to do this with an integrated research program bringing together genetics, cell biology, differentiation and development to provide a platform upon which significant insights will be based.

## MOLECULAR GENETICS OF HUMAN DISEASES



### Group Leader

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### Research Assistants

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Emily Riley  
Hania Lada

### Honours Student

Kim Hanchard

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.

Our group examines the molecular pathology of two distinct genetic diseases.

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.

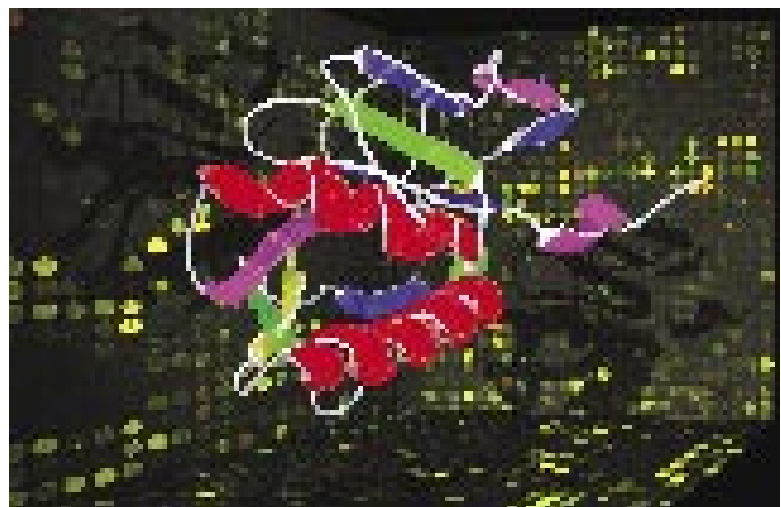
A powerful approach to the analysis of human genetic disease is the use of model systems, such as the mouse.

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.

Our group undertakes specific projects analysing:

- 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; and
- Novel mouse modifier genes affecting lung development and inflammation.



'Cornering Hedgehog' by David Ingram and Wendy Ingram.



## MACROPHAGES AND OSTEOCLASTS



### Group Leader

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Guy Barry

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Vera Ripoll

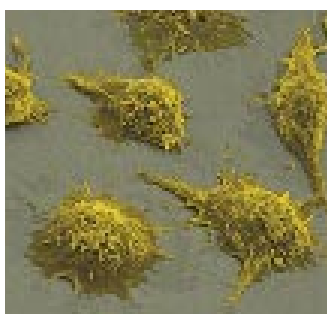
Kate Irvine

Kate Schroder

Nicole Walsh

Nick Meadows

Christine Wells



**M**acrophages and osteoclasts are cells that are critical to the body's ability to repel pathogens, remove damaged tissue and dying cells caused by normal growth and development, as well as decalcify bone. Understanding how these cells function could help boost their normal function and also limit the damage caused in inflammatory and infectious diseases when these cells unleash their destructive capabilities inappropriately.

The research interests of the Hume Laboratory centre on the biology of macrophages and osteoclasts. These are cells of haematopoietic origin that are closely related to each other but have distinctly different activities.

Macrophages are cells of the innate immune system that have critical roles in regulating not only immune response but tissue development and homeostasis.

On the other hand osteoclasts have specialised roles in resorbing bone and in maintaining bone and mineral homeostasis.

The dysregulation of macrophage function mediates several human diseases such as rheumatoid arthritis, inflammatory bowel disease and chronic obstructive pulmonary disease.

The pathological role of macrophages in these diseases is being characterized with the aim of developing novel therapeutic approaches to their treatment.

The bone group led by Dr Ian Cassedy focuses on the biology of osteoclasts. These cells mediate the pathology of a number of bone diseases including osteoporosis.

The aim is to characterise osteoclast function so that we may be able to manipulate it to yield new treatments of osteoclast-mediated bone diseases.

A central area of our investigations is focused on the mechanisms controlling the differentiation of macrophages and osteoclasts from their progenitors.

Macrophage Colony-Stimulating Factor (CSF-1) is the essential growth factor regulating differentiation, activation and survival of macrophages and osteoclasts.

(Cont.)



## MACROPHAGES AND OSTEOCLASTS (continued)

### Research Assistants

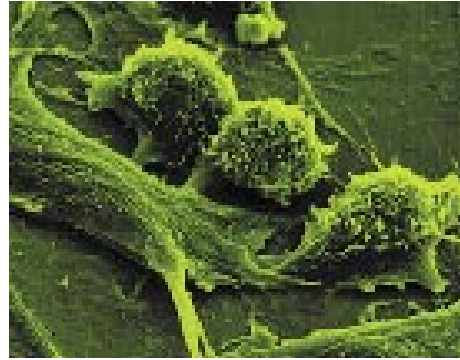
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Jane Clarkson  
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Jill Gillmore



The action of CSF-1 is mediated by its receptor, *c-fms*, and we have defined the elements within the *c-fms* gene required for its expression in macrophages thereby identifying lineage-related transcriptional processes.

The study of macrophage and osteoclast biology has been facilitated by our generation of transgenic mice bearing the *c-fms* promoter-green fluorescent protein; the "MacGreen" mice.

The macrophages and osteoclasts in MacGreen mice are fluorescently tagged so the cells can be monitored in a living animal.

Work is also progressing on development of transgenic mice with macrophage and osteoclast specific, inducible transgenes.

Studying the responses of macrophages to activating signals such as lipopolysaccharide (LPS) and bacterial CpG DNA, has opened new avenues for therapeutic intervention in infectious disease, as well as identifying the novel biology of these cells.

cDNA microarrays are being used to profile global changes in gene expression resulting from macrophage activation by LPS, bacterial CpG DNA and CSF-1 and during osteoclast differentiation and activation. Several novel macrophage/osteoclast specific genes have been identified and are being characterised as part of the structural genomics program, in collaboration with IMB's Jenny Martin and Joint Appointment Bostjan Kobe.



## MOLECULAR GENETICS OF MAMMALIAN DEVELOPMENT



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### Honours Student

Sonjia Layton

**W**e 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.

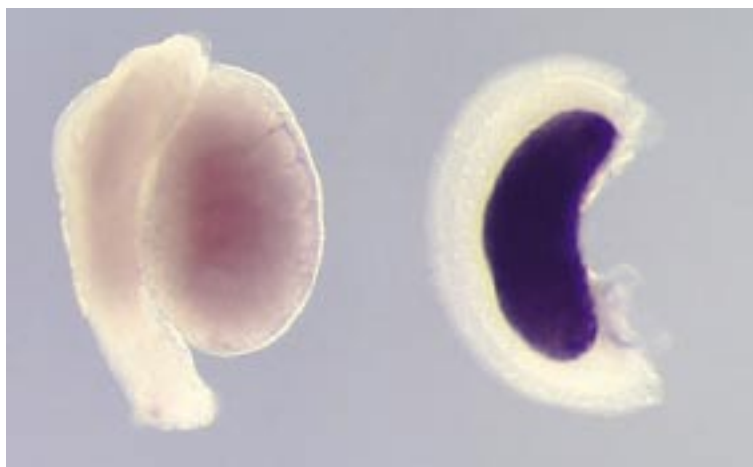
### Molecular genetics of sex determination

Sexual development is regarded as a paradigm for the study of how genes control mammalian development, involving a pathway of gene regulation under the control of a “switch” gene on the Y chromosome, *Sry*.

Our group is continuing to study the molecular biology of *Sry* in order to understand its role in male sex determination and the defects that can result in sex reversal. We discovered a gene, *Sox9*, which plays a critical role in male sex determination and acts downstream of *Sry*.

Current studies are aimed at understanding the molecular and cellular role of *Sox9* in this pathway. We are also searching for other genes downstream in the sex-determining pathway, using expression screening approaches such as microarrays.

Several novel genes have been identified, and we are developing assays to study the functions of these genes in the regulation of gonadal development.



### Molecular genetics of vascular development

In collaboration with the group of fellow IMB researcher George Muscat, we discovered a gene, *Sox18*, that is expressed transiently in endothelial cells during vascular formation in the embryo and in the adult. Mutations in *Sox18* disrupt vascular development and/or function.

We are currently studying the genetics and biology of the role of *Sox18* in vascular development, and exploring the possibility that angiogenesis can be modulated – for example to slow the growth of tumours, or promote wound healing - by enhancing or suppressing *Sox18* activity.



## RENAL DEVELOPMENT AND DISEASE



### Group Leader

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Michael Piper

### Research Assistant

DaYing Wen

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### Administrative Assistant

Kylie Georgas

The kidneys not only filter the blood to produce urine but also regulate blood pressure and red blood cell number, various hormones and growth factors. If your kidneys fail, you will need dialysis or organ transplantation to survive, both of which have serious side effects. This laboratory focuses on developing new treatments by understanding how the kidney develops and what causes renal disease.

Chronic renal failure (CRF) is a devastating disease which is expensive to treat. It is estimated that 60,000 Australians from 12 to 74 years of age have CRF.

Each year, approximately 4000 Australian adults will be diagnosed with CRF, costing the health system more than \$30 million.

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

A greater understanding of the processes involved in normal kidney development and CRF are critical to the development of new therapeutic strategies. This is the focus of our laboratory.

### Towards renal regeneration

It has long been assumed that kidney development ceased at birth with no prospect of regeneration of new functional units.

Over the past five years stem cell biology has questioned similar assumptions about other organs and we now know that the brain con-

tains neural stem cells which can indeed change into many cell types.

Could there be a renal stem cell and could these be used to treat renal disease?

Another milestone in stem cell biology has been the isolation of human embryonic stem cells.

This brings with it the prospect of regenerating tissues even if there is no persistent stem cell population. Could we regenerate a kidney or repair kidney damage using embryonic stem cells?

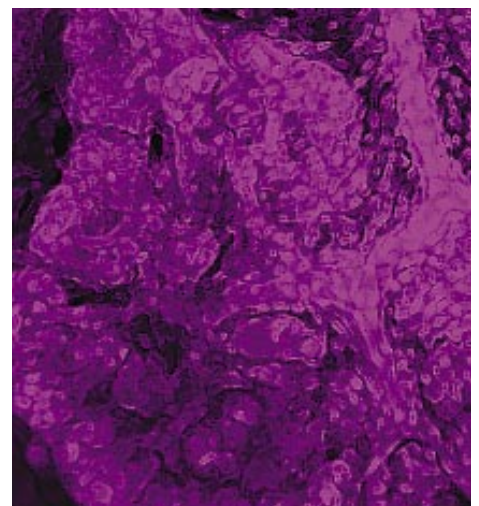
These two questions are being tackled by systematically cataloging all the secreted and cell surface proteins made during kidney development.

To do this we are using the genomic technique of expression profiling. Novel growth factors isolated from these screens are then assessed for their role in kidney development using organ culture assays.

They can then be assayed for their ability to direct embryonic stem cells towards a renal fate.

Novel cell surface markers are being used to isolate putative renal stem cells or purify renal progenitors from differentiating embryonic stem cells.

This work is a national collaboration with other laboratories within the IMB, Monash University and the Monash Institute for Reproduction and Development, and The University of Queensland.



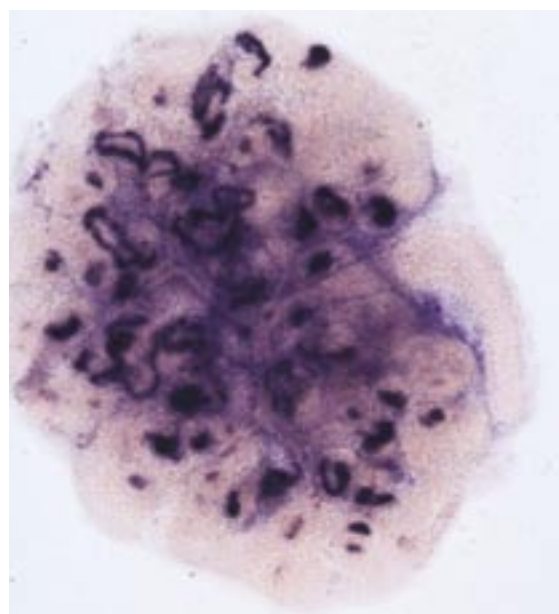
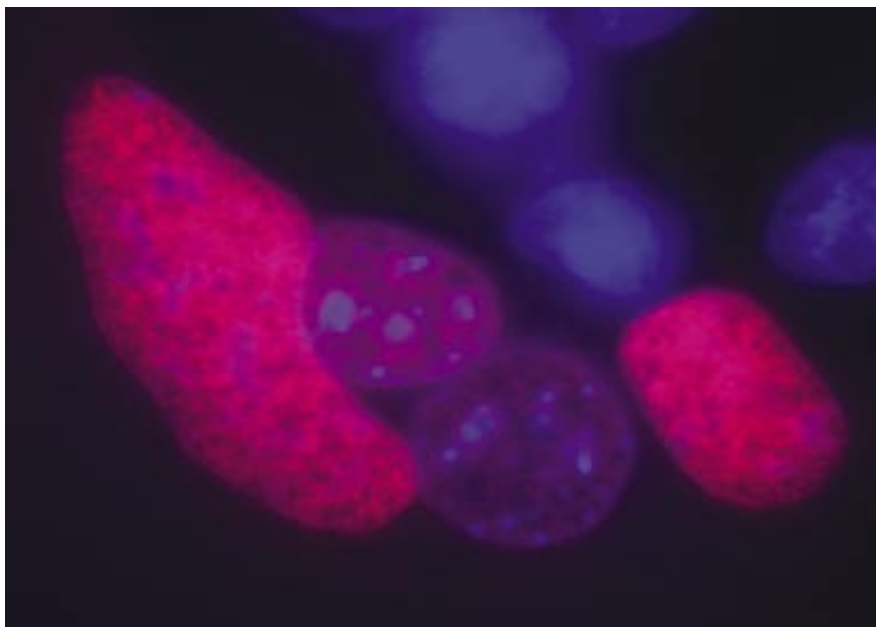
### From Wilms' tumour to kidney development

The childhood renal tumour, Wilms' tumour, is one of the most common solid tumours. Wilms' tumour can arise due to the loss of a gene, *WT1*, whose role in normal development is to direct differentiation rather than cell growth.

This laboratory has investigated the role of *WT1* mutation in Wilms' tumour and several other conditions.

While mutated in renal disease, normal function of *WT1* is critical for both kidney development and the ongoing function of the kidney after birth. Hence *WT1* is also mutated in several rare renal failure conditions.

*WT1* is also a regulatory protein in the nucleus of the cell. We are investigating how this regulatory protein works to create a kidney and keep it functioning by examining what genes it regulates, what proteins and nucleic acids it interacts with and to what end.



### Crim1 in TGFbeta signalling and kidney development

*Crim1* is a novel gene expressed in the developing kidney and also the eye, spinal cord, brain and tooth. The *Crim1* gene encodes a protein with an ability to interact with members of the TGFbeta growth factor superfamily.

We are currently investigating the interaction between *Crim1* and the TGFbeta superfamily by increasing or decreasing its expression in the fish and mouse.

This has shown that *Crim1* plays a very critical role in a number of organ systems, including the kidney and in the development of the blood vessels.



## NUCLEAR HORMONE RECEPTORS AND GENE REGULATION



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Paul Rohde  
Jyotsna Pippal  
Tamara Allen

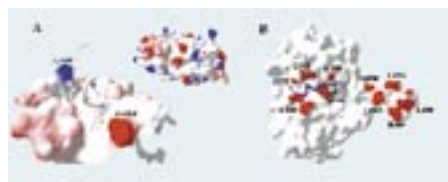
**Research Assistants**  
Shayama Wijedasa  
Rachel Burow

Our research focuses on the regulation of gene expression during differentiation by nuclear hormone receptors (NHRs), and chromatin remodeling factors. Specifically, we aim to decipher the mechanism of action of orphan NHRs, and their functional role in skeletal muscle with respect to lipid homeostasis and cardiovascular disease.

Nuclear hormone receptors (NHRs) function as ligand activated transcription factors that bind DNA and recruit chromatin remodelling factors to regulate gene expression involved in reproduction, development and metabolism. NHRs are the conduit between physiology and gene expression.

Furthermore, these hormone regulated DNA binding proteins and chromatin remodeling proteins mediate the link between genome and phenome by operating at the nexus of pathways that control cell specific transcription, signalling, differentiation and metabolism.

The importance of NHRs in human physiology is underscored by the pharmacopeia created to combat disorders associated with dysfunctional hormone signalling. Twenty of the 100 top selling drugs in the USA are directed at nuclear receptor targets and have annual sales in excess of \$US5 billion. These diseases affect every field of medicine, including reproductive biology, inflammation, cancer, diabetes, and cardiovascular disease.



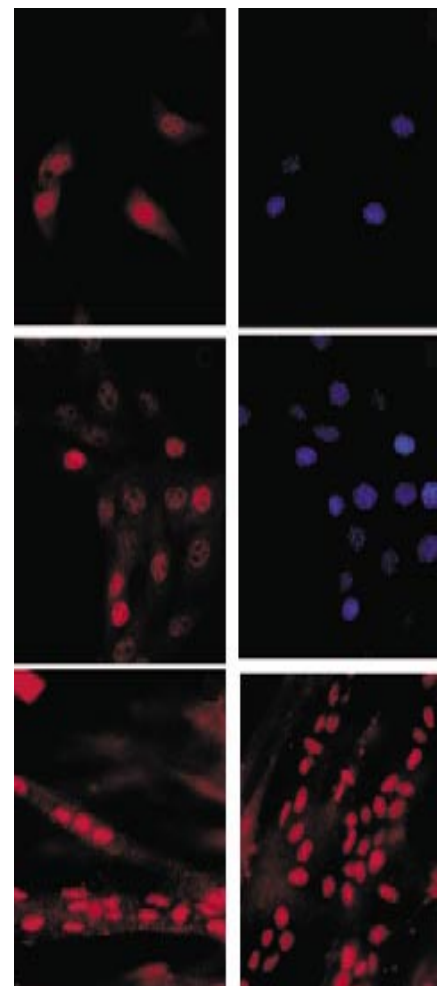
A decade ago, gene products that appeared to belong to the NHR superfamily on the basis of their nucleic acid sequence identity were identified. However, the endogenous signaling molecules which bound to these proteins were unknown and thus the term “orphan NHR” was coined. One of the challenges facing biomedical science is to decipher the function of orphan nuclear receptors and their mechanism of action. The potential impact of such a discovery cannot be overstated, since every known nuclear receptor has been implicated in human disease.

The ‘orphans’ herald an enormous yet unexploited opportunity for the discovery of important new therapeutic agents. Recent studies on previously denoted orphans have uncovered new hormone signaling pathways that regulate glucose, lipid and drug metabolism, and provided new insights and possible treatments for many human diseases including diabetes, dyslipidemia, obesity and metabolic syndrome X.

Furthermore, skeletal muscle is a major mass peripheral tissue accounting for approximately 40 percent of total body weight and is a primary site of glucose metabolism and fatty acid oxidation. Consequently, it plays a very significant role in insulin sensitivity, and the blood lipid profile. The heightened occurrence of cardiovascular disease, obesity and diabetes is

associated with lipid disorders. Accordingly, the projects in our laboratory include:

- Genetic programs induced by the oxy-cholesterol dependent nuclear receptor, LXR, in skeletal muscle regulation of cholesterol metabolism;
- Understanding the role of Peroxisome Proliferator-Activated Receptors in skeletal muscle energy and lipid homeostasis;
- Structure/function and mechanistic analysis of orphan nuclear receptor mediated transcription (e.g Nur 77, NOR-1, ROR, and Rev-erb); and
- Regulation of gene expression and mammalian differentiation by tissue specific transcription factors (e.g *Sox18*) and chromatin remodeling factors (e.g protein arginine methyl transferases).



## THE CELL SURFACE IN HEALTH AND DISEASE



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### Research Assistants

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Amanda Carozzi

Annika Stark

Charles Ferguson

Our research focuses on the cell surface and, in particular, on the structure and function of caveolae. Caveolae are small pits in the plasma membrane which have been linked to tumour formation and muscular dystrophy. We are investigating the role of caveolae in cell physiology and their exploitation by pathogens.

Caveolae, small pits in the surface of many mammalian cell types, have been implicated in regulation of cell proliferation, endocytosis, and lipid transport.

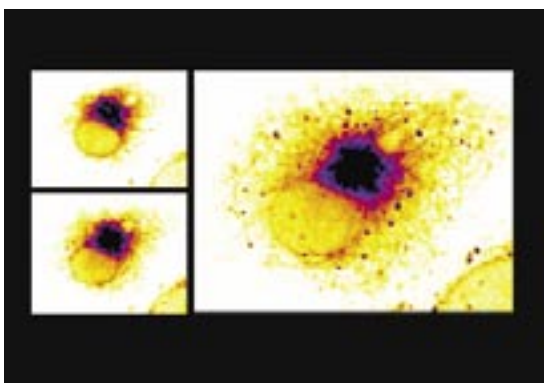
In addition, caveolae and caveolins, the major proteins of caveolae, have been linked to a number of disease states.

Caveolins are fatty acid and cholesterol-binding proteins which have been implicated in regulation of cellular lipids.

All cells maintain a delicate balance of cholesterol, through regulation of influx, efflux, synthesis, and esterification, which is crucial to the correct functioning of the cell.

Our studies have shown that cholesterol is involved in organising plasma membrane signalling domains termed 'lipid raft' domains, and that this process is regulated by caveolins.

We are using a number of tools to dissect caveolae function including dominant negative caveolin mutants, caveolin-1 knockout mice, and novel Ras assay systems (in collaboration with John Hancock, University of Queensland Medical School).



In addition, we have utilised lower eukaryotic systems, such as zebrafish (in collaboration with Brian Key, School of Biomedical Sciences), to understand the role of caveolae and caveolins in development and in normal cellular function.

*In vitro* studies show that caveolin mutants perturb very specific cholesterol-dependent signalling pathways and disrupt lipid metabolism.

Our *in vivo* studies have shown a role for caveolins in evolutionarily conserved developmental pathways. We have also developed novel quantitative immunoelectron microscopic techniques which have allowed us to visualise lipid raft domains in sheets of plasma membrane prepared from cultured cells for the first time.



## PROTEIN TRAFFICKING



### Group Leader

Jenny Stow

### Research Officers

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Lubomira Jamriska

### PhD Students

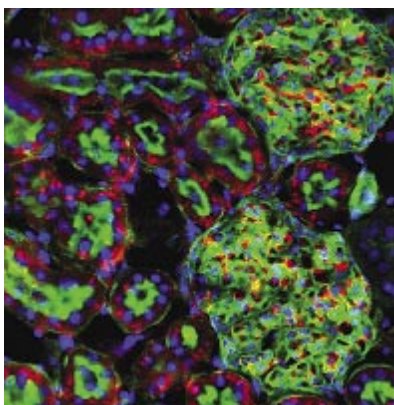
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Juliana Venturato

### Honours Students

David Bryant  
Daniel Sangermani



Our research is focused on sorting, trafficking and secretion of proteins in epithelial cells and in macrophages. This work provides insights into how proteins are delivered to different membrane domains in healthy and diseased tissues. In macrophages we are studying the regulation of cytokine secretion and trafficking, a key aspect of inflammation and disease.

Epithelial cells have a series of complex mechanisms to ensure the correct, polarized trafficking of key proteins to the top or bottom cell surface. E-cadherin is a membrane protein which must be delivered to the basolateral surface of epithelial cells to function in cell-cell adhesion and cell polarity. E-cadherin is also a powerful tumour suppressor and its loss or dysfunction is an early event in many metastatic tumours. Our studies aim to show how E-cadherin is sorted and delivered to and from the cell surface in kidney epithelial cells and in tumour cells.

We have previously shown that surface E-cadherin is first delivered to the cell surface and then endocytosed and recycled via a novel pathway. Our current studies now focus on identifying the molecules and signaling pathways that control the trafficking of E-cadherin to and from the cell surface.

Sorting in the trans-Golgi network of epithelial cells allows E-cadherin to be trafficked in a polarized fashion. In collaboration with IMB's Rohan Teasdale, we are studying targeting signals responsible for E-cadherin sorting and trafficking. This work has major implications for cell-cell adhesion and epithelial polarity regulation during development and in cancer.

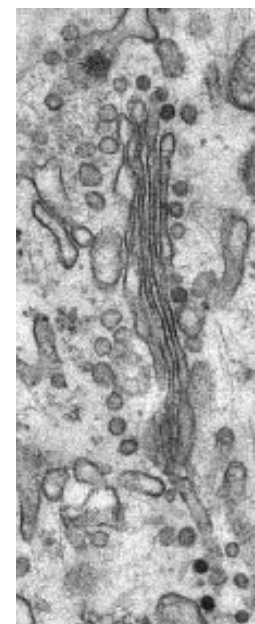
We are also interested in characterising the carrier vesicles that transport proteins throughout cells. This work involves the expression and real-time imaging of

fluorescently-tagged proteins in live cells. In a second approach the vesicles are reconstituted in an *in vitro* assay and then isolated for proteomic analysis.

Most recently we have shown that regulators of G protein signaling (RGS) family proteins have an essential role in regulating vesicle budding. This work contributes to our understanding of basic cell processes and also provides the means to experimentally or therapeutically manipulate secretion in cells.

Macrophages are professional secretory cells with finely-tuned but little-studied secretory pathways. It is now becoming evident that macrophages have evolved specialized trafficking pathways to accommodate their diverse roles in immunity. Our work is focused on the mechanisms for secretion of tumour necrosis factor (TNF $\alpha$ ) in immune-activated macrophages.

We are developing a detailed understanding of the intracellular trafficking of TNF $\alpha$ . We are employing novel approaches and assays to identify immune-responsive trafficking proteins regulating the post-Golgi transport of TNF $\alpha$ . This work may lead to new strategies for anti-TNF $\alpha$  therapies in inflammatory disease.





## MOLECULAR GENETICS OF PIGMENTATION



### Group Leader

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### Research Officers

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### PhD Students

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Anthony Cook  
Luke Kirkwood  
Helene Johanson

### Research Assistants

Darren Smit  
Wei Chen

Our work on human pigmentation genetics has provided a framework to understand normal variation in this physical trait and the associated genotypic risk for skin cancer development. The genes that determine an individual's skin phototype and the cellular mechanisms that result in the tanning response of melanocytes after UV-exposure of the skin are actively being investigated.

Skin colour and skin cancer – MC1R, the genetic link

Pigmentary traits such as red hair and fair skin, lack of tanning ability and propensity to freckle have been identified as genetic risk factors for skin cancer when combined with the environmental risk factor of high ultraviolet exposure.

A major area of investigation is the role of the human melanocortin-1 receptor (MC1R) gene variants in directing skin phototype and response to UV-induced ligand binding and receptor activation.

The MC1R coding sequence is highly polymorphic in human populations and we have examined MC1R variant allele frequencies in the general community as well as a collection of adolescent dizygotic and monozygotic twins with defined pigmentation characteristics.

Variant allele frequencies have also been determined in several case-control studies of sporadic melanoma, basal cell carcinoma and squamous cell carcinoma, and in familial melanoma kindreds collected within Australia.

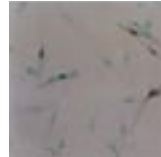
These studies have shown that three MC1R alleles – Arg151Cys, Arg160Trp and Asp294His – were associated with increased risk in all forms of skin cancer and with penetrance and age of onset in familial melanoma in CDKN2A mutation carriers.

There is a significant MC1R variant allele heterozygote carrier effect on skin phototype and skin cancer risk, which indicates that these alleles do not behave in a strictly recessive manner.



Characterisation of melanoblast stem cell differentiation

The process of development and differentiation of the melanocytic cell lineage is being investigated using primary melanoblast and melanocyte cells cultured *in vitro* from human skin.



This will provide information to allow the genes and processes involved in melanoma tumour formation and metastasis to be examined.

These studies focus on the identification and molecular characterisation of the genes involved in melanocyte function.

Mechanisms of melanoma metastasis

Expression of the  $\beta 3$  integrin gene in melanoma *in situ* has been found to be the single most important marker of metastasis yet discovered.

Experiments to investigate the effects of this expression has involved the use of Adenoviral gene transduction of the  $\beta 3$  integrin subunit into radial growth phase (RGP) melanoma cell lines and differential gene screening.

A skin reconstruction model was used to assay the invasiveness of RGP melanoma cells after ectopic  $\beta 3$  integrin expression and these studies have discovered induction of the anti-adhesive protein osteonectin is required for melanoma metastasis.



## DEVELOPMENTAL GENES AND HUMAN DISEASE



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Jenny Bennetts  
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### Research Assistant

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### Honours Student

Natalie Butterfield

Defects arising from abnormal embryonic development are a major cause of infant mortality and childhood disability. We are involved in isolation of novel genes involved in embryonic development, as well as more fully characterising the role of these and other known genes in embryogenesis and disease.



### Identification of genes involved in craniofacial development

Defects in facial development are a common feature of human dysmorphism syndromes.

Using the mouse as a model system, we have adopted a genomics approach based on subtractive hybridisation to enrich for genes expressed in pharyngeal arches, the precursors to the mammalian face.

As a result we have isolated a large number of both novel and previously identified genes whose expression pattern during embryogenesis suggests a specific role in the development of a range of organ systems.

Functional and cell biological characterisation of a number of these genes is currently underway.

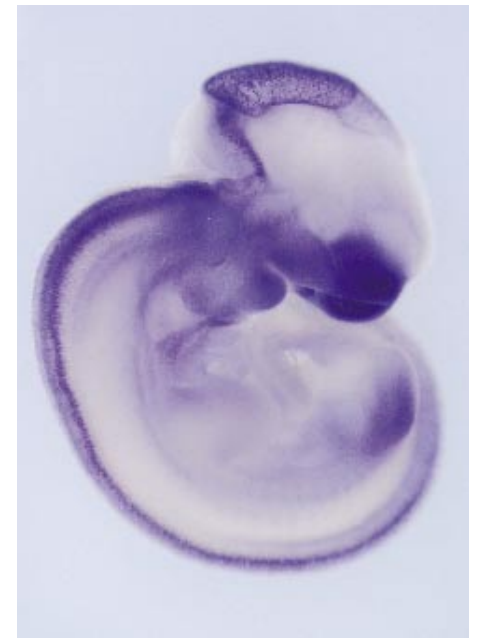
### Regulation of the hedgehog pathway by intracellular trafficking and sterol levels

The hedgehog signalling pathway is central to embryonic development as well as tumorigenesis.

The regulation of this pathway at the cellular level involves complex intracellular trafficking events which appear to be linked to sterol levels.

We are investigating the subcellular localisation of members of the hedgehog pathway under a range of sterol depleting conditions.

Concurrently we are analysing the effect of cholesterol depletion on hedgehog pathway activity in a signalling-competent cell line.

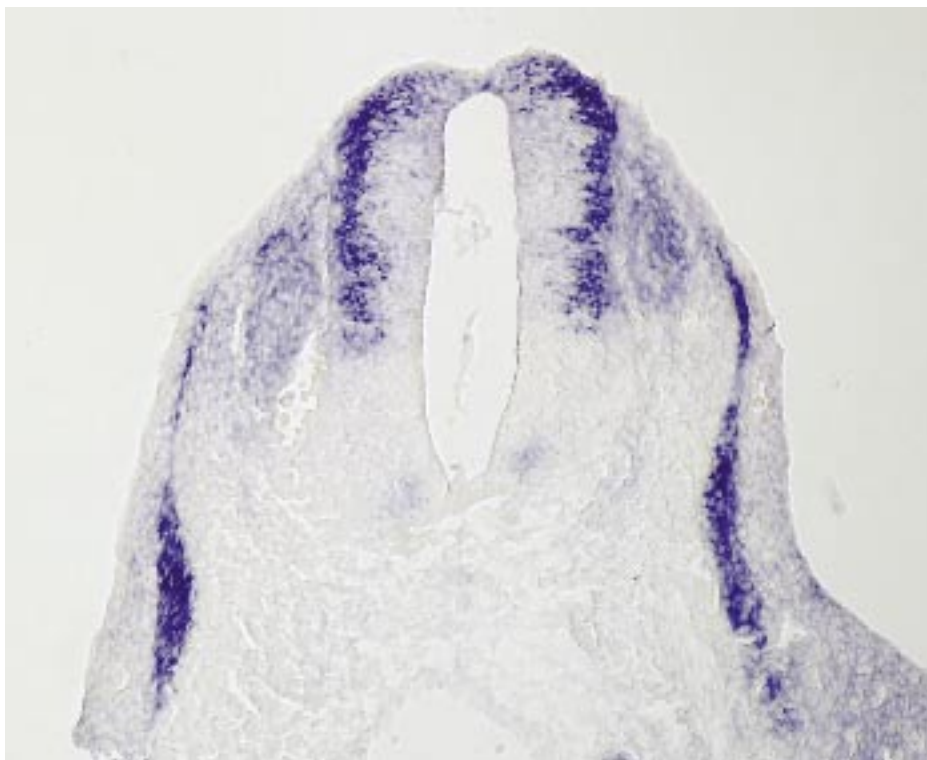


## Microarray analysis in a mouse model of limb development

We have used microarray technology to investigate the large-scale expression differences in the embryonic limb of the polydactylous mouse mutant extra-toes ( $Xt^1$ ) versus the wild-type limb bud.

This mutant involves a spontaneous deletion of the gene encoding the Gli3 transcription factor which, together with Gli1 and Gli2, is involved in mediating the output of the hedgehog signalling pathway.

As a result of our microarray analysis we have identified a number of both novel and previously identified developmental genes, and their role in the polydactyl phenotype is currently under investigation.



## DEVELOPMENTAL NEUROBIOLOGY



15.10.60 - 12.05.01

### Group Leader

Murray Hargrave

(Continuing the work of Dr Toshi Yamada)

### PhD Students

Asanka Karunaratne

Gabriel Kolle

### Research Assistants

Ning Huang

Ian Wilson

**We** are investigating the processes that generate the nervous system during embryonic development, particularly focussing on the molecular mechanisms that produce the many different cell-types found in the adult nervous system. Ultimately, this will clarify how the nervous system is made and how nervous system disease might be treated.

During embryogenesis, thousands of different cell-types are produced in the nervous system.

As well as developing different functions, these cells must develop in the correct numbers, at the correct position and connect precisely with other cells.

How this is controlled at molecular level during embryonic development is a fascinating question and the focus of our research team.

We chose to investigate these issues in mice, chicken and zebrafish using different experimental approaches.

Previous research has indicated that cell-type diversity in the nervous system is determined by concentration gradients of secreted signalling proteins. Many aspects of these signalling processes are still unknown.

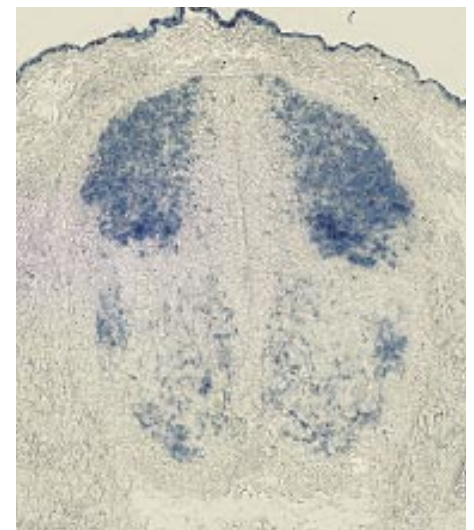
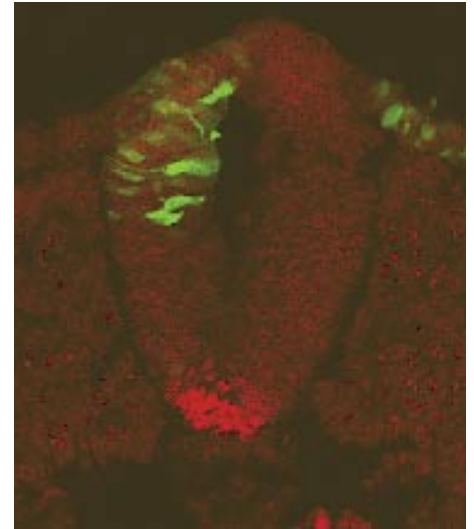
We are investigating the mechanisms of the Sonic hedgehog signalling protein and its receptor protein, Patched, in the developing chick spinal cord.

We also aim to uncover the functions of Crim I, a more recently discovered protein expressed in developing nervous system.

We hypothesise that Crim I regulates other signalling molecules and we are seeking to uncover the function of Crim I in mouse, chick and zebrafish embryos.

In response to secreted signals, neuronal precursor cells express a variety of transcription factors which lead to differentiation of these cells.

We are concentrating on the transcription factors Sox14, GATA2, GATA3, SCL and FOG2. We aim to elucidate their role in mouse and chick spinal cord development and to characterise the small groups of neuronal cells that express them.





# Structural Biology and Chemistry

Understanding the three dimensional characteristics of biologically important molecules is vital to structure-based drug design. Using this information in combination with advanced chemistries to study protein-protein interactions, develop libraries of small molecule mimetics, and synthesise bioactive compounds, the Division of Structural Biology and Chemistry pursues drug leads to develop candidate pharmaceuticals for clinical evaluation.

## BIOACTIVE MOLECULES, CHEMICAL PROTEIN SYNTHESIS AND PROTEOMICS



### Group Leader

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### Research Officers

Peter Cassidy  
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### Research Assistant

Angie Morrison

### Honours Student

Aaron Poth

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, as well as development of new synthetic and analytical methods, and proteomics. Special emphasis is placed on determining the structure-function relationships of natural and designed molecules.

### Toxins

Venom peptides make interesting pharmacological tools due to their action on ion channels and receptors.

Conotoxins are small cysteine-rich peptides isolated from the venom of predatory marine snails. We have developed new synthetic approaches to access fully cyclic analogues with improved physical properties.

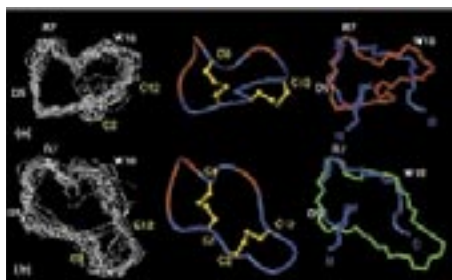
These analogues nicely mimic the original native structure and maintain high potency. We have also designed the most potent, selective conotoxin that recognises the alpha-7 nicotinic receptor.

### Milk proteomics

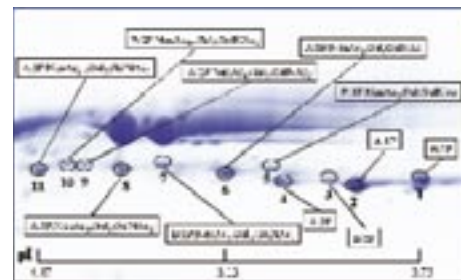
Glycosylation is a post-translational modification which introduces great diversity into the proteome allowing numerous distinct molecular species to be generated from a single gene product.

We have identified numerous different glycoforms of the major milk protein,  $\kappa$ -casein. Using 2D electrophoresis and MALDI-ToF mass spectrometry, differences in phosphorylation and glycosylation were identified.

By analyzing the glycopeptides generated from individual species we have been able to assign molecular identities to 11 of these in terms of genetic variant, number and location of phosphorylation sites, and the number of tri- and tetra-saccharides attached.



*C1m1 structures*



*Different glycoforms of  $\kappa$ -casein*

## New generation antibiotics

The replication of DNA in eubacteria involves many proteins organised into a complex multifunctional machine termed the replisome. A central enzyme involved in replication is the multi subunit DNA polymerase (pol III).

The processivity of the polymerase is conferred by the  $\beta$  subunit of pol III, which forms a clamp around the DNA.

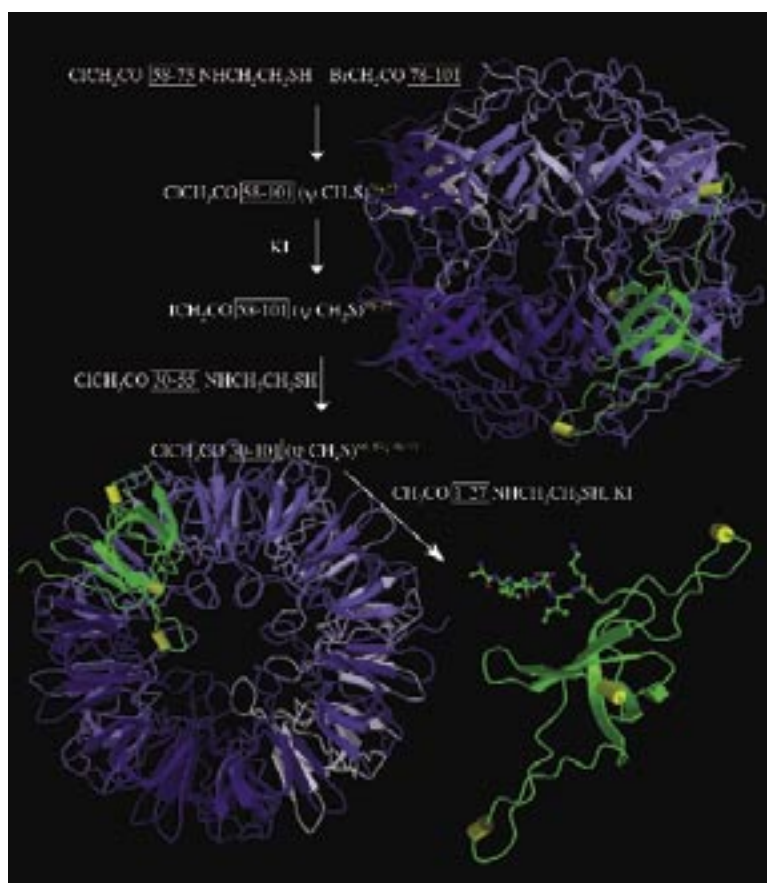
The subunit  $\beta$  is in turn loaded onto the DNA by a clamp loader complex comprised of single  $\delta$  and  $\delta'$  subunits and three or four  $\tau/\gamma$  subunits.

The  $\delta$  subunit of the clamp loader and the polymerase  $\alpha$ , bind the  $\beta$  subunit at the same site or overlapping site.

In a collaborative program with CSIRO Livestock Industries, an initial lead pentapeptide has now delivered a suite of novel peptidomimetic lead compounds with nanomolar potency that inhibit *in vitro* interaction of the  $\alpha:\delta$  and  $\alpha:\beta$  proteins.

## Protein chemical synthesis

We have synthesised the 101 residue protein Early Pregnancy Factor (EPF), also known as human chaperonin 10, from four functionalised peptides by a novel sequential thioether ligation strategy. The high efficiency, generality and flexibility of this approach will broaden the scope and versatility of chemical protein synthesis by establishing a methodology that will routinely allow synthesis of larger (>200 amino acid) proteins.



Early Pregnancy Factor synthesis

## NMR SPECTROSCOPY



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Rekha Bharathi

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Emryn Maclachlan

Our work focuses on the application of NMR spectroscopy in drug design and development. By determining the structures of biologically active molecules it is possible to identify functional regions of these molecules and use this information to design novel drugs. We have a particular interest in the concept of stabilising proteins by joining their ends to make circular molecules.



We are developing the use of small disulfide-rich proteins as leads in drug design. Such proteins often have potent biological activities and, because of their cross-linking disulfide bonds, usually have well defined three-dimensional structures that can be determined using NMR spectroscopy.

The proteins we study come from animal and plant sources, as well as "designer" proteins we produce in the lab. In particular we have been exploring the bioengineering of circular proteins.

By cyclising proteins and creating embedded knots within the structures using disulfide bonds we are able to significantly enhance the stability of proteins.

Our goal is to overcome current limitations on the use of conventional proteins as drugs, i.e. their poor bioavailability and susceptibility to degradation *in vivo*.

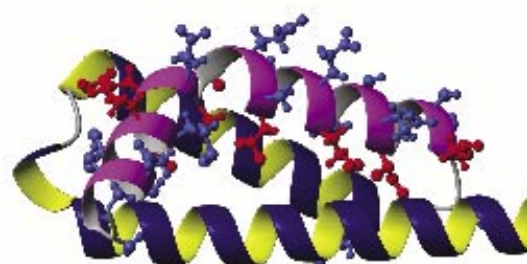
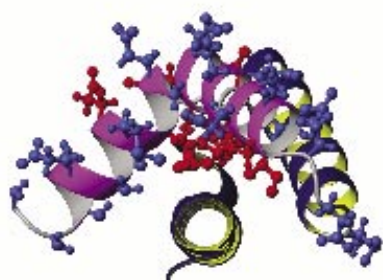
A company, Kalthera Pty Ltd, has been formed to commercialise research outcomes relating to a particularly stable protein motif that we discovered called the cyclic cystine knot.

We are currently determining relationships between structure and activity in a wide range of cystine knot proteins, including those from plants, cone-snail venoms, snakes, spiders and frogs.

Cystine knot proteins have applications in agriculture as well as in the development of pharmaceuticals, and in collaboration with Dr Marilyn Anderson at La Trobe University we have been examining the insecticidal properties of a range of disulfide rich proteins.

The cyclotide proteins discovered in our laboratory show particular promise as "natural" insecticides against pests in a range of crop plants.

A company, Cyclagen, has been formed to commercialise opportunities arising from this research.





## CHEMISTRY AND HUMAN THERAPEUTICS



### Group Leader

David Fairlie

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Huy Hoang  
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### Research Assistants

Renee Beyer  
Bernadine Flannigan  
Tom Guthrie



*NMR-derived structure of a new anti-tumour drug*

Chemistry underpins all aspects of molecular biosciences. Our group studies chemical reactivity, chemical structure, molecular interactions, and the molecular basis for biological processes, disease development, and drug action. We also design potent new enzyme inhibitors and receptor antagonists and develop drugs for viral and parasitic infections, cancer, inflammatory and neurodegenerative diseases.

Our group has internationally recognized strengths associated with chemical design, chemical synthesis, and structures of chemically reactive and biologically active small molecules.

While many group members are synthetic chemists, others are heavily committed to studying protein-ligand interactions using computer modelling, NMR or crystallographic structure determination, biochemistry, and pharmacology.

In recent years our group has devoted a great deal of chemical effort towards tailoring new molecular shapes analogous to elements of secondary and tertiary protein structure.

This has resulted in new and in some cases the first, generic approaches to small molecules that mimic strands, turns, helices, helix bundles, multi-loop bundles, and their combinations (supramolecular nanostructures).

This effort has produced new molecular classes that are structural and/or functional mimics of bioactive protein surfaces.

In the drug arena, we have developed generic approaches to the discovery of protease and lipase inhibitors, G protein-coupled receptor antagonists, and transcriptional regulators.

As a result we have created multiple classes of small orally active organic molecules and demonstrated their potent ( $IC_{50} < 100$  nM) anti-tumour activity, anti-parasitic activity (malaria, giardia, schistosomal proteases), anti-inflammatory activity (blocking human TNF- $\alpha$ , IL-1 $\beta$ , IL-6, complement receptors, phospholipases), anti-viral activity (low resistance inhibitors of HIV and Dengue proteins), and anti-Alzheimer's activity (against secretase enzymes). Compounds are in various stages of pharmacological, preclinical or clinical development.

To cover so much ground we acknowledge our many local, national and international collaborators in pharmacology, biochemistry, virology, parasitology, neurobiology, and tumour biology.

## MEMBRANE PROTEIN STRUCTURES



**Group Leader**  
Ben Hankamer

**M**y research is focussed on determining the structure of membrane protein and macromolecular assemblies. This is conducted using single particle analysis, electron and X-ray crystallography.

Cryo-electron microscopy is ideally suited for solving the structures of membrane proteins and macromolecular assemblies using single particle analysis and electron crystallography.

### Single particle analysis

For the purposes of a single particle analysis, randomly orientated, macromolecular assemblies and membrane protein molecules can be imaged in a thin layer of vitreous ice to recover high-resolution information.

The projection images of the particles are then classified according to particle orientation and the class averages obtained used to produce 3D reconstructions.

### Electron crystallography

Electron crystallography requires the use of two-dimensional crystals which are ideally suited for determining the structures of membrane proteins under near-native conditions as arrayed protein molecules are embedded in a lipid bilayer.

The 2D crystals are then tilted and the processed tilt images merged to generate 3D reconstructions of the protein of interest.

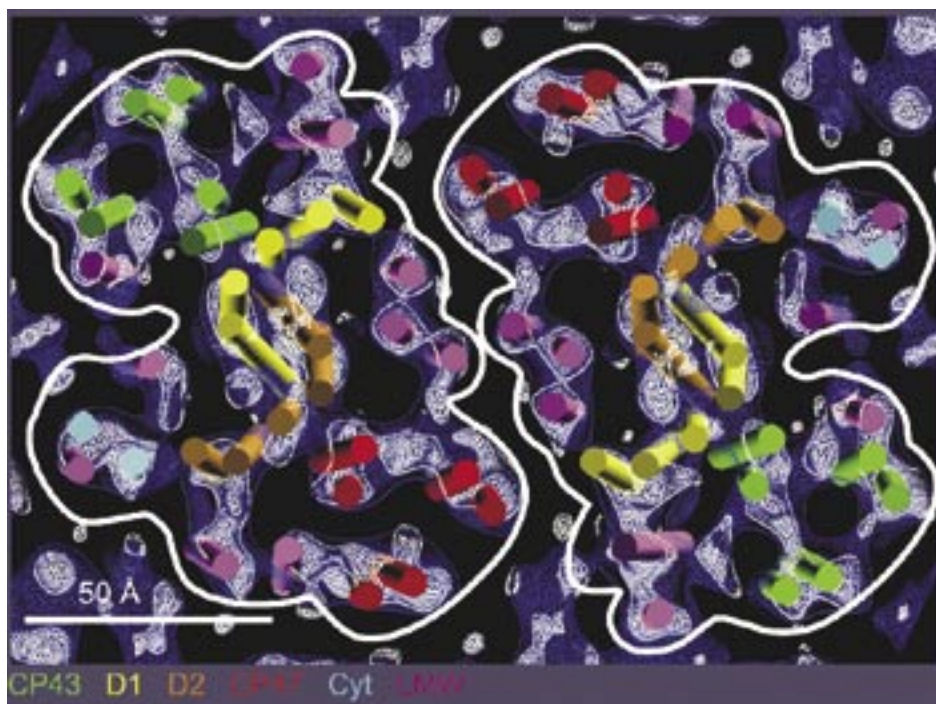
### X-ray crystallography

The use of cubic phase lipids for the purpose of membrane protein crystallisation is also being explored.

Many lipids form highly ordered contorted bilayers. These can be thought of as continuous bilayers organised in 3D space.

Membrane proteins can be inserted into these cubic phase lipid bilayers and induced to form highly ordered three-dimensional crystals well-suited for X-ray crystallographic analysis.

A strong research focus is automation of all three techniques to increase the rate of protein structure determination.



*Photosystem 2 structure solved by electron crystallography*

## MOLECULAR PHARMACOLOGY



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### Research Assistants

Linda Thomas  
Trudy Bond

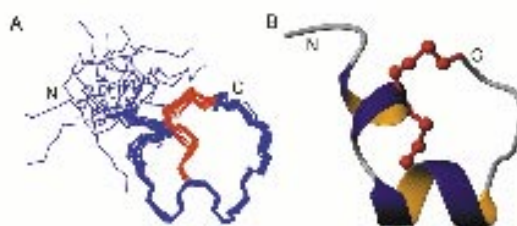
Our research focuses on the discovery and characterisation of conotoxins acting at ion channels and receptors and transporters present in neurons. Currently we are investigating conotoxins that selectively target the nicotinic acetylcholine and NMDA receptors, the voltage sensitive calcium and sodium channels, and the noradrenaline transporter. Complimentary interactions between conotoxins and their receptor are being established to better understand where and how they act at the molecular level.

The aim of this research is to develop research tools and potential therapeutics for poorly treated diseases such as chronic pain.

This research involves assay-guided isolation of venom peptides, peptide synthesis, tissue pharmacology, radioligand binding and electrophysiological studies, as well as receptor mutagenesis, modelling and docking.

Specific projects include:

- The nicotinic acetylcholine receptor is a non-selective cation channel stimulated by acetylcholine and selectively inhibited by  $\alpha$ -conotoxins. We have discovered several new  $\alpha$ -conotoxins using receptors expressed in oocytes to guide crude venom fractionation. Several had unusual structure and subtype selectivity. Homology modelling and docking studies are allowing us to understand, at the molecular level, how these selectivity differences arise
- The NMDA receptor, an important non-selective cation channel in the brain, is inhibited by conantokins. Using conantokin analogues, we recently found that specific subtypes of the NMDA receptor are lost in Alzheimer's disease. Currently we are trying to establish their identity to better understand how Alzheimer's disease develops
- The voltage sensitive N-type calcium channel, a neuronal calcium channel found in pathways involved in the transmission of painful stimuli, is inhibited by  $\omega$ -conotoxins. We recently identified a novel variant of this channel using CVID. This variant is currently under investigation to understand its role in chronic pain
- The voltage sensitive sodium channels, particularly those found in neurons inhibited by  $\mu$ -conotoxins, are also under investigation. We have established that  $\mu$ -conotoxins selectively target persistent forms of the TTX-sensitive sodium channel. The nature and role of these sodium channels is currently under investigation
- The noradrenaline transporter (NET) is the primary route of noradrenaline removal from synapses. We have identified  $\chi$ -conotoxins as the first peptide inhibitor of NET, and its effectiveness in treating neuropathic pain and depression. We are presently establishing the complimentary interactions between  $\chi$ -conotoxins and NET to understand where and how they act at the molecular level.



## PROTEIN STRUCTURE AND PROTEIN INTERACTIONS



**Group Leader**  
Jenny Martin

### Research Officers

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### PhD Students

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### Research Assistants

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Russell Jarrott  
Kirra McConnell

### Visitor

Glyn Truscott

Our work focuses on the determination of protein structure to provide a better understanding of protein interactions, protein evolution, protein function and protein folding. We target the structures of medically relevant proteins, through collaborations within the IMB and with other research teams in Australia and worldwide.

We have focused on two of our projects from 2002 highlighting how protein structure aids understanding of protein interactions and protein function.

Sulfotransferases play an important role in chemical defense against xenobiotics but can also bioactivate carcinogens.

We determined the structure of a major human sulfotransferase, *SULT1A1*, in collaboration with Professor Mick McManus (UQ).

Unexpectedly, the structure shows two molecules of the substrate *p*-nitrophenol at the active site and suggests that the active site can adapt its architecture to accept hydrophobic substrates of varying sizes, shapes and flexibility.

Thus the crystal structure provides the molecular basis for substrate inhibition of *SULT1A1* and reveals clues as to how the enzyme sulfonates a wide variety of lipophilic compounds.

The second example is that of DsbE, now also known as CcmG. This is one of a family of Dsb proteins that play a critical role in cellular redox control and assists in the folding and function of many proteins, including toxins and virulence factors.

Amid the highly oxidizing environment of the periplasm, there is a need for selected protein cysteines to be kept in a reduced form. Thus



*SULT1A1*

the protein CcmG (DsbE) is necessary to keep apocytochrome C in the reduced form.

Unlike other periplasmic thioredoxin-like proteins, CcmG has a specific reducing activity in the highly oxidizing periplasmic environment and has a high fidelity of interaction.

In collaboration with Dr Linda Thöny-Meyer from ETH-Zürich we determined the structure of CcmG, showing it to incorporate a modified thioredoxin fold with an acidic active site and a groove formed from two inserts. Both these structural features are necessary for CcmG function.



*CcmG (DsbE)*

## COMBINATORIAL CHEMISTRY AND MOLECULAR DESIGN



### Group Leader

Mark Smythe

### Research Officers

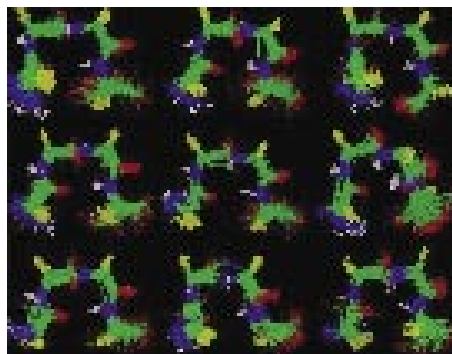
Greg Bourne  
Andreas Ruhmann  
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Stephen Long  
Gerald Hartig

### Research Assistants

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Jill Turner  
Ngari Teakle  
Jonathon Nielson  
Carolyn Jacobs  
Warren Oliver  
Marc Campitelli



Our research focus is on developing drug design, combinatorial chemistry and biological methodologies for the discovery of small molecule protein mimetics by studying the chemical and conformational diversity of protein surfaces. The approach is to combine protein structural information with combinatorial chemistry, resulting in the design and synthesis of molecules that mimic protein structure, ultimately leading to the discovery of compounds that mimic protein function. We are actively pursuing small molecules for cytokine and G-protein coupled receptors.

#### Protein-protein interactions

Many biological processes are carried out, or regulated, through protein-protein interactions.

Despite their physiological significance, they remain one of the most difficult molecular recognition events to inhibit or mimic.

We have developed molecular design processes that successfully identify small molecular candidates which modulate the function of protein-protein interactions.

We currently have several lead molecules against numerous protein-protein interaction targets.

#### Molecular design

We have developed an integrated design platform for library design and structure-based design of molecules that modulate protein-protein interactions.

This approach includes a set of unique biological descriptors for library design, a purpose-built virtual screening of virtual library platform and databases comprising large virtual libraries of compounds.

Using these methodologies we design and synthesise arrays of molecules that sample biologically relevant diversity space for primary screening, as well as arrays of molecules specifically targeted for a therapeutic protein of interest.

(Cont.)

## COMBINATORIAL CHEMISTRY AND MOLECULAR DESIGN (continued)

### Combinatorial chemistry

Current strategies in library design involve the calculation of hundreds of potential descriptors that define various chemical characteristics, and selecting a diverse set of compounds in this descriptor space.

With hundreds of available descriptors it is difficult to know which descriptors, if any, are important or essential for describing biological activity.

Consequently such procedures result in the optimisation of libraries in chemical descriptor space, which has little impact on biologically-relevant regions of that space.

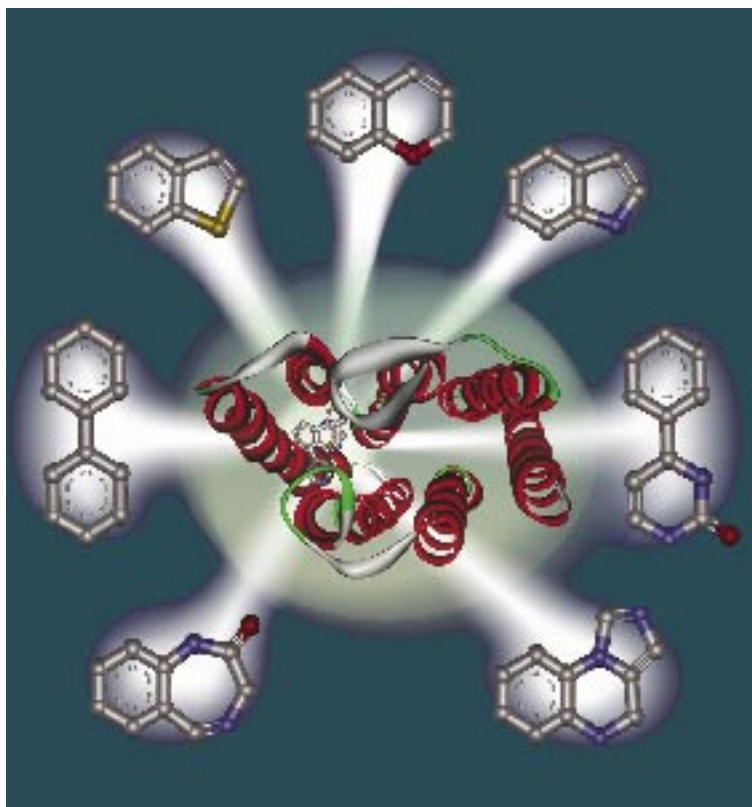
To overcome this we have developed a series of biologically-relevant descriptors that are used in library design.

As a consequence, we aim to identify the biologically-relevant structural regions of chemical diversity and design and synthesise arrays of molecules that match this diversity space.

We have developed new linkers and auxiliaries to aid combinatorial synthesis and a molecular design platform to achieve these objectives.

We have synthesised various constrained cyclic peptide libraries (molecular toolkit libraries) and libraries of macrocycles and heterocycles.

We have a particular focus on the discovery and exploitation of privileged structures.



Several privileged structures binding to a representative G-protein coupled receptor. 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.



# Office of Public Policy and Ethics

IMB's Office of Public Policy and Ethics undertakes research and analysis of the new ethics and public policy issues raised by biotechnology. The Office aims to enhance public awareness and discussion of the issues concerning the application of biotechnology.

## OFFICE OF PUBLIC POLICY AND ETHICS



### Group Leader

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Angela Wallace  
Sarah Yeates

### Gene CRC UROP Student

Max Yeh

**T**he Office of Public Policy and Ethics (OPPE) investigates the ethical and policy implications of biotechnology and genetics, specifically the policy implications of research on the genetics of addiction, mental disorders and cancer, as well as research on human embryonic stem cells.

As part of our ongoing research into the genetics of addiction, our group has explored ethical issues raised by neuroscience research into the addiction and the development of a cocaine vaccine as well as the contribution made by illicit drug use to the global burden of disease. The policy implications of research on the genetics of tobacco use and dependence and a vaccine to treat nicotine dependence also falls under this area.

Another of our projects has been considering the ethical and policy implications of research into the genetics of depression, and the impact anti-depressant prescription had on suicide mortality in Australia from 1990 to 2000.

We have developed collaborations with the Queensland Cancer Fund and the School of Population Health (UQ Medical School), to undertake community surveys assessing public understanding of the implications of research in the cancer genetics and new treatments derived from advances in biotechnology.

OPPE investigated the ethical and policy implications of human embryonic stem cell research. We presented seminars on this contentious research to various scientific, public and government audiences in Brisbane and Sydney.







# Joint Appointments

## ARTHROPOD EVOLUTIONARY GENOMICS



**Group Leader**  
Steve Barker

While most animals are arthropods, their genomes and evolutionary genetics are poorly understood. Our research focuses on the mitochondrial genomics of ticks and lice, the evolution of resistance to insecticides in lice and mosquitoes, and the phylogenetic relationships of lice and other insects.

### Mitochondrial genomics

Mitochondria have their own genomes, and in most groups of animals the order of genes is remarkably similar.

However, we discovered two extraordinary exceptions: a group of hard ticks, and lice and their kin. The arrangement of the 37 genes in the mitochondrial genomes of these animals has changed so many times it is difficult to reconstruct the evolutionary path of these mitochondrial genomes.

By studying the mitochondrial genomes that have changed a lot, we hope to learn why the arrangements of genes in mitochondria evolve so slowly.

### Resistance to insecticides

The insecticides that people rely on to control pests like lice and mosquitoes do not always work effectively because the insect develops resistance to the chemicals in the insecticide.

Our group studies the epidemiology of resistance and also seeks to understand the genetic and biochemical basis behind it.

### Evolutionary relationships of lice

Human head lice are a severe social problem in developed countries yet body lice, which are associated with diseases like Typhus, are not.

The two are closely related and may even be the same species. We are studying whether the head and body lice of humans are interbreeding and therefore conspecific.

We also study the evolution of all lice (order Phthiraptera) and their relationships to the free-living Psocoptera.

## STRUCTURAL BIOLOGY OF PROTEIN-PROTEIN INTERACTIONS



**Group Leader**  
Bostjan Kobe

Our primary research theme involves understanding how the three-dimensional structure of a protein translates into function, and in particular how proteins interact with each other. To do this we combine crystallography, with computational techniques, biophysical methods for evaluating interactions, protein chemistry and molecular biology.

### Specificity of signal transduction pathways

The specificity of signal transduction pathways stems from specific recognition and regulatory properties of proteins involved in these pathways. The ongoing experimental structure-function studies involve protein kinases, the phosphopeptide-binding FHA domains, a novel class of G-proteins, and proteins involved in plant development and disease resistance.

In parallel, we are carrying out computational work aimed at developing bioinformatic tools for functional annotation of new protein sequences obtained by genome sequencing. In particular, we have developed methodology to predict the substrate specificity of novel Ser/Thr kinases based on their sequence alone, providing a powerful tool for genome-wide analysis of signaling pathways and identifying therapeutic targets.

### Regulation of nuclear import

Nuclear proteins are synthesized in the cytoplasm and are imported into the nucleus through the nuclear pore complexes. Such transport is directed by special signals, the most common termed the nuclear localization sequences (NLSs). Importin-alpha is the nuclear import receptor that recognizes these NLSs.

The ongoing crystallographic, biophysical and mutagenesis studies are aimed at shedding

light on both regulation and NLS recognition by importin-alpha, as well as using this protein as a structural framework for engineering new binding specificities useful for diagnostic and biotechnology purposes.

### Structural genomics of macrophage proteins

Structural genomics is a large-scale effort to determine 3D structures of all representative proteins, as this information is one of the most effective ways to infer protein function.

Our strategy is to use gene expression information from cDNA microarrays for target selection, and therefore selectively determine the structures of medically relevant proteins via a high-throughput approach.

The structures will be used to infer biochemical and cellular function and will serve as templates for structure-based drug design.

Macrophage proteins are of central importance in a wide range of immunopathology, including infectious and inflammatory disease, cardiovascular disease and cancer.

## MOLECULAR ANALYSIS OF CUTANEOUS SYSTEMS



**Group Leader**  
Joe Rothnagel

The epidermis provides a barrier that protects us from harmful radiation, environmental toxins and infection, as well as preventing desiccation. We are studying the contribution of individual genes to the development and maintenance of the epidermis and associated structures such as the hair follicle, sebaceous glands and nail bed.

A major focus of our group is identifying the signals and messages involved in specifying the formation of the integument. We are studying several genes and their protein products including, *Smoothed*, *Frizzled-3* and *Gli1*.

Analysis of the *Gli1* oncogene revealed alternatively-spliced exons that generate 5' leader sequences with differing translational capacities. The transcript with the highest translational capacity was associated with basal cell carcinoma. We have also characterised the mouse and human *Frizzled-3* genes and identified several alternatively spliced variants that are predicted to interact with each other to modulate Wnt signalling.

A primary function of the epidermis is to protect us from environmental assault as well as preventing desiccation. A major keratinocyte protein involved in both these functions is profilaggrin. This large (>600kDa), abundant protein is expressed late in epidermal differentiation and is thought to regulate skin water content, have innate anti-microbial activity, modulate the skin's response to UV damage and act as a calcium sink.

We have cloned the mouse profilaggrin gene as well as related genes in both human and mouse that form a large protein family which has not been previously described. Antibodies to various domains of profilaggrin have identified a region that is actively transported to the nucleus in late stage differentiating keratinocytes. It is postulated that this domain signals the final stages of terminal differentiation.

## GROWTH HORMONE AND CYTOKINE SIGNALLING



**Group Leader**  
Mike Waters

We study structure and function of class 1 cytokines and their receptors, particularly growth hormone and prolactin. This extends from small molecule analogs through hormone mutants to investigation of mechanisms of receptor activation. Receptor function is studied with knockin mice mutants, gene arrays, transcriptional activation assays and physicochemical approaches.

### Receptor activation mechanism

We have developed a new model for hormone-induced receptor activation involving rotational conformational change within a preexisting dimer.

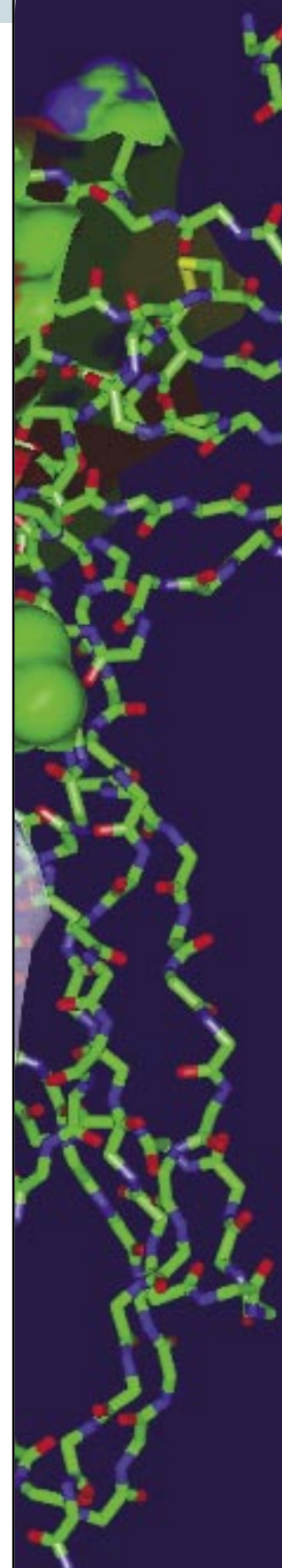
We continue to develop small molecule antagonist candidates for the GH receptor together with Protagonist Pty Ltd.

We have created a number of "super" porcine growth hormones of higher than wildtype potency.

We have created the first knockin mice mutants for signalling domains within the GH receptor. These are providing information about the requirements for promotion of somatic growth *in vivo*. They will be studied with gene chip arrays. We published the first gene array study on peptide hormone activation of transcription.

We have shown that the GH receptor in the endoplasmic reticulum traffics to the nucleus in response to the hormone binding at the surface. The extracellular domain is a transcriptional activator, and binds to identified co-activators. Nuclear localized receptor provides hormone independent growth and survival, and regulates a novel set of genes.

We have proposed important roles for suppressors of cytokine signalling in the breast response to milk engorgement and in the process of luteolysis.



## ARTHROPOD EVOLUTIONARY GENOMICS



**Group Leader**  
Alpha Yap

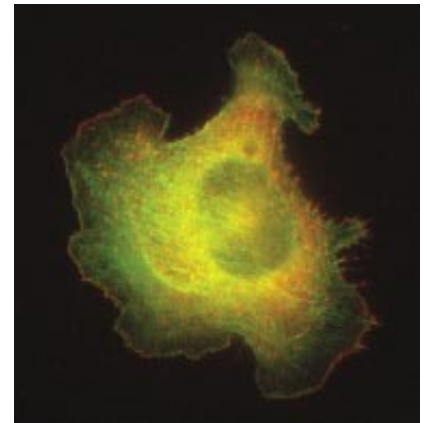
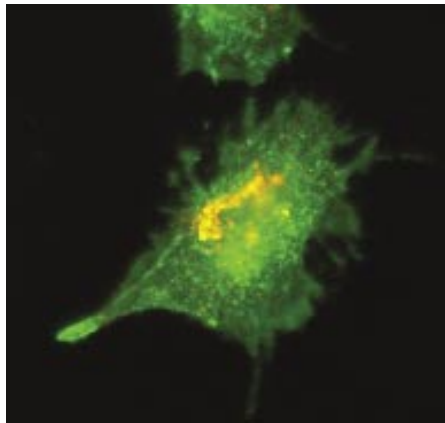
**M**y group studies the role of cadherin cell adhesion molecules in morphogenesis and tumor development. E-cadherin is a key mediator of cell-cell recognition. It participates in tissue patterning and its dysfunction contributes to tumor progression and invasion. We seek to understand the cellular basis of cadherin recognition, and how this controls cell movement and organisation.

We are studying the molecular and cellular mechanisms by which cadherin cell adhesion molecules mediate cell-cell recognition. Our current work builds on two recent discoveries made by my lab.

Firstly, we found that E-cadherin, the principal cadherin molecule found in epithelial tissues, functions as an adhesion-activated cell signaling receptor. In particular, upon adhesion E-cadherin activates signaling via the small GTPase, Rac, and the lipid kinase PI3-kinase.

Finally, an important potential target of this signaling receptor is the Arp2/3 protein complex, a protein machine that nucleates assembly of actin filaments. We were the first to discover that E-cadherin interacts with the

Arp2/3 complex to mark sites for actin assembly within cells. We are now exploring the general hypothesis that cadherin-activated signaling controls the subcellular localization and activity of Arp2/3 to modulate cell shape changes and motility in response to productive cell-cell recognition.





IMB  
Associates

## BIOINFORMATICS



**Group Leader**  
Kevin Burridge

Our group works on developing simulation and visualisation methodologies for understanding the behaviour of genetic regulation. The simulation models take into account stochastic effects, while the visualisation focuses on three dimensional display.

### Stochastic models and simulations for chemically reacting systems

In microscopic systems formed by living cells, the small numbers of reactant molecules can result in dynamic behavior that is discrete and stochastic rather than continuous and deterministic.

This research introduced a new class of discrete stochastic methods based on Poisson processes which 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 modeling of cellular behavior and regulation.

However, this method can be computationally quite demanding. We introduced a new class of numerical methods, called Poisson Runge-Kutta methods, that generalise this approach.

A general formulation and order theory for this class of Poisson Runge-Kutta methods is given, and high order methods constructed. Attention was given to such issues as stiffness and efficient implementation.

Numerical simulations illustrated the performance of these new simulations on some important cellular models.

We have investigated bi-stability and switching issues in the genetic regulatory networks of lambda phage using these approaches.

## EPITHELIAL AND TUMOUR IMMUNOLOGY



**Group Leader**  
Ian Frazer

Our research focuses on understanding how the immune system can identify and destroy cancers arising from the skin and skin-like surfaces throughout the body. This is particularly important in finding a vaccine to prevent papillomavirus, the major cause of cervical cancer.

The immune system is an incredibly complex defence mechanism capable of distinguishing between infections and the host body. Tumours are so different from the host that the immune system recognises them as foreign yet for some reason it does not attack them.

### Epithelial tumours

We are currently using mouse models to explore the molecular and cellular mechanisms of self tolerance and of rejection. We are particularly interested in what prevents the immune system from attacking the body, especially the skin, and how to harness the immune system to fight against tumours.

### Papilloma virus and codon usage

Papilloma viruses utilise codons which are rarely used in mammalian genomes and this represents an exciting avenue for the development of a vaccine to treat and prevent a papilloma infection. Currently much of our work is focusing on mismatches between codon usage and amino acids.

## SIGNAL TRANSDUCTION



**Group Leader**  
John Hancock

Our group studies mammalian intracellular signalling, particularly 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.

## CELL AND MOLECULAR ARCHITECTURE



**Group Leader**  
Alasdair McDowall

Using state-of-the-art cryo-electron microscopy, single particle reconstruction techniques, protein electron crystallography and whole cell tomography, our group studies the molecular structure and function of protein structures to provide a clear view of the complex interactions occurring inside a cell.

Ras proteins operate as molecular switches in signal transduction pathways downstream of tyrosine kinase and G-protein coupled receptors. This is a fascinating model system because there are three highly homologous Ras isoforms that generate different signal outputs despite sharing a common set of effector and activator proteins.

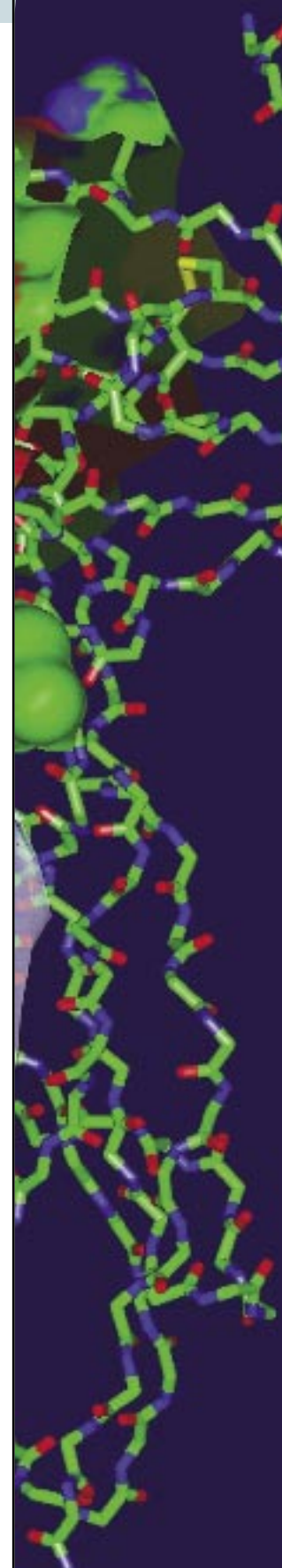
Our studies strongly suggest the existence of parallel Ras signalling pathways that are based on different plasma membrane microdomains. A major thrust of our current program is to dissect the composition and function of these microdomains. Specific themes include:

- Molecular mapping of the proteins and lipids of plasma membrane microdomains;
- EM visualization and quantitative characterization 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 localization of Ras and Ras-interacting proteins in response to physiological stimuli;
- Mechanism of Raf-1 activation, to characterize the multistep Raf-1 activation process spatially within the plane of the plasma membrane; and
- Characterization of the mechanism(s) whereby K-ras is transported to the plasma membrane and how Ras proteins engage different endocytic pathways.

High resolution ultrastructure of macromolecules is essential for virus identification and classification. We are applying the high resolution cryo-electron microscopy technique to study macromolecular complexes to gain insights into the molecular basis of virus and cell interactions.

Discovering an *in vitro* method for the measurement of drug release from nanoparticulate drug delivery systems is a joint project with groups at CSIRO Molecular Science, and DBL Pty in Victoria. We are investigating the preparation of novel surfactants with the aim to understanding potential components to be used as carriers for the delivery of anti-cancer drugs.

Our research focuses on protein localisation by electron microscopy of the Tax protein, human T-cell leukemia virus type I. Tax is a potent activator of viral transcription. Together with Dr F Bex from the University of Brussels we are using immunocytochemistry to characterize the intracellular localization of Tax and identify cellular factors which colocalized with Tax and are potential targets for its activation.



## MOLECULAR GENETICS OF SCHIZOPHRENIA



**Group Leader**  
Bryan Mowry

Schizophrenia is estimated to be 70 to 80 percent inherited and our work aims to identify genes for this devastating disease affecting one percent of the world's population.

Evidence from family, twin and adoption studies clearly demonstrate that schizophrenia aggregates in families, with this clustering largely attributable to genetic rather than cultural or environmental factors.

However, epidemiological data and molecular genetic studies demonstrate that susceptibility to schizophrenia is likely to be the result of a number of interacting genes of small to moderate effect that interact with each other and with non-genetic risk factors.

Candidate-gene and genome-wide linkage studies provide some evidence for the involvement of a number of specific genes and as yet unidentified factors localised to specific chromosomal regions including 1q, 2q, 6p, 6q, 8p, 13q and 22q.

In collaboration with national and international colleagues, we are studying both ethnically diverse and genetically isolated populations, to account for two different possibilities:

- The same, frequently occurring causative genes occur in all populations; and
- Rare genes may exist in one or more genetically homogeneous populations.

## CENTRE FOR NANOTECHNOLOGY & BIOMATERIALS



**Group Leader**  
Matt Trau

We are focused on the formation of novel materials and devices for medical and diagnostic needs including devices for rapid DNA sequencing, genetic screening, and drug discovery as well as artificial tissue matrices for human bone, liver and pancreas tissue.

Nanotechnology, the ability to control and manipulate nanometer-sized features of matter, is a fundamental tool which is used to fashion such materials and devices.

The overall goal of the research within our centre is to develop biologically related materials and devices which will ultimately improve human health.

Our research work is divided into two main categories:

- Genetic screening and drug discovery devices; and
- Artificial tissue matrices for implants into the human body.

Both of these areas require the preparation of novel materials and devices which have been fashioned to contain designed nanostructure.

Genetic screening and drug discovery devices

Rapid access to genetic information is central to the revolution occurring in the pharmaceutical industry, particularly in relation to novel drug target identification and drug development. Genetic variation, gene expression, gene function and gene structure are just some of the important research areas requiring efficient methods of screening DNA.

We are currently developing colloidal devices (ie, devices that are comprised of microscopic particles) which can be used for rapid DNA sequencing, genetic screening and drug discovery applications.

Artificial tissue matrices

Many human ailments arise as a result of the body's inability to fully re-generate damaged tissue (eg, bone, liver, pancreas). Common medical therapies in these cases involve the use of autografts (implants from one's own body), allografts (implants from cadavers), or other synthetic (non-biological) materials, each of which have their associated problems. Our research focuses on developing novel biological, degradable and "living" implants for the human body.

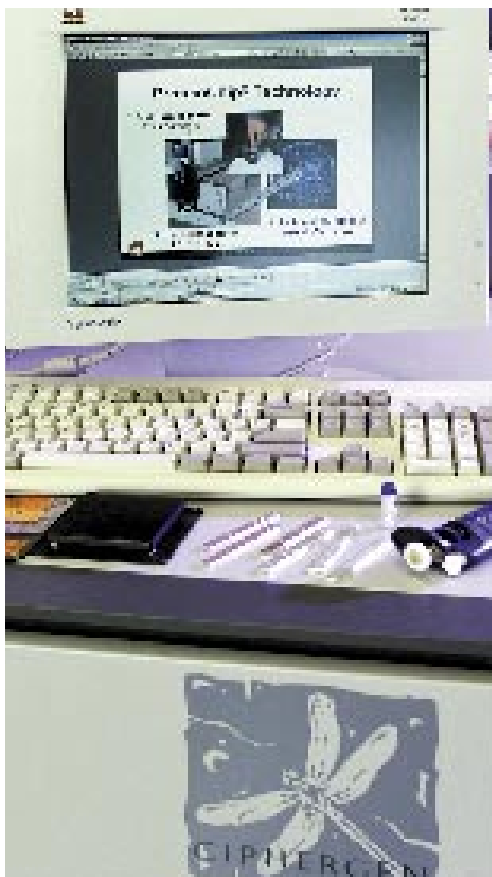




# Joint Ventures

## AUSTRALIAN RESEARCH COUNCIL SPECIAL RESEARCH CENTRE FOR FUNCTIONAL AND APPLIED GENOMICS

The ARC Special Research Centre for Functional and Applied Genomics provides and develops rate-limiting technologies that can enable world-class genomics research in the field of genomics. An integrated network of core technologies including computational biology, structural biology, proteomics, animal transgenics service and a microarray facility is already established.



The SRC has been operating for three years and the last 12 months has seen the consolidation of the physical infrastructure and personnel.

### Microarray Facility

The SRC Microarray Facility, directed by Sean Grimmond was commissioned for the purpose of facilitating bacterial clone archiving, high-density microarray manufacture, sample labelling and hybridisation and bioinformatics support for comprehensive gene expression profiling.

In the last year the facility has continued to produce a 16,000 cDNA array based on the NIH-NIA clone set. More recently, we pioneered the fabrication of long-oligo arrays and now provide 22,000 mouse and 19,000 human gene arrays.

The facility has also continued to generate custom arrays from a wide variety of organisms (eg. specialised libraries from the mouse, *Arabidopsis*, soybean, cow). Work has commenced on other microarray fabrication including antibody and reverse transfection arrays.

Storage of microarray data became internationally standardised in 2002 with the implementation of the Minimum Information about a Microarray Experiment (MIAME) guidelines.

In collaboration with researchers at the University of Lund, Sweden, the facility

was involved in the implementation of BioArray Software Environment (BASE), an open source web-based comprehensive database server to manage the massive amounts of data generated by microarray.

BASE collates biomaterial, raw data, and a series of integrated analysis for normalisation, visualisation and analysis tools.

Finally a series of web-based tools have been established for annotating the biological function and pathway data for all genes on the arrays fabricated by the facility.

### Mass spectrometry

The mass spectrometry section houses the very latest instrumentation required for the investigation of biological molecules ranging from small molecular weight organic compounds to large proteins.

The section has five mass spectrometers with complementary capabilities and is involved in a diverse range of activities encompassing almost all divisions of IMB.

These include protein characterisation, post-translationally modified amino acid determination, quantification of potential therapeutics including cyclotides and peptidomimetics in biological matrices, selenomethionine incorporation for crystallographic analysis, integrity of synthetic products and intermediates, structural determination and exact mass measurement of organic molecules.

*(L to R) IMB Co-director Peter Andrews, Advanced Laboratory Solution's Rick Holder, IMB Co-director John Mattick, UQ Vice Chancellor Professor John Hay and Hon. Paul Lucas Minister for Innovation and Information Economy at the launching of the Ciphergen SELDI-ToF mass spectrometer.*



This wide range of involvement in all aspects of IMB's division of Structural Biology and Chemistry means that mass spectrometry is represented in most publications from this division.

We also have a number of collaborations with the Queensland Department of Primary Industries, in the investigation of milk proteins and fish toxins and CSIRO Molecular Genetics Division, which rely heavily on our spectrometry capabilities.

The latest mass spectrometer to join the section is Australia's first Ciphergen SELDI-ToF, mass spectrometer which was purchased through an ARC Research Infrastructure and Equipment Fund Grant.

This instrument, enables us to develop methods of studying protein-protein and protein-DNA interactions, protein expression differences in diseased and healthy cells, ligand fishing and binding type experiments, protein identification and characterization, immunoaffinity isolation, antibody-antigen interactions.

The Ciphergen spectrometer complements our existing facilities, which are already at the forefront of high sensitivity structural determination of organic molecules, peptides and proteins, together with the investigation of post-translationally modified amino acid residues, and the rapid characterisation and quantitation of biomolecules in a range of matrices.



Further enhancing our mass spectrometry capabilities, the SRC has very powerful and fast database searching software and hardware.

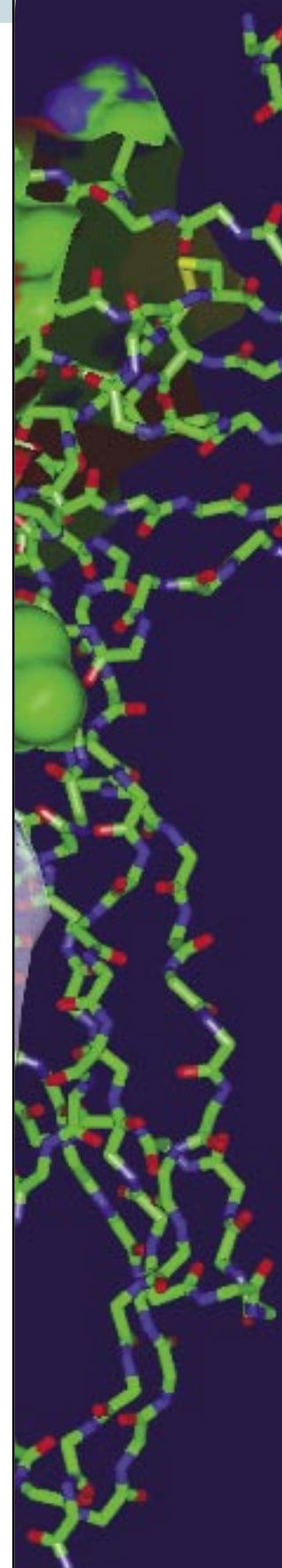
#### Protein Expression Facility

The SRC's Protein Expression Facility has established a downstream processing unit for large-scale processing and purification of recombinant proteins using affinity chromatography in conjunction with FPLC. Also the infrastructure to produce recombinant proteins in baculovirus systems is in place.

#### Transgenic Service

In keeping pace with growing demand the SRC's Transgenic Service has increased staff numbers to ensure a prompt and reliable service for users. New targeting approaches to achieve tissue-specific, inducible gene expression in transgenic animals and knockouts are in development further enhancing the suite of services available

In 2002 the SRC underwent a successful review with funding approved for a further three years. In its report the Australian Research Council Review Panel commented that the SRC was 'outstandingly successful'.



## AUSTRALIAN GENOME RESEARCH FACILITY



The Australian Genome Research Facility (AGRF) comprises of laboratories in Melbourne and Brisbane equipped and staffed to ensure Australia plays a leading role in the worldwide genomics revolution.



*Senator George Brandis (right) launching AGRF's new sequencers.*

The AGRF provides national and international research and industry groups with large scale DNA sequencing, genotyping, microarray production and bioinformatics services.

The AGRF is a major national research facility (MNR) of the Federal Government and is the largest supplier of genotyping and sequencing services in Australia. Additionally the AGRF has the largest customer base of any existing MNR in the country.

In 2002 the AGRF invested over \$2.5 million purchasing four new Applied Biosystems 3730 capillary sequencers to increase the Facility's sequencing output while maintaining competitive costs and ensuring quality data.

Further complementing this, the services and laboratories of the AGRF were inspected and officially accredited by the National Association of Testing Authorities (NATA) in 2002.

NATA accreditation is an essential component of analytical service laboratories and confirms that AGRF's methods and procedures are reproducible while offering customers further assurance that data is accurate and correct.



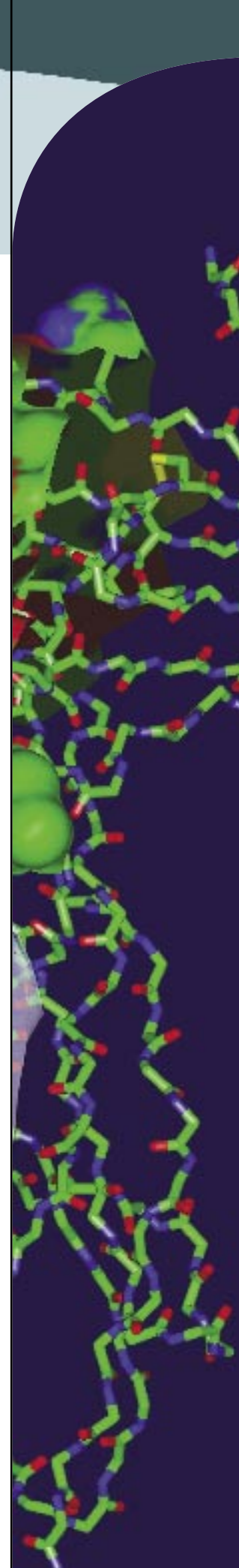
One of the highlights this year has been AGRF's collaboration with Professor Ben Adler's group at Monash University in sequencing the *Leptospira* genome.

Upon completion in early 2003, this will be the first genome fully sequenced in Australia, and the AGRF has played a vital role in sequencing and annotating this 4.1 Megabase spirochete genome.

Finally, expansion of the AGRF with the development of a facility in Adelaide, South Australia is reaching fruition with the completion of the design phase of the new laboratory. This facility sees the AGRF providing services focused on agricultural genomics, in conjunction with the University of Adelaide's Waite Institute and the South Australian Research and Development Institute.

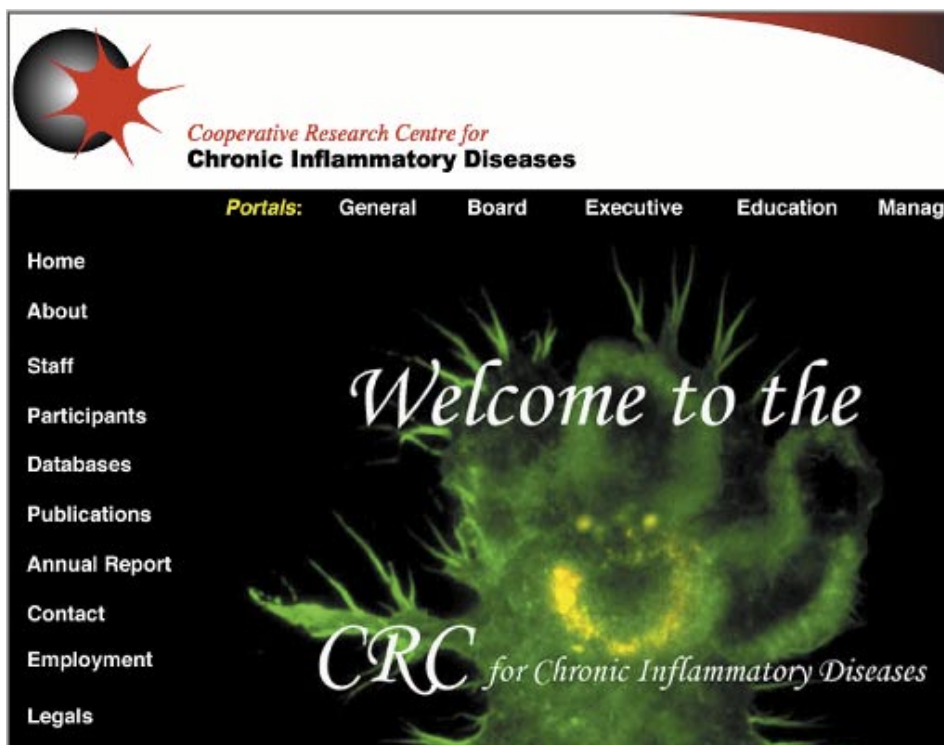


AGRF's Susan Forrest and Elizabeth Kuczek (second and third from left) with representatives of Applied Biosystems.



## COOPERATIVE RESEARCH CENTRE FOR CHRONIC INFLAMMATORY DISEASES

The IMB is a core participant in the Cooperative Research Centre for Chronic Inflammatory Diseases (CRC-CID), established in September 2001. The major objective of the CRC is to discover new molecular targets involved in the pathogenesis of chronic inflammatory lung and joint disease and use this information to develop novel treatments for these disorders.



The CRC is using gene microarrays, proteomics, cell-based assays and genetically modified animal models of disease to understand how macrophages cause chronic inflammation. The CRC is structured to facilitate the entire drug discovery cycle from primary target identification using functional genomic and proteomic approaches, target validation in disease models and human tissues, high throughput cell-based assay development, lead target screening, generation of therapeutic and research antibodies, and the development of macrophage-targeted drug delivery strategies.

The IMB's Professor David Hume is Deputy Director of the CRC and Chair of the Education Committee. Several key appointments were

made at the Queensland node during 2002 including Dr Ian Ross (proteomics) and Dr Dmitri Ovchinnikov (transgenics) and Dr Tim Ravasi (microarray technology).

The focus of the CRC Education program is postgraduate training and the Queensland node has been successful in recruiting ten PhD students. These students have the opportunity to undertake courses in drug design, intellectual property and commercialisation and to gain industry experience with short-term placements with our commercial partner Astra-Zeneca.

The CRC was successful in its supplementary funding application and will receive \$5 million to develop new methods to treat debilitating

joint diseases, particularly osteoarthritis, and the development of new biomaterials to repair injured joints. Dr Ian Cassady (IMB) will be joint program leader of Macrophage Lineage Cells and the Inflammatory Reaction to Joint Prostheses and Professor Hume is the program leader of Computational Biology and Structural/Functional Genomics.

## CO-OPERATIVE RESEARCH CENTRE FOR THE DISCOVERY OF GENES FOR COMMON HUMAN DISEASES

The Co-operative Research Centre for the Discovery of Genes for Common Human Diseases has developed a research portfolio to unravel the genetic causes behind conditions such as endometriosis, type I diabetes and multiple sclerosis. This research is complimented by an education and ethics program addressing many of the issues associated with medical genetics in our society.



The IMB is part of the Co-operate Research Centre for the Discovery of Genes for Common Human Diseases (Gene CRC) along with the Queensland Institute for Medical Research, the Walter and Eliza Hall Institute of Medical Research, the Murdoch Childrens Research Institute and associate member The Menzies Centre for Population Health Research. Cerylid Biosciences is the administrative centre and commercial partner of the Gene CRC.

A major objective of the Gene CRC is to identify and study genes that are important in determining susceptibility to common human diseases. Many of the common diseases which afflict us have both genetic and environmental components. In some cases the genetic component is distinct enough to allow identification of genes responsible using genomic approaches. Such discoveries have applications as diagnostics and the development of therapies including pharmaceuticals. The basal cell carcinoma research conducted at the IMB by Professor Brandon Wainwright and Dr Carol Wicking contributes to the Gene CRC's project portfolio.

The Gene CRC is committed to engaging the Australian community in an informed debate on the applications of human genetic technology. To this end, an education and ethics program, geneEDUCATION, has been developed.

This program seeks to provide knowledge and skills related to human genetic research to a wide range of people in the community, including primary and secondary students and their teachers, health professionals, financiers and the general public.



# Graduate programme

The mission of the IMB graduate programme is to be recognised nationally and internationally in the field of research training, providing students with a stimulating, supportive environment in which to develop. The programme provides training beyond the boundaries of each student's specific research incorporating topics such as bioethics and biobusiness.

The IMB graduate programme now has over 60 students enrolled through the Institute. As 2002 was the third year since the programme's inception we are expecting our first students to be awarded their PhDs in the coming year.

This year, mandatory sessions on ethics and biobusiness were conducted in-house. These courses provided relevant new perspectives and encouraged active discussion of research-related issues.

There was an 'Introduction to BioBusiness' workshop conducted by staff from IMBcom in May and a workshop covering 'Ethical and Social Issues in Biomedical Research' in July. This workshop was conducted by Professor Wayne Hall and Angela Wallace from IMB's Office of Public Policy and Ethics and covered issues associated with HIV/AIDS.



Another highlight was the two day BioBusiness Retreat, held at the Sunshine Coast in August. It covered commercialisation topics such as ethical issues, career options, leadership and interpersonal skills.

## AWARDS

Melissa Edeling received an Australian Society for Biochemistry and Molecular Biology (ASBMB) student poster award at the 2002 COMBIO conference 29 Sept-03 Oct 2002.

Gabrielle Kolle received the Australia New Zealand Society for Cellular and Developmental Biology Keith Dickson poster award at the 2002 COMBIO conference.

Julie Dutton won a Travel Fellowship to attend the Second International Conference on Structural Biology and Functional Genomics, Singapore, 2002.

Gerald Hartig won the Angstrom Art 'Expose Your Science' competition and John Lock and Dan Sangermani were runners-up in the same competition.

Grant Challen was awarded both the Student Presentation Prize - Frontiers in Tissue Engineering 2002 and Queensland Health Young Achiever of the Year - Queensland Health and Scientific Meeting 2002.

The gATAAg seminar series was also instigated. An initiative of IMB's Christine Wells, Chris Johns and QIMR's Steff Williams, it was started to give students and early postdoctoral researchers a forum to discuss and question new techniques, ideas and applications. The series opens the door to "big" science speakers for students, in a less formal environment.

## PhDs AWARDED IN 2002

Scott Beatson  
Shen-liang Chen  
Bryan Fry  
Brett Hosking  
Michael Kelso  
Wai Fun (Patrick) Lau  
Donmienne Leung  
Carney Matheson  
Delvac Oceandy  
Budi Utama

## NEW STUDENTS

Tamara Allen  
Guy Barry  
Jennifer Bennetts  
Grant Challen  
Sebastien Dutertre  
Jenny Ekberg  
Alex Garcia  
Michael Höhl  
Jean Jin  
Shannon Joseph  
Marcus Kerr  
Matthew Kirkham  
Luke Kirkwood  
Erica Lovelace  
Nicholas Meadows  
Andrew McDevitt  
Emma Millard  
Michael Pheasant  
Alisa Poh  
Vera Ripoll  
Lillian Sando  
Ivana Saska,  
Nicholas Shepherd  
Bo Wang

## HONOURS STUDENTS IN 2002

Rajith Aturaliya  
David Bryant  
Natalie Butterfield  
Damon Cheyne  
Alexander Combes  
Kevin Gillinder  
Tom Guthrie  
Kim Hanchard  
David Ireland  
Sonjia Layton  
Rebecca McDonald  
Madhavi Maddugoda  
Christopher Moore  
Aaron Poth  
Daniel Sangermani  
Elaine Thomas





# Staff and students

## Directors

Peter Andrews, Co-director  
John Mattick, Co-director  
Ian Taylor, Deputy Director (Systems and Administration)  
Brandon Wainwright, Deputy Director (Research)  
Wayne Hall, Director, Office of Public Policy and Ethics

## Group leaders

Paul Alewood  
David Craik  
David Fairlie  
Sean Grimmond  
Wayne Hall  
Jennifer Hallinan  
Ben Hankamer  
David Hume  
Bostjan Kobe  
Peter Koopman  
Richard Lewis  
Melissa Little  
Jenny Martin  
George Muscat  
Rob Parton  
Mark Ragan  
Mark Smythe  
Jenny Stow  
Rick Sturm  
Rohan Teasdale  
Carol Wicking

## Joint appointments

Steve Barker  
Bostjan Kobe  
Joe Rothnagel  
Mike Waters  
Alpha Yap

## Associates

Kevin Burrage  
Bernie Carroll  
Ian Finlay  
Ian Frazer  
John Hancock  
Stuart Kellie  
Tom Loy  
Alasdair MacDowall  
Brian Mowry  
Matt Trau

## Adjunct appointments

Derek Kennedy  
Robert Raven  
Tracie Ramsdale  
Judy Halliday  
Michael James  
Sue Treloar

## Senior research officers

John Abbenante  
Paramjit Bansal  
Gregory Bourne  
Jo Bowles  
Ian Cassady  
Peter Cassidy  
Norelle Daly  
Murray Hargrave  
John Holland  
Richard Kidd  
Stephen Love  
Sally Martin  
Amanda Nourse  
Jane Olsson  
Bob Reid  
Andreas Ruhmann  
Yogendra Singh  
Kate Stacey  
Trung Tran

## Research officers

Anna Agard  
Denise Adams  
Peter Bailey  
Annemiek Beverdam  
Ross Brinkworth  
Richard Brown  
Jens Buchardt  
Caspar Christensen  
Richard Clark  
Michelle Colgrave  
Elaine Costelloe  
Nathan Cowieson  
Uwe Dressel  
Tammy Ellis  
Barb Fletcher  
Matthias Floetenmeyer  
Lindsay Fowles  
Michael Gagen  
Niranjali Gamage  
Matthew Glenn  
Ulf Goransson  
Roland Govers  
Karl Hansford  
Begona Heras  
Roy Himes  
Brett Hosking  
Shu-Hong Hu  
Ben Huang  
Lubomira Jamriska  
Pia Kahnberg  
Joanna Kelly  
Eva Kovacs  
Astrid Kraemer  
Sarah Kruger  
Patrick Lau  
Agnes Lichanska  
Marion Loughnan  
Andrew Lucke  
Tina Maguire

Gemma Martinez  
Fiona McMillan  
Brendan McMorran  
Juan Molero Navajas  
Leonard Motin  
Richard Newton  
Annette Nicke  
Dmitry Ovchinnikov  
Josef Pánek  
Nasrin Perskvist  
Bernhard Pfeiffer  
Fiona Rae  
Paavo Rahkila  
Timothy Ravasi  
Thomas Robertson  
Ian Ross  
Horst Schirra  
Iain Sharpe  
Philip Sharpe  
Graeme Shepherd  
Fiona Simpson  
Yogendra Singh  
Darren Smyth  
Martin Stoermer  
Ylva Strandberg  
Matthew Sweet  
Shuji Takada  
Johan Trygg  
Joel Tyndall  
Parimala Vajjhala  
John Whitehead  
Dagmar Wilhelm  
Lorine Wilkinson  
Megan Wilson  
Fiona Wylie  
Clarissa Wynne  
Zheng Yuan

#### PhD students

Udani Abeypala  
Christelle Adolphe  
Azita Ahadzadeh  
Tamara Allen  
Radiya Ali  
Chris Armishaw  
Shannon Armstrong  
Daniel Barry  
Guy Barry  
Scott Beatson  
Jenny Bennetts  
Wang Bo  
Jennifer Bolton  
Trudy Bond  
Robert Breinl  
Grant Challen  
James Clark  
Becky Conway-Campbell  
Anthony Cook  
Larry Croft  
Meredith Downes  
Nick Drinnan

Sebastien Dutertre  
Julie Dutton  
Jenny Eckberg  
Melissa Edeling  
Timothy Evans  
Juliet French  
Alex Garcia  
Brooke Gardiner  
Susan Gillies  
Kevin Gillinder  
Andrew Goodall  
Marita Goodwin  
Brett Hamilton  
Tamarind Hamwood  
Gerald Hartig  
Fredrik Hellqvist  
Michael Höhl  
Douglas Horton  
Gene Hopping  
Wendy Ingram  
Darryl Irwin  
Kate Irvine  
Jean Jin  
Shannon Joseph  
Asanka Karunaratne  
Markus Kerr  
Matthew Kirkham  
Luke Kirkwood  
Gabriel Kolle  
Michael Korsinczky  
Cath Latham  
Chi-Yan Lau  
Chris Le  
Andrew Leech  
Donmienne Leung  
John Lock  
Kelly Loffler  
Erica Lovelace  
Fred Martinson  
Carney Matheson  
Ailsa McCormack  
Karen McCue  
Andrew McDevitt  
Edwina McGlenn  
Nick Meadows  
Emma Millard  
Kevin Miranda  
Isabel Morrow  
Jason Mulvenna  
Susan Nixon  
Ryan O'Donnell  
James Palmer  
Andrew Paterson  
Leonard Pattenden  
Rebecca Pelekanos  
Michael Pheasant  
Michael Piper  
Jyotsna Pippal  
Manuel Plan  
Alisa Poh  
Mariel Quimio  
Lotten Ragnarson

(Cont.)



# Staff and students

## STAFF AND STUDENTS (continued)

Ayanthi Richards  
Vera Ripoll  
Tara Roberts  
Paul Rohde  
Johan Rosengren  
Angela Salim  
Lillian Sando  
Ivana Saska  
Tedjo Sasmono  
Robert Sbaglia  
Kate Schroder  
Tina Schroeder  
Jeannie Scott  
Hasnawati Seleh  
David Sester  
Nicholas Shepherd  
Annetete Shewan  
Shane Simonson  
Ben Skellett  
James Smith  
Stefan Stanley  
Khairina Tajul Arifin  
Manuela Trabi  
Vicky Tsai  
Budi Utama  
Carmel Walsh  
Nicole Walsh  
Yu Wan  
Mary Wang  
Senali Abayratna Wansa  
Jong Wei  
Chris Wells  
Charlotte Widberg  
Budi Utama  
Sundy Yang  
Taka Yasuda

### Honours students

Charlie Ahn  
Rajith Aturaliya  
Natalie Butterfield  
Alex Combes  
Kevin Gillinder  
Jill Gillmore  
Tom Guthrie  
Kim Hanchard  
Elizabeth Holliday  
David Ireland  
Sonjia Layton  
Madhavi Maddugoda  
Emryn Maclachlan  
Rebecca McDonald  
Christopher Moore  
Aaron Poth  
Daniel Sangermani  
Elaine Thomas  
Nhi Tran  
Brendan Tse  
John Wei Wooh

### Research assistants

Shirlene Badger  
Ian Bailey-Mortimer  
Renee Beyer  
Rekha Bharathi  
Selena Boyd  
Darren Brown  
Daniel Bryant  
Rachel Burow  
Marc Campitelli  
Amanda Carozzi  
Adrian Carter  
Lucy Carter  
Rowena Cecil  
Wei Chen  
Jane Clarkson  
Alexander Combes  
Justin Coughlan  
Stephen Cronau  
Melissa Davis  
Christina Denman  
Joanne Dowd  
Julie Dutton  
Brydie Edwards  
Geoffery Faulkner  
Charles Ferguson  
Bernadine Flanagan  
Cameron Flegg  
Barb Fletcher  
Alistair Forrest  
Christine Gee  
Kylie Georgas  
Milena Gongora  
Anne Hardacre  
Suzanne Hardy  
Timothy Harlow  
Edith Hii  
Michael Hines  
Rhonda Hobb  
Daryl Horton  
Brett Hosking  
Ning Huang  
Carolyn Jacobs  
Kristy James  
Russell Jarrott  
Chris Johns  
Sonya Kaiser  
Gregory Kelly  
Michael Kelso  
Tatiana Khromykh  
Gabriel Kolle  
Hania Lada  
Kellie Lammerts van Bueren  
Hung-Teck Lee  
Pawel Listwan  
Robert Luetterforst  
Andrew McDevitt  
Kirra McConnell  
Suzanne McHardy  
Allison McLean  
Adrian Miranda  
Thea Monks

Katherine Morley  
Angie Morrison  
Christine Mulford  
May Myint  
Jonathon Nielson  
Delvac Oceandy  
Warren Oliver  
Katherine Palethorpe  
Sarah Penning  
Darren Pickering  
Elena Piotto  
Michael Piper  
Alisa Poh  
Ramakrishnan  
Min Rao  
Emily Riley  
Ashley Rosetta  
Ke-lin Ru  
Elke Seppanen  
Iain Sharpe  
Darren Smit  
Annika Stark  
Anita Swallow  
Matthew Tatkovics  
Darrin Taylor  
Ngari Teakle  
Trazel Teh  
Linda Thomas  
Bradley Tonkes  
Liam Town  
Angela Trieu  
Brendan Tse  
Jill Turner  
Laurence Veness  
Juliana Venturato  
Suzie Verma  
Tom Watson  
Christine Wells  
Daying Wen  
Jacqueline Wicks  
Shayama Wijedasa  
Elizabeth Williams  
Shaiyena Williams  
Sarah Yeates  
Michael Young

#### Scientific support

Selena Boyd  
Karl Byriel  
Kylie Georgas  
Alun Jones  
Colin Macqueen  
Julie Osborne  
Darren Paul  
Greg Young

#### Visitors

Sari Alto  
Alisa Becker  
Mohit Chaturvedi  
Carolyn Dong

Carolyn Geczy  
J. Peter Gogarten  
Ruchi Gupta  
Thomas Lauber  
Ute Marx  
Paul Pavli  
George Ramm  
Michel Rheli  
Dietmar Schomburg  
Glyn Truscott  
Wendy van Zuylen  
Carl Wibom

#### Administration and finance

Teresa Buckley, Executive Secretary  
Jodie Campbell, Administrative Assistant  
Barb Clyde, Administrative Officer  
Robyn Craik, Purchasing Officer  
Ann Day, Executive Officer  
Mileta Duggleby, Purchasing Officer  
Barbara Feenstra, Reception/Secretary  
Angela Gardner, Administrative Officer  
Carole Key, Principal Administration Officer  
Karen Korenromp, Finance Manager  
John Spooner, Finance Manager  
Santa-Maria Trubshaw, Reception/Secretary  
Rhonda Turk, Reception/Secretary

#### Technical and laboratory services

Robyn Baird, Sterilisation Facility Manager  
Chris Barnett, Infrastructure Manager  
Henk Faber, Technical Officer  
Jeremy Kroes, Technical Assistant  
Karleen Marsh, Glassware attendant  
Greg McHugh, Technical Officer  
Charles Nelson, Safety Officer  
David Scarce, Workshop Manager  
Michael Tetley, Glassware attendant  
Dawn Walsh, Glassware attendant

#### Information technology services

Calvin Evans, Computer Systems Officer  
Ondrej Hlinka, Computer Systems Officer  
Luke Kirkwood, Computer Systems Officer  
Maria Maddison, Computer Systems Officer  
Nelson Marques, Computer Systems Officer  
Ireneusz Porebski, Computer Systems Officer  
Lance Rathbone, Computer Systems Officer  
Calvin Wang, Computer Systems Officer

#### Marketing and communications

Russell Griggs, Communications Officer  
Tania Hudspith, Marketing Officer  
Angela Wallace, Education Officer  
Helen Weatherley, Marketing and Communications Manager



## Statement of operating income and expenditure Year ended 31 December 2002

| INCOME   |      | 2000<br>\$        | 2001<br>\$        | 2002<br>\$                   |
|--|------|-------------------|-------------------|------------------------------|
|  | Note |                   |                   |                              |
| University of Queensland (operating grant)           | 1    | 2,942,718         | 6,664,365         | 6,023,929                    |
| University of Queensland research grants             |      | 200,990           | 100,000           | 269,358                      |
| State Government                                     |      | 5,500,000         | 2,500,000         | 6,000,000                    |
| SRC grant (Australian Research Council)              |      | 1,631,153         | 1,039,320         | 1,148,975                    |
| Australian Research Council                          | 2    | 1,131,271         | 1,668,000         | 1,599,576                    |
| Clive and Vera Ramaciotti Foundation                 |      | 43,545            | 9,545             | 0                            |
| CRC for Discovery of Genes for Common Human Diseases |      | 220,958           | 232,415           | 122,469                      |
| CRC for Chronic Inflammatory Diseases                |      |                   |                   | 943,401                      |
| Department of Primary Industries                     |      |                   |                   | 98,040                       |
| Diabetes Australia Research Trust                    |      | 33,409            | 35,791            | 37,700                       |
| Department of Industry Science and Technology        |      | 166,400           | 0                 | 0                            |
| Human Frontiers Science Program                      |      | 127,242           | 0                 | 0                            |
| Glaxo Wellcome Australia                             |      | 670,000           | 62,000            | 0                            |
| Government Employees Medical Research Fund           |      | 45,000            | 0                 | 0                            |
| Juvenile Diabetes Foundation International           |      | 299,626           | 267,704           | 77,084                       |
| Mayne Bequest Foundation                             |      | 60,000            | 0                 | 0                            |
| The Merck Genome Research Institute                  |      | 261,559           | 0                 | 0                            |
| National Institute of Health (US)                    |      |                   |                   | 1,391,005                    |
| National Health and Medical Research Council         | 2    | 2,938,586         | 5,359,112         | 4,306,397                    |
| National Heart Foundation                            |      | 45,000            | 0                 | 50,000                       |
| Postgraduate Scholarships                            |      | 28,209            | 15,882            | 38,214                       |
| QIMR   |      |                   |                   | 53,908                       |
| Queensland Cancer Fund                               |      | 230,072           | 116,447           | 92,750                       |
| Sylvia and Charles Viertel Charitable Foundation     |      | 165,000           | 165,000           | 165,000                      |
| Wellcome Trust                                       |      | 28,011            | 23,829            | 0                            |
| Commercial income                                    |      | 1,371,664         | 2,589,861         | 2,127,649                    |
| Miscellaneous income                                 |      | 415,591           | 272,136           | 19,593                       |
| <b>TOTAL INCOME</b>                                  |      | <b>18,556,004</b> | <b>21,121,405</b> | <b>24,565,049</b>            |
| <b>FUNDS BROUGHT FORWARD FROM PREVIOUS YEAR</b>      | 3    | <b>1,009,031</b>  | <b>3,843,597</b>  | <b>3,594,479</b>             |
| <b>TOTAL FUNDS AVAILABLE</b>                         |      | <b>19,565,034</b> | <b>24,965,002</b> | <b>28,159,528</b>            |
| <b>EXPENDITURE</b>                                   |      |                   |                   |                              |
| Salaries   |      |                   |                   |                              |
| Research   |      | 6,549,841         | 7,809,255         | 9,066,745                    |
| Administration                                       |      | 1,090,220         | 1,117,375         | 1,342,520                    |
| Infrastructure                                       |      | 541,043           | 813,527           | 1,012,400                    |
| Research services                                    |      | 2,635,745         | 6,034,723         | 4,865,433                    |
| Education programs                                   | 4    | 317,726           | 378,436           | 500,939                      |
| Administration                                       | 5    | 937,703           | 550,574           | 452,021                      |
| Infrastructure                                       | 6    | 357,436           | 928,651           | 786,809                      |
| Capital equipment                                    | 7    | 2,307,116         | 3,132,769         | 1,840,664                    |
| IMBcom   |      | 984,608           | 605,214           | 746,896                      |
| <b>TOTAL EXPENDITURE</b>                             |      | <b>15,721,437</b> | <b>21,370,523</b> | <b>20,614,427</b>            |
| <b>Funds carried forward</b>                         | 8    | <b>3,843,597</b>  | <b>3,594,479</b>  | <b>7,545,101<sup>#</sup></b> |

<sup>#</sup> Of this, \$1.1 million is the carry forward on core IMB accounts, \$3.7 million relates to commitments on equipment for the new building, \$1.3 million relates to a new NIH grant awarded in late 2002 and \$1.4 million relates to research grants.

## Explanatory notes to statement of income and expenditure

### 1/ In-kind contributions

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

|               |                           | %   |
|---------------|---------------------------|-----|
| S. Barker     | Parasitology              | 80  |
| D. Hume       | Biochemistry              | 20  |
| T. Loy        | Anthropology & Sociology  | 100 |
| J. Mattick    | Biochemistry              | 20  |
| R. Parton     | Micoscopy & Microanalysis | 10  |
| J. Rothnagel  | Biochemistry              | 80  |
| B. Wainwright | Biochemistry              | 20  |
| M. Waters     | Physiology & Pharmacology | 100 |
| A. Yap        | Physiology & Pharmacology | 80  |
| B. Kobe       | Biochemistry              | 80  |

### 2/ Fellowship/projects from government agencies

|                                    | \$               |
|------------------------------------|------------------|
| <b>Australian Research Council</b> |                  |
| Projects                           | 903,615          |
| Fellowships                        | 695,961          |
|                                    | <b>1,599,576</b> |

|   |                  |
|---|------------------|
| <b>National Health and Medical Research Council</b> |                  |
| Projects  | 3,839,431        |
| Fellowships   | 466,966          |
|   | <b>4,306,397</b> |

### 3/ Funds brought forward from 2001

|  |                  |
|--|------------------|
| University of Queensland operating grant       | 1,619,317        |
| University of Queensland research grants       | -232             |
| Postgraduate scholarships                      | 3,544            |
| State Government                               | -150,411         |
| SRC Grant                                      | 164,880          |
| Fellowships (as approved by funding bodies)    | 77,703           |
| Project grants (as approved by funding bodies) | 1,879,678        |
|  | <b>3,594,479</b> |

### 4/ Education programs

|                                       |                |
|---------------------------------------|----------------|
| Postgraduate scholarships             | 445,930        |
| Postgraduate recruitment and training | 14,204         |
| Public Policy and Ethics Unit         | 40,805         |
| Total education services              | <b>500,939</b> |

### 5/ Administration

|                                    |                |
|------------------------------------|----------------|
| Annual report                      | 15,810         |
| Marketing                          | 46,241         |
| Personnel recruitment and training | 64,115         |
| Visiting scientists/seminars       | 17,639         |
| Fees                               | 167,713        |
| Entertaining                       | 703            |
| Equipment lease                    | 80             |
| Photocopying                       | 35,155         |
| Postage and freight                | 5,439          |
| Printing and stationery            | 55,862         |
| Telephone                          | 44,660         |
| Travel expenses                    | 14,757         |
| Sundries                           | 18,734         |
| Cost recovery                      | -34,886        |
| Total administration               | <b>452,021</b> |

### 6/ Infrastructure

|                                       |                |
|---------------------------------------|----------------|
| Building maintenance                  | 16,250         |
| Rental - demountables/storage         | 22,706         |
| Safety equipment                      | 29,210         |
| Laundry                               | 1,960          |
| Minor equipment and furniture         | 13,198         |
| Equipment maintenance                 | 142,048        |
| Animals                               | 144,063        |
| Computer services                     | 326,355        |
| Glass-washing and replacement         | 23,052         |
| Reticulated gases, RO water & dry ice | 62,935         |
| Sundries                              | 14,958         |
| Stores                                | -9,925         |
| Total Infrastructure                  | <b>786,809</b> |

### 7/ Capital equipment

|                         |                  |
|-------------------------|------------------|
| Scientific equipment    | 1,712,810        |
| Minor equipment         | 127,853          |
| Total capital equipment | <b>1,840,664</b> |

### 8/ Funds carried forward to 2003

|  |                              |
|--|------------------------------|
| University of Queensland operating grant       | 4,047,449                    |
| University of Queensland research grants       | 69,686                       |
| Postgraduate scholarships                      | 4,371                        |
| State Government                               | 346,758                      |
| SRC grant                                      | 373,794                      |
| Fellowships (as approved by funding bodies)    | 91,919                       |
| Project grants (as approved by funding bodies) | 2,611,123                    |
|  | <b>7,545,101<sup>#</sup></b> |

<sup>#</sup> Of this, \$1.1 million is the carry forward on core IMB accounts, \$3.7 million relates to commitments on equipment for the new building, \$1.3 million relates to a new NIH grant awarded in late 2002 and \$1.4 million relates to research grants.

# How can we help you?

The IMB is committed to building partnerships and collaborations with industry, government and other research organisations, contributing to world knowledge in terms of human and animal biology as well as health benefits for the global community, and ethics of the new genetics. In particular, the IMB is developing:

- **partnerships** with hospitals and medical research institutes to provide a better understanding of the genetic and biochemical basis of disease, and to develop and trial clinical candidates emerging from its research programs.
- **strategic alliances** with national and international pharmaceuticals to build technology platforms and develop novel pharmaceuticals based on the Institute's research programs.
- **collaborations** with mathematicians and computational scientists to develop new programs in bioinformatics and biological information theory which will have an impact on future design of computers and information systems.
- **joint ventures** with the CSIRO and Queensland Department of Primary Industries to transfer IMB's technologies and utilise its facilities for the development of products for plant and livestock industries.
- **exchange programs** with national and international educational institutions to build a diversity of skills across cultures and disciplines, and to enhance the IMB's ability to contribute to the developing world.

To explore how the IMB can build its relationship with your organisation or research group, please call the IMB today or alternatively, please complete and return this page.

- ( ) Please arrange for a representative of the Institute for Molecular Bioscience to call me to discuss potential collaborations.
- ( ) Please send me more information about supporting the work of the Institute.
- ( ) Please send me the Institute's Scientific Annual Report and newsletter.

Name:.....

Address:.....

..... Postcode:.....

Ph:..... Fax:.....

Email address:.....

My area of interest:.....

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