



**IMB**

# Annual Report 2012





## SHARE IN OUR DISCOVERIES

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This report is an accurate record of IMB's achievements from 1 January - 31 December 2012 and was published by IMB's Advancement team in May 2013. For any enquiries regarding this publication, please email [advancement@imb.uq.edu.au](mailto:advancement@imb.uq.edu.au).

## COVER ARTWORK

The artwork featured on the front cover of this report is entitled *Garden of Rebirth* (mixed media 91cm x 122cm) by IMB artist-in-residence Joannah Underhill. This artwork was created as part of Ms Underhill's residency collection entitled *Envisaging the Invisible*.

You can read more about Ms Underhill's residency and view her full collection at [www.jounderhill.com](http://www.jounderhill.com).

You can buy official prints from the collection, which are signed by the artist, at [www.imb.uq.edu.au](http://www.imb.uq.edu.au), with all proceeds supporting IMB's vital research.



## THANKS TO OUR MAJOR SUPPORTERS IN 2012



**welcome**trust



**The Simon Axelsen  
Memorial Fund**

**Dr Rosamond Siemon**

**JAMES S.  
MCDONNELL  
FOUNDATION**



# ANNUAL REPORT 2012

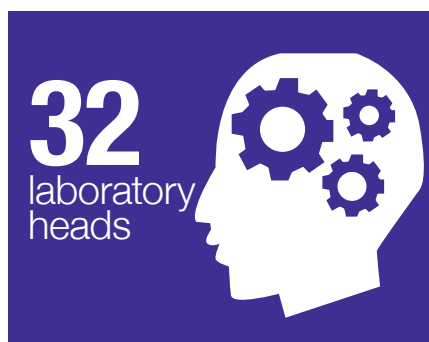
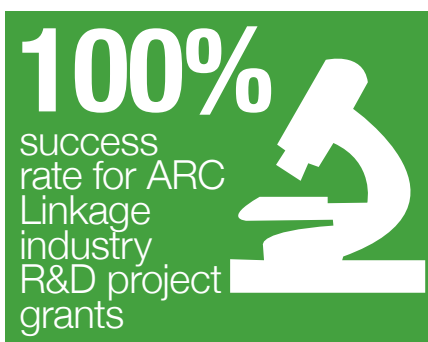
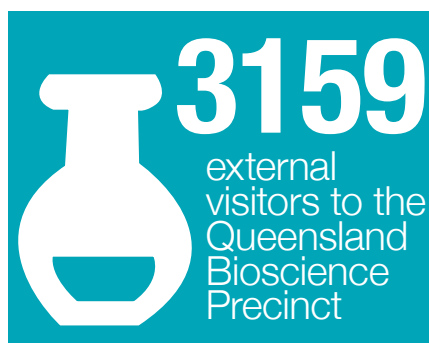
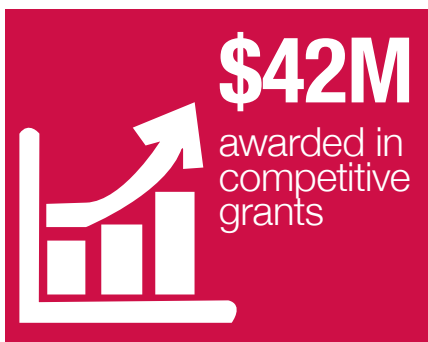
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**IMB is committed to improving quality of life for all by pursuing discoveries through fundamental research, inventing biotechnologies, and advancing cures for disease.**

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During the past 12 months, IMB has made great progress in its efforts to advance scientific knowledge through pioneering research, transferring discoveries into commercial outcomes, and training the next generation of research scientists to continue the Institute's vital work.

# 2012 SNAPSHOT





**\$5**

delivered to the community for every \$1 invested

**337**



refereed journal articles published, with 30 achieving an impact factor >10



**32**

new discoveries lodged and 27 patents managed



**498**

researchers, support staff and students



**30**

PhD and masters students graduated



**196**

undergraduate UQ lectures delivered

## About IMB

The University of Queensland's Institute for Molecular Bioscience is a leading global research institute. IMB was established in 2000 as UQ's flagship research institute and is the cornerstone of one of the largest bioscience research precincts in Australia.

Every day, 500 scientists, support staff and postgraduate students from more than 40 countries are working to improve quality of life for all.

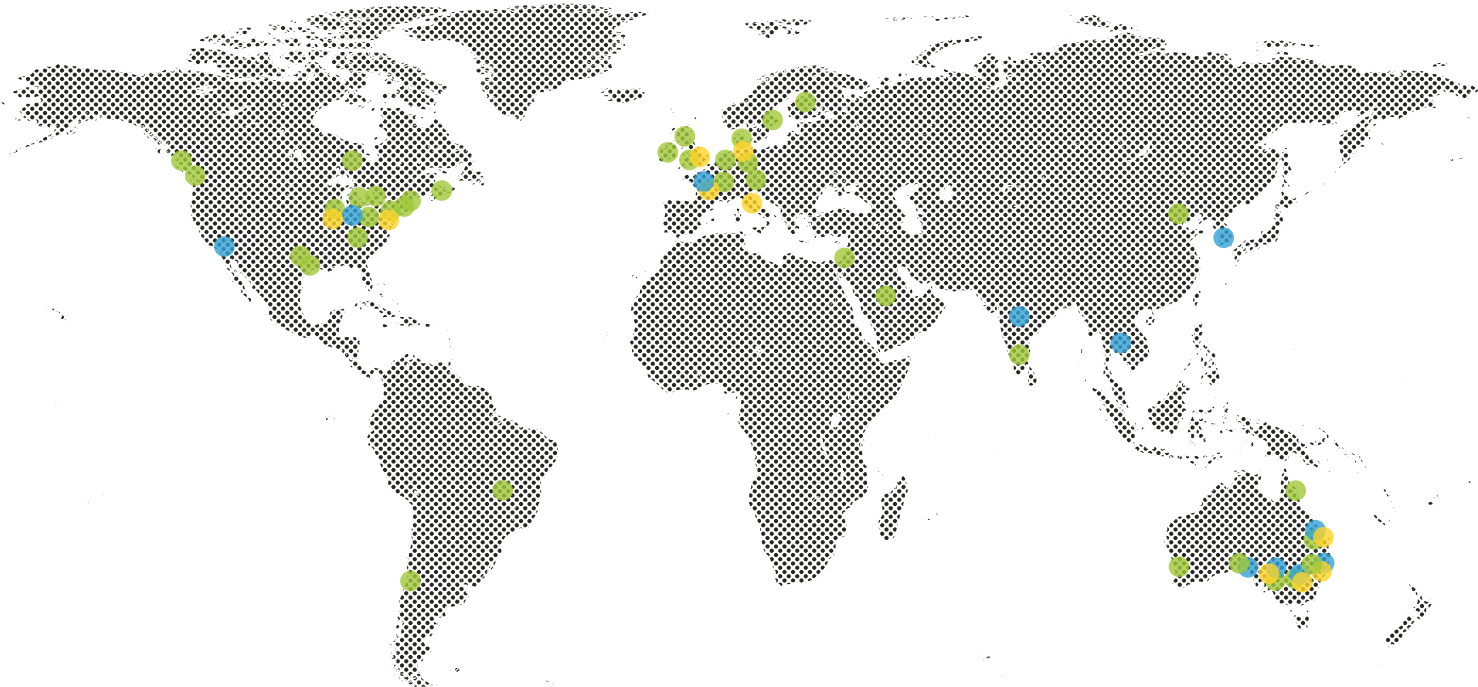
IMB's multidisciplinary research programs focus on advancing personalised medicine, drug discovery and biotechnology. By investigating the basis of growth and development at the genetic, molecular, cellular and organ level, our researchers aim to better understand the development processes and pathways involved in human and animal health and disease.

They also work to translate these findings into diagnostics, technologies and therapeutics to more effectively prevent, detect and treat disease, and deliver a sustainable future for Australia through initiatives such as clean energy and environmentally friendly agricultural insecticides.

IMB's research outcomes are actively protected and commercialised by UniQuest, UQ's own and one of Australia's leading technology transfer companies.

**IMB is a globally recognised research institute with a strong network of collaborators and alumni around the world. IMB's scientific impact continues to grow, helping to solve some of the greatest challenges facing our community.**

# 2012 GLOBAL COLLABORATIONS



Major collaborators



Sources of competitive funding



Alumni destinations

## Major 2012 collaborators

### Asia

**Academic:** Beijing Genomics Institute, Centre for Cellular and Molecular Platforms (Bangalore), Institute of Microbiology Chinese Academy of Sciences (Beijing), King Abdullah University of Science and Technology (Saudi Arabia), Kunming Institute of Zoology Chinese Academy of Sciences (Beijing), Weizmann Institute (Israel)

**Industry:** Advanta India

### Australia

**Academic:** Australian National University (Canberra), European Molecular Biology Laboratory (EMBL) Australia (Melbourne), Garvan Institute (Sydney), La Trobe University (Melbourne), Macquarie University (North Ryde), Mater Medical Research Institute (Brisbane), Monash University (Melbourne), Murdoch Childrens Research Institute (Melbourne), Peter MacCallum Cancer Centre (Melbourne), Prince Henry's Institute (Melbourne), Princess Alexandra Hospital (Brisbane), Queensland Institute of Medical Research, Queensland University of Technology, RMIT University (Melbourne), The University of Queensland, The University of Western Australia, University of Adelaide, University of Melbourne, University of New South Wales, University of Southern Queensland, University of Sydney, UQ Centre for Clinical Research (Brisbane), UQ Diamantina Institute (Brisbane), UQ Queensland Brain Institute (Brisbane), UQ School of Chemistry and Molecular Biosciences (Brisbane), UQ Veterinary Science (Gatton), Western Australian Institute for Medical Research

**Industry:** Alchemia (Brisbane), Alere Australia (Brisbane), Amgrow (Sydney), Antisense Therapeutics (Toorak), Barmac Pty Ltd (Ipswich), BioAustralis (Smithfield), Bioplatforms Australia (North Ryde), Bioproton (Brisbane), Biota (Notting Hill), Cement Australia (Brisbane), Grains Research and Development Corporation (Canberra), Growth Agriculture (Wee Waa), Hexima (Melbourne), Innovate Ag (Wee Waa), IOR Energy (Brisbane), Johnson & Johnson (Sydney), KBR (Brisbane), Kintan Pty Ltd (Corowa), Microbial Screening Technologies (Sydney), North Queensland and Pacific Biodiesel (Cairns), Pacific Seeds (Palm Cove), Phylogica (Perth), Protagonist Pty Ltd (Brisbane), SYNthesis med chem (Melbourne), Virgin Australia (Brisbane)

**Not-for-profit:** Australian Red Cross Blood Service (Brisbane), Cancer Council Queensland (Brisbane), Great Barrier Reef Foundation (Brisbane), Joannah Underhill – IMB artist-in-residence (Brisbane), Kidney Health Australia (Melbourne), National Breast Cancer Foundation (Sydney), The Kids' Cancer Project (Sydney)

### Europe

**Academic:** Bielefeld University (Germany), Cambridge Institute for Medical Research University of Cambridge, Curie Institute (Paris), Defence Science and Technology Laboratory (Wiltshire), German Cancer Research Centre (Heidelberg), Great Ormond Street Hospital (London), Guy's Hospital (London), Imperial College London, Institute of Child Health (London), Karlsruhe Institute of Technology (Münich), Karolinska Institute (Sweden), King's College London, Ludwig-Maximilian University (Münich), Max Planck Institute for Experimental Medicine (Göttingen), Max Planck Institute for Molecular Physiology (Dortmund), Medical University of Graz (Austria), Trinity College (Dublin), University College London, University of Copenhagen, University of Edinburgh, University of Essex, University of Lausanne, University of Leipzig, University of Münster, University of Oxford, University of Stockholm, VU University (Amsterdam), Wellcome Trust Sanger Institute (Cambridgeshire)

**Industry:** Adenium Biotech (Denmark), Boehringer Ingelheim (Germany), Bruker BioSpin (Germany), Clondiag (Germany), GlaxoSmithKline (London), Neste Oil (Finland), Siemens (Germany), Zealand Pharma (Denmark)

**Not-for-profit:** Association for International Cancer Research (Scotland), Wellcome Trust (London)

### North America

**Academic:** Baylor College of Medicine (Houston), Children's National Medical Centre (Washington), Dalhousie University (Canada), Harvard University (Massachusetts), Howard Hughes Medical Institute (Maryland), Institute for Metabolic Disease Baylor College of Medicine (Texas), Johns Hopkins University (Baltimore), Oak Ridge National Laboratory (Tennessee), Ontario Institute for Cancer Research (Canada), Rockefeller University (New York), Rutgers University (New Jersey), Stanford University (California), State University of New York (Buffalo), The Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases (Texas), The Hospital for Sick Children (Toronto), University of California Davis, University of California San Francisco, University of California Santa Cruz, University of Chicago, University of Pittsburgh, University of Southern California (San Diego), University of Tennessee (Knoxville), University of Texas at Austin, University of Texas Health Science Centre (Houston), University of Texas Medical School (Houston), University of Washington, Wayne State University (Michigan), Yale University (Connecticut)

**Industry:** Alere (San Diego), Amyris (California), BioSite Incorporated (San Diego), Boeing (Illinois), Courtagen Life Sciences, Inc. (Massachusetts), GenoLogics (Canada), Illumina (California), Ironwood Pharmaceuticals (Massachusetts), Isis Pharmaceuticals (California), Johnson & Johnson Pharmaceutical Research and Development (San Diego), Pfizer (Groton and Boston), Progenra (Philadelphia), Protagonist Therapeutics Inc. (California), Versatis Inc. (California)

### South America

**Academic:** Universidad Católica de Brasilia (Brazil), Universidad de Chile (Santiago)

## Sources of competitive funding

**National sources of competitive grant funding in 2012 included:** Australian Cancer Research Foundation, Australian Stem Cell Centre, Cancer Council Queensland, Diabetes Australia Research Trust, Education Investment Fund, G08 Australia-Germany Joint Research Cooperation, Grain Research and Development Cooperation, Heart Foundation, National Breast Cancer Foundation, National Health and Medical Research Council, Pharmaceutical Society of Australia, Prostate Cancer Foundation of Australia, Queensland Government, Wesley Research Institute

**International sources of competitive grant funding in 2012 included:** Cariplo Foundation, Centro San Raffaele del Monte Tabor Foundation, Human Frontier Science Program, International Association for the Study of Pain, James S. McDonnell Foundation, Wellcome Trust, US National Institutes of Health

## Alumni destinations

The strong talent and determination of IMB's 2012 alumni granted many the opportunity to secure positions within their laboratories of choice. At IMB, we were proud to offer positions to many of our graduating students and retain their knowledge and expertise as they commenced their careers. Our students also secured positions at a range of leading institutes and commercial organisations, including the University of California, Khon Kaen University (Thailand), Cook Medical Australia, Bruker Daltonics, and the Office of the Chief Scientist of Australia.

For a full list of alumni destinations, please see the PhD conferrals table on page 37.



# PRESIDENT AND VICE-CHANCELLOR'S MESSAGE

Since commencing as Vice-Chancellor in October 2012, I have been very impressed with the level of expertise at UQ's research institutes.

It is the dedication and determination of our researchers that has helped position UQ as one of the top four universities in Australia and in the top 100 universities in the world in the four leading independent university ranking tables.

As the University's first research institute, the Institute for Molecular Bioscience (IMB) is integral to UQ's ongoing success. For more than a decade, IMB has advanced its position as one of Australia's leading multidisciplinary research institutes. The achievements highlighted in this report reaffirm the global quality and relevance of the Institute's collaborative research.

The culture of excellence at IMB is ever present, with many of its researchers leading the way in discovering innovative outcomes to some of the greatest challenges facing society today. The National Health and Medical Research Council has recognised IMB's research, naming Professor Richard Lewis' cone snail research and IMB Director Professor Brandon Wainwright's skin cancer and brain tumour research in its *Ten of the Best Research Projects* in 2011 and 2012, respectively.

Further, in 2012, IMB made a significant contribution to UQ's research credentials, achieving well above world standard in the Excellence in Research for Australia exercise. Areas the Institute excelled in were biological sciences, chemical sciences, technology, and medical and health sciences. This was an outstanding result for the Institute and assisted UQ in achieving more specialised fields of research well above world standard than any other university in Australia.

As an internationally respected research university, UQ has many advantages. It is the combination of these advantages – access to the latest technology, modern infrastructure and multidisciplinary teams – and the dedication and talent of its people that gives IMB its continued strength and energy.

These world-class advantages assisted IMB in securing a recent record of 42 new postgraduate research students in 2012 and encouraged many of the Institute's most promising and talented graduating students to continue their novel research right here at UQ. This year also saw the introduction of the University's new UQ Career Advantage PhD program, which gives PhD students more opportunities to engage with industry and alumni networks to accelerate their careers.

Our achievements as a university have played an important role in helping Queensland realise its potential during the past century. Moreover, we know there will be more work for the University to do as Queensland grows. As a learned community, we will continue to move forward in a collective and determined way to make UQ stronger and better than ever – better performing, better connected and better supported.

Engaging with industry has been an area of renewed focus across the University in 2012. UQ's commercialisation company UniQuest benchmarks in the top 10 per cent worldwide for university-based technology transfer, specialising in connecting researchers with leading industry partners. The results across the board have been impressive – IMB has entered into six new research agreements with companies including KBR and Adenium Biotech, and managed an intellectual property portfolio of 27 patents ranging from drug discovery tools to therapeutics and agriculture.

It has been due to the hard work of many that these successes have been possible and I sincerely thank everyone at IMB for their ongoing contribution. It is my ambition – an ambition I share with the UQ community – to make The University of Queensland Australia's most globally connected university. I congratulate and thank Brandon and his team for working towards this goal in 2012 and look forward to moving ever closer to this ambition in 2013.

**Professor Peter Høj**

President and Vice-Chancellor

The University of Queensland





# DIRECTOR'S MESSAGE

It has been a busy and rewarding year for UQ's IMB as we advanced our mission to improve quality of life for all through our research in personalised medicine, drug discovery and biotechnology.

Our commitment to research excellence was recognised early and often in 2012 through our competitive grant funding successes. IMB achieved 50 per cent and 53 per cent success rates in the Australian Research Council and National Health and Medical Research Council grant rounds respectively, which were more than double the national average success rates of 22 per cent (ARC) and 22.9 per cent (NHMRC). We also saw funding commence for 34 competitively awarded grants and 14 fellowships.

In January, we transferred our commercial operations to UniQuest, the largest of UQ's commercialisation companies, to expand our industry engagement and manage our intellectual property pipeline. Since this time, the UniQuest team has proven to be a strong advocate for IMB, working alongside our researchers to bring our scientific endeavours to commercial reality.

During the past 12 months, IMB has partnered with Johnson & Johnson's Corporate Office of Science and Technology and its Janssen affiliates to develop components of spider venom as treatments for pain relief; collaborated with US biotech company Viral Genetics Inc. on an innovative biofuel production system; and worked alongside the world's largest pharmaceutical company, Pfizer, to develop improved treatments for type 2 diabetes, obesity and cardiovascular disease.

This year we also turned our minds to the challenges confronting our communities and worked to help reduce their impact through our discoveries. We unmasked the genetic mutations that lead to pancreatic cancer; we pursued promising new treatments to improve the relief of chronic pain; we made a difference in the fight against superbugs; and we discovered how microalgae can develop sustainable solar-driven fuel production systems.

Along the way, we continued to guide and support the next generation of scientists, graduating a recent record of 30 PhD and masters students, including UQ's 10,000th PhD conferral since the University's first PhD students were conferred on 30 April 1953.

A highlight for the Institute was Dr Nick Hamilton's pioneering collaboration with young Brisbane artist and cancer survivor, Joannah Underhill. As IMB's official artist-in-residence, Ms Underhill worked with Dr Hamilton, a world leader in scientific visualisation, and John Griffin, a microscopy expert at the Australian Cancer Research Foundation Cancer Biology Imaging Facility located at IMB, to produce images of diseased and healthy cells, including some of her own cells, and gain a unique visual insight into how our researchers study cancer. Ms Underhill used these images to produce a series of about 20 original artworks that explored the nexus of art and science. We launched this collection with a public reception at Brisbane's Galley of Modern Art in August, and it has been a pleasure watching the artworks capture the imagination of the community ever since.

We continued efforts to build a sustainable future for IMB, commencing work on a renewed strategic plan to guide us through the coming years. The challenge ahead will be to finalise this plan and put it to work early in 2013 for the benefit of the Institute.

This report is a record of our collective achievements in 2012 and I commend and thank each of our staff, students and supporters for their hard work and dedication. The scientific impact of our research goes far beyond our laboratory walls, and together, we are making a lasting difference we can all be proud of now and into the future.

**Professor Brandon Wainwright**

Director

Institute for Molecular Bioscience



# EXECUTIVE COMMITTEE

## 1. Professor Mark Ragan

**BA (Hons) (Chicago), PhD (Dalhousie)**  
**Head, Genomics and Computational Biology Division**

Professor Ragan was appointed as the founding Head of IMB's Genomics and Computational Biology Division in 2000. In this role, he leads a team of five laboratory heads and their respective research teams, as well as managing his own laboratory.

Professor Ragan completed his undergraduate studies in biochemistry at the University of Chicago and postgraduate studies in biology at Dalhousie University in Canada. Before joining IMB, Professor Ragan worked for more than 20 years as a research scientist for National Research Council Canada, and for six years as a Fellow of the Canadian Institute for Advanced Research's Program in Evolutionary Biology.

Professor Ragan is the Director of the Australian Research Council Centre of Excellence in Bioinformatics and a Co-Founder of QFAB Bioinformatics.

## 2. Professor David Fairlie

**BSc (Hons) (Adelaide), PhD (NSW)**  
**Head, Chemistry and Structural Biology Division**

Professor Fairlie was appointed Head of IMB's Chemistry and Structural Biology Division in 2009. He is one of a team of ten IMB laboratory heads and four affiliates working on chemistry, biochemistry and pharmacology.

Professor Fairlie undertook undergraduate studies at The University of Adelaide, postgraduate studies at Australian National University and The University of New South Wales, and postdoctoral studies at Stanford University and The University of Toronto. He has held ARC Federation and Professorial fellowships, chief scientific officer and scientific director company roles, and has collaborated with some of the world's largest biopharmaceutical companies.

Professor Fairlie is currently a National Health and Medical Research Council (NHMRC) Senior Principal Research Fellow.

## 3. Professor Jennifer L. Stow

**BSc (Hons) PhD (Monash)**  
**Deputy Director (Research)**

Professor Stow was appointed IMB's Deputy Director (Research) in 2008, previously holding the position Head of IMB's Molecular Cell Biology Division. As Deputy Director (Research), Professor Stow is responsible for managing the scientific and competitive funding performance of the Institute, as well as IMB's postgraduate program.

Professor Stow completed her undergraduate and postgraduate studies at Monash University in Melbourne, after which she undertook postdoctoral training at Yale University's School of Medicine as a Fogarty International Fellow. She was soon appointed as Assistant Professor in the Renal Unit at Massachusetts General Hospital, where she established an independent research group in cell biology. She returned to Australia in 1994 as a Wellcome Trust Senior International Fellow to join UQ's Centre for Molecular and Cellular Biology (now IMB).

Professor Stow leads her own IMB laboratory and is a current National Health and Medical Research Council (NHMRC) Principal Research Fellow.

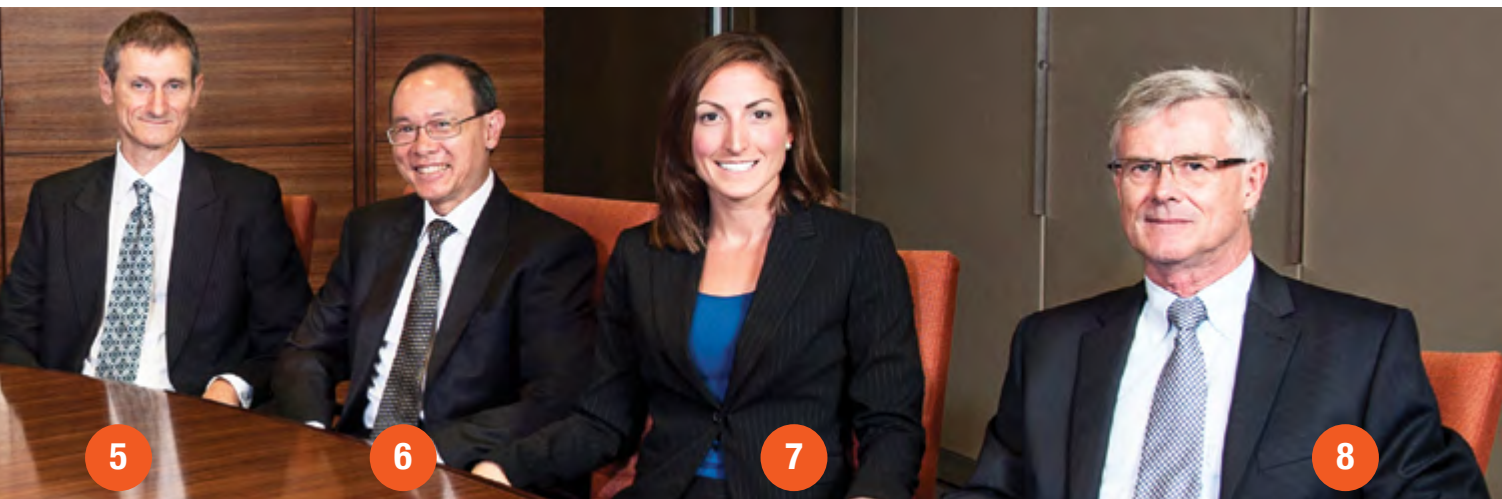
## 4. Professor Brandon Wainwright

**BSc (Hons) PhD (Adelaide)**  
**Director**

Professor Wainwright was appointed Director of IMB in 2006, previously holding the position of IMB's Deputy Director (Research) from 2002. As Director, Professor Wainwright is responsible for advancing the Institute's research initiatives, strengthening the Institute's global connections and leading IMB's scientists in their work to improve quality of life for all.

Professor Wainwright completed his undergraduate and postgraduate studies at The University of Adelaide, after which he secured a postdoctoral fellowship at St Mary's Hospital at Imperial College London (ICL). During his six years at ICL he worked on the first Human Genome Project and also became a Medical Research Council Senior Research Fellow. He returned to Australia in 1990 to join UQ's Centre for Molecular and Cellular Biology (now IMB).

Professor Wainwright leads his own IMB laboratory and serves on the boards of the Mater Medical Research Institute, The Australian Genome Research Facility, and a number of national and international scientific review committees.



**IMB's leadership team moves the Institute forward by ensuring all strategic initiatives are supported with the energy, knowledge and resources needed to make them a success.**

## 5. Professor Peter Koopman

**BA BSc (Hons) PhD (Melbourne)  
Head, Molecular Genetics and Development Division**

Professor Koopman was appointed Head of IMB's Molecular Genetics and Development Division in 2006. In this role, he leads a team of eight laboratory heads and their research teams, as well as managing his own laboratory.

Professor Koopman received a Bachelor of Arts (Fine Arts and Dutch), a Bachelor of Science with Honours (Genetics), and a PhD (Paediatrics) at The University of Melbourne. After this time, he spent six years as a postdoctoral researcher and staff scientist with the Medical Research Council in London, where he was part of the team that discovered the Y-chromosome sex-determining gene SRY.

He joined UQ's Centre for Molecular and Cellular Biology (now IMB) in 1992.

Professor Koopman has published more than 230 papers, is a member of five scientific journal editorial boards, and is a Fellow and Council Member of the Australian Academy of Science.

## 6. Professor Alpha Yap

**MBBS PhD (Queensland), FRACP  
Head, Molecular Cell Biology Division**

Professor Yap was appointed Head of IMB's Molecular Cell Biology Division in 2008. In this role, he leads a team of six laboratory heads and their respective research teams, as well as managing his own laboratory.

Professor Yap trained as a physician and endocrinologist at The University of Queensland and the Royal Brisbane Hospital, after which he completed a PhD in epithelial physiology at UQ.

Before joining IMB, Professor Yap was a CJ Martin Fellow at Memorial Sloan-Kettering Cancer Center (New York) and a Wellcome Trust International Senior Medical Research Fellow (UQ).

Professor Yap is a current National Health and Medical Research Council (NHMRC) Principal Research Fellow.

## 7. Ms Amanda Whelan

**BSc (Hons) MPA (Florida State)  
Deputy Director (Advancement)**

Amanda Whelan was appointed IMB's Deputy Director (Advancement) in 2011 and is responsible for managing philanthropic development, government relations and communications.

Prior to joining IMB, Amanda was a senior advisor and advocate in the US for the Florida Association of Counties and Florida-based law firm Hopping Green & Sams.

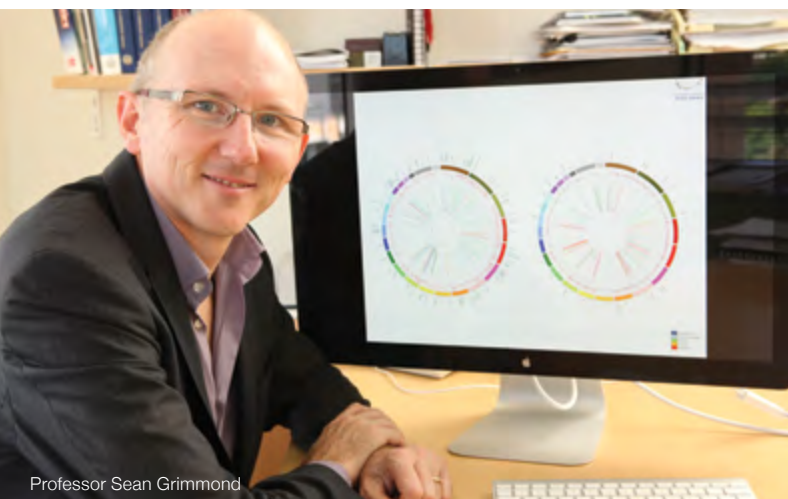
## 8. Dr Ian Taylor

**BSc (Hons) (Strathclyde), PhD (London), MBA (Queensland)  
Deputy Director (Operations)**

Dr Taylor was appointed IMB's founding Deputy Director (Operations) in 1998, working to establish the Institute from the ground up. In this role, he is responsible for the administration and operations of the Institute, including management of Institute finances, infrastructure, safety, and support services and staff.

Dr Taylor completed his undergraduate studies in biochemistry and postgraduate studies in radiation biology in the UK, working as a research officer for several years. In the 1980s, he relocated to Australia to work as a Research Fellow at the Ludwig Institute for Cancer Research and a lecturer at the University of Sydney, before becoming the Queensland Institute for Medical Research's first Scientific Manager in Brisbane.

Dr Taylor has more than 10 years of experience in research and 30 years of experience in scientific management and laboratory design and construction.



Professor Sean Grimmond



Professor Matt Cooper

# RESEARCH PRIORITIES

## Personalised medicine

Personalised medicine allows patients to be diagnosed and treated on an individual level, generally using their genome. Since the human genome was first sequenced around a decade ago, the speed of sequencing has increased at a marked rate while the cost has dropped dramatically. These two factors combined ensure that personalised medicine is about to make an enormous impact on human society comparable to that of antibiotics or X-rays, completely changing how medicine is practised.

Genomics will improve the accuracy of diagnosis, reduce the cost of genetic testing and improve public health by targeting lifestyle advice to those predisposed to certain diseases as determined by their genome sequence.

IMB's focus on personalised medicine is built on research excellence, technical capacity and critical mass in genome sequencing, bioinformatic analysis, computational systems biology and laboratory validation. This combination is unique in Australia and positions IMB as a world leader in this emerging field.

In 2012, IMB research contributed to some significant advances in personalised medicine.

Professor Sean Grimmond was senior author on a *Nature* paper that sought to identify the gene mutations that drive pancreatic cancer. He and his collaborators examined the genomes of 100 pancreatic tumours and discovered over 2000 mutated genes. Each tumour differed greatly in the genes that were mutated, with some being common to most tumours, while others were only found in one or two per cent of cases. This discovery highlighted that patients who seemingly have the same disease, in this case pancreatic cancer, may need very different treatments.

Further success was achieved by Dr Ryan Taft, who used genome sequencing to investigate the case of a toddler with a rare paediatric brain disorder. Dr Taft sequenced the genome of three-year-old Massimo Damiani, who was diagnosed with Leukodystrophy, and compared it to his parents' genomes to find the genetic differences and identify genes that may be responsible. Dr Taft successfully discovered a candidate gene and is investigating further to determine if it is responsible for Massimo's illness. He hopes to repeat this process for the benefit of other children affected by rare diseases.

## Drug discovery

Compounds with the potential to prevent or treat disease are present everywhere, including in bacteria, plants and even the venom of spiders. But in order for this potential to be harnessed, an institution requires the necessary level of expertise and equipment.

IMB houses some of the most advanced equipment in Australia for drug discovery, which supports the world-class work of its researchers. Companies such as Pfizer, the world's largest research-based pharmaceutical company, have chosen to collaborate with IMB because of its scientific expertise in modern drug discovery.

IMB research has also led to spin-out companies including Protagonist, established by Associate Professor Mark Smythe. In 2012, Protagonist expanded its collaboration with Massachusetts-based Ironwood Pharmaceuticals, with the latter funding Protagonist scientists based at IMB in exchange for access to their proprietary technology platform to design, discover and optimise drugs.

Professor David Fairlie is head of a drug design laboratory with experts in both chemistry and biology. His lab's interdisciplinary focus enabled them to advance work into the development of drugs to treat inflammatory bowel disease, other inflammatory conditions such as arthritis, and obesity. Professor Fairlie was also involved in a 2012 *Nature* paper that told of the discovery that Vitamin B metabolites produced by *Salmonella* bacteria can activate the immune system.

Professor Matt Cooper and Professor Jenny Martin are both engaged in discovering new drugs to combat superbugs, which are bacteria that have become resistant to multiple antibiotics. If these bacteria become widespread, it could herald a return to a pre-antibiotic era when more than half of deaths were due to bacterial infection, making procedures such as surgery very risky.

Professor Cooper is developing drugs to treat a range of resistant bacteria. In 2012, he received funding from the National Health and Medical Research Council for several projects, including one to develop treatments for resistant strains of tuberculosis.

Professor Martin's approach attempts to reduce the chance of bacteria developing resistance to a drug by targeting the protein machinery in bacteria that causes disease, rather than actually killing the bacteria. In 2012, Professor Martin and her laboratory were developing a library of the proteins involved in this machinery to form a resource for structure-based drug design.



Professor Glenn King. Image credit: Lyndon Mechielsen Source: The Australian

## IMB's multidisciplinary research programs focus on advancing personalised medicine, drug discovery and biotechnology to improve the health of our community.

### Biotechnology

IMB differs from most, if not all, Australian biomedical institutes in that its investigative focus extends beyond disease. The Institute's third research stream, biotechnology, reflects this. While biotechnology does encompass medical applications, it also includes agricultural and industrial uses. Biotechnology refers to any technology that uses living organisms, or some component thereof. This technology can be as simple as the use of yeast to make bread rise or as advanced as the Human Genome Project.

Biotechnology is a vital area of research that will provide the tools needed to 'heal, fuel and feed the world' as the global population rises to an expected level of more than nine billion people by 2050. IMB researchers are working on projects with the potential to improve health and agriculture and provide alternative fuel sources.

Professor Glenn King is developing eco-friendly insecticides from spider venom. Spiders have successfully been killing insects for more than 400 million years and have evolved a complex chemical cocktail of toxins. Professor King and his lab are investigating which of these toxins would be suitable for use in a commercial pesticide, discarding any that are harmful to vertebrates and could pose a threat to humans, pets or livestock. This research would benefit agriculture by eliminating insect pests that prey on crops, but it also has medical applications. In 2012, Professor King received an Australian Research Council grant to explore methods of taking natural insecticidal compounds from spider venom and delivering them to insects using parasitic fungi to stop the spread of human disease.

Another researcher leading IMB's efforts in the area is Professor Ben Hankamer, who is harnessing biotechnology to provide clean fuels. Algae naturally use solar energy to produce biofuels such as hydrogen, so Professor Hankamer and his lab are optimising this process to create a fuel production system that is economically viable. They have spent years studying different strains of algae to determine which are the most efficient at biofuel production under different conditions. The team then engineers these strains to ensure they are even more productive. Professor Hankamer, with the support of industry and academic partners, is taking this work from the laboratory to larger-scale production with the launch of a pilot plant. This plant will measure the effectiveness of various algae biofuels production systems and potentially pave the way for greener fuels in the vehicles of tomorrow.



Dr Ryan Taft's young Leukodystrophy patient, Massimo Damiani



Professor Jenny Martin using the UQROCX Crystallisation Facility at IMB



Professor Ben Hankamer's algae ponds in action



# RESEARCH SUPPORT FACILITIES

## 1. ACRF Cancer Biology Imaging Facility and ACRF Dynamic Imaging Facility

The Australian Cancer Research Foundation's (ACRF) Cancer Biology Imaging Facility is one of the largest and most comprehensively equipped facilities in Australia for both the imaging and screening of chemical and biological libraries. It houses image data analysis workstations and 23 high-performance microscopes, which have been tailored to meet the specific needs of IMB researchers.

Each year, more than 230 unique users throughout IMB and UQ use the Facility to conduct advanced live imaging of cancer cells to help unravel the molecular reasons why healthy cells turn into cancerous cells and spread through the body.

Data generated from Facility equipment in 2012 featured in 11 publications, highlighting a range of discoveries, including investigating the coordination of subcellular activity and its role in determining the biological impact of Rho; and exploring the essential role of 25-hydroxycholesterol (25HC), an oxysterol with emerging roles in immunity, in regulating metabolism and immunity.

The ACRF Cancer Biology Imaging Facility was founded in 2010 with a \$2.5 million ACRF grant and was designed to complement and extend the work of the existing ACRF Dynamic Imaging Facility, which was established in 2005.

## 2. LISA Facility

IMB's Life Science Automation (LISA) Facility uses its genome-wide RNA interference libraries and robotic equipment to assist both internal and external research clients in performing cell-based RNA interference screens in human and murine tissue cultures.

Each year, more than 70 users throughout Australia access the Facility's services. Using key technologies, LISA provides screening services to assist researchers working across the life sciences to develop and transport assays from the bench to automation.

Data generated from Facility equipment in 2012 featured in five publications, and five new research grants, which detailed their plans to use LISA, commenced funding.

LISA is funded by IMB and the Australian Phenomics Network.

## 3. High-Throughput Genomics Facility

IMB's Queensland Centre for Medical Genomics (QCMG) recently established a high-throughput DNA sequencing and microarray facility that is capable of delivering genomic data at unprecedented speeds and scales. More than 30 scientists and bioinformaticians working within the QCMG use the technology daily to conduct pioneering research and meet the objectives and milestones for the International Cancer Genome Consortium (ICGC) project.

Some of the internal sample processing capabilities of the Facility include: robotic sample preparation; an integrated Laboratory Information Management System (LIMS); Illumina HiSEQ, MiSEQ and iScan instrumentation; dedicated high-performance computing and data archiving; and extensive automation of genome sequencing informatics.

Our scientists use the Facility to produce high-quality genomic data and analyses to primarily investigate genome variation, which is used to deliver novel applications to improve human health and patient outcomes.

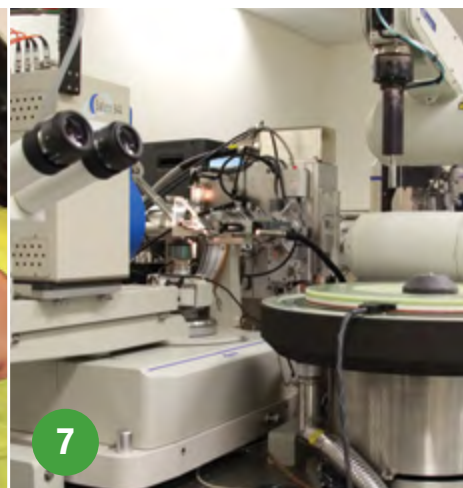
The High-Throughput Genomics Facility is funded by IMB and operates on a cost recovery basis.

## 4. Mass Spectrometry Facility

IMB's Mass Spectrometry Facility (MSF) is home to a suite of state-of-the-art mass spectrometry, high-performance liquid chromatography and robotic instrumentation that have been refined and optimised to investigate biological systems in a high-throughput qualitative and quantitative manner. The 11 available systems within the Facility provide researchers with the resources to investigate a broad range of mass spectrometric applications, including molecular discovery, identification, characterisation and quantification. The latest addition to the Facility is the Triple TOF 5600 mass spectrometer. Its high resolution and fast acquisition in both ms and ms/ms characteristics make it an ideal system for proteomic and small molecule applications.

In 2012, the Facility provided expert advice and research and training support for 120 unique users from across Queensland working on a diverse range of projects. Through the use of this facility, our scientists hope to gain new insights into protein interactions and structures; amino acid sequence; post-translational modifications; compound stability; and bioavailability of potential therapeutics in a range of biological systems.

Discoveries made in 2012 using the Facility included: novel protein interactions from proteomic analyses of whole cell lysates; potential protein biomarker discovery and quantification via targeted organelle proteomics; discovery and characterisation of potential therapeutic molecules from natural product extracts using de-novo peptide sequencing; and quantitative bioavailability characteristics of new



## IMB scientists have on-site access to a range of leading technologies and facilities allowing them to conduct faster, more comprehensive research.

molecules in the discovery and development of potential therapeutic molecules for a number of targeted diseases.

The Facility acknowledges funding from ARC LIEF Project LE110100186.

### 5. NMR Facility

IMB's Biomolecular NMR Facility makes the powerful technique of nuclear magnetic resonance (NMR) spectrometry accessible to our research and industry clients. The Facility comprises a 600 MHz spectrometer with a recent upgrade of a cryoprobe and a 500 MHz spectrometer equipped with a robotic sample changer. Access is also available to the extensive NMR infrastructure housed throughout IMB, most notably a 900 MHz spectrometer equipped with a cryoprobe and soon-to-be installed sample changer. The latter is an instrument of the Queensland NMR Network and is the most powerful state-of-the-art NMR spectrometer in Australia.

The available instrumentation is particularly useful for the determination of high-resolution structures of biological macromolecules such as proteins, as well as characterisation of protein/ligand interactions; determination of molecular size and oligomerisation state; investigation of dynamic properties; and metabolomic studies of various biofluids.

Key discoveries made in 2012 using the Facility include: using NMR analysis to show how synthetic micasin adopts a 'hallmark' cysteine stabilized  $\alpha$ -helical and  $\beta$ -sheet fold, representing a valuable approach to explore novel peptide antibiotics from a large resource of fungal genomes; and using NMR to help discover a new approach for the synthesis of lanthionine-like cyclic peptides and evaluating the chemical synthetic advantage of substituting thioethers by selenoethers.

The Facility is available on a user-pays system to researchers from a range of scientific disciplines both within IMB and across UQ. The Facility also holds several international collaborations, most recently with scientists from China, Brazil and Austria.

### 6. QFAB Bioinformatics

QFAB Bioinformatics provides bioinformatics services for life science researchers to analyse and manage large-scale datasets.

The QFAB team has completed 130 projects for more than 50 unique research groups from industry, universities, medical research institutes, and government departments. Their support ranges from the experimental design, data capture and mining through to genomics, proteomics and metabolomics analyses. They are also expert in cross-domain integration with clinical data.

QFAB's tools and platforms support a range of evolving technologies used by life scientists, including microarrays, mass spectrometry, genotyping, high-throughput genomics and pathology/clinical data.

The data can then be used for custom bioinformatics and biostatistics applications within academic research, healthcare, agriculture, environment, pharmaceutical research and development or biotechnologies.

QFAB combines two critical infrastructure platforms linking leading software packages and data repositories with a web service workflow engine and visualisation technology deployed in a scalable, high-performance computational environment. This allow for investigations across the biological continuum from systems and chemi-biology perspectives.

QFAB mediated analysis assisted with a range of discoveries in 2012, including demonstrating that Independent Principal Component Analysis (IPCA) offers a better visualisation of large biological data sets, and identifying the widespread divergence in human versus mouse model innate immune responses, which can be used to understand the limitations of the mouse as a model for immune-related diseases.

QFAB Bioinformatics was established in 2007 and is a successful collaboration between UQ, Queensland University of Technology, Griffith University and the Queensland Government's Department of Agriculture, Fisheries and Forestry.

### 7. UQROCX Crystallisation Facility

The UQ Remote Operation Crystallisation and X-ray Diffraction (UQ ROCX) Facility provides research training and support for protein structure determination. This support includes protein crystallisation condition screening, crystal diffraction screening, data collection, data processing, and structure determination. Nano-litre liquid handlers and automated imaging means that large numbers of crystallisation conditions can be investigating with little protein. The diffraction facility has Queensland's brightest research X-ray source and the only robotic sample storage and retrieval system, which allows for multiple data sets to be collected without user intervention.

In 2012, 59 unique users accessed the Facility for its high-throughput applications, namely crystallisation condition screening, especially for membrane proteins, and screening fragment libraries for drug leads. Diffraction data collected during the past 12 months assisted with the publication of ten protein structure papers.

Discoveries made in 2012 using the Facility included: new insights into the molecular basis of a number of features of the classical nuclear transport pathways specific to plants; promising new leads for osteoporosis therapeutics; and discovering how membrane protein APPL2 structures reveal unexpected domain motion that could have function implications and may be crucial for its role in the cell signalling process.

UQ ROCX is funded by the Australian Research Council and UQ.



Dr Reena Halai

## Division Head

Professor David Fairlie

## Laboratory Heads

Professor Paul Alewood, Professor Rob Capon, Professor Matt Cooper, Professor David Craik, Professor Ben Hankamer, Professor Glenn King, Professor Richard Lewis, Professor Jenny Martin and Associate Professor Mark Smythe

# RESEARCH HIGHLIGHTS

## CHEMISTRY AND STRUCTURAL BIOLOGY

### Division overview

IMB's Chemistry and Structural Biology Division conducts pure, strategic and applied research in chemistry, structural biology, biochemistry, pharmacology, virology and bacteriology.

IMB scientists discover, design and synthesise new compounds, investigate the molecular and structural basis of physiology and disease, and invent new treatments to improve health.

Researchers within the Division have expertise along the drug discovery pipeline and work together with academic and industry partners around the world to make important contributions towards understanding and treating a range of human diseases and conditions. These include: cancer; chronic pain; inflammatory, cardiovascular and neurodegenerative diseases; obesity and type 2 diabetes; and bacterial, viral and parasitic infections.

During 2012, the Division supported research in the following areas:

- › chemistry and human therapeutics
- › protein structure in drug and insecticide design
- › algal biofuels and protein structural biology
- › biodiscovery: learning from nature
- › drugs and diagnostics for superbugs, viruses and cancer
- › antibiotic discovery, protein structure and drug design
- › bioactive peptides and proteins in venomous fauna
- › pharmacology of marine toxins
- › bugs and drugs
- › combinatorial chemistry and molecular design.

The Division uses advanced technologies in NMR spectroscopy, protein crystallography, computational design, chemical synthesis, protein and cell activation and signalling, tissue analysis and rodent pharmacology.

Major funders of the Division include the NHMRC, ARC, Queensland Government, and industry partners.

### Featured publications

**Ciguatoxins activate specific cold pain pathways to elicit burning pain from cooling.**

**Vetter, Irina,** Touska, Filip, Hess, Andreas, Hinsbey, Rachel, Sattler, Simon, Lampert, Angelika, Sergejeva, Marina, Sharov, Anastasia, Collins, Lindon S., Eberhardt, Mirjam, Engel, Matthias, Cabot, Peter J., Wood, John N., Vlachova, Viktorie, Reeh, Peter W., **Lewis, Richard J.** and Zimmermann, Katharina (31 July 2012) *EMBO Journal*, 31 19: 3795-3808.

Ciguatoxins are sodium channel activator toxins that cause ciguatera, an unusual form of seafood poisoning characterised by intense stabbing and burning pain in response to mild cooling. This paper explored the mechanisms underlying ciguatoxin-induced pain and showed that intraplantar injection of P-CTX-1 elicits cold allodynia in mice by targeting specific unmyelinated and myelinated primary sensory neurons.

**Low-resolution solution structures of Munc18: Syntaxin protein complexes indicate an open binding mode driven by the Syntaxin N-peptide.**

**Christie, Michelle P., Whitten, Andrew E., King, Gordon J., Hu, Shu-Hong, Jarrott, Russell J., Chen, Kai-En, Duff, Anthony P., Callow, Philip, Collins, Brett M., James, David E. and Martin, Jennifer L.** (19 June 2012) *Proceedings of the National Academy of Sciences of the United States of America*, 109 25: 9816-9821.

When nerve cells communicate, vesicles from one neuron fuse with the presynaptic membrane releasing chemicals that signal to the next. Similarly, when insulin binds its receptor on adipocytes or muscle, glucose transporter-4 vesicles fuse with the cell membrane, allowing glucose to be imported. This paper described the innovative combination of complementary techniques used to derive the first structural information for activated SNARE Syntaxin protein required for membrane fusion in complex with its regulatory protein Munc18.



## CHEMISTRY AND HUMAN THERAPEUTICS

Professor David Fairlie

DIVISION HEAD

Our researchers work at the interface of chemistry and biology to better understand the molecular mechanisms of life, ageing, disease and death.

Our chemists study medicinal chemistry, organic synthesis, computer aided drug design; use nuclear magnetic resonance (NMR) spectroscopy to investigate the structure and dynamics of proteins; and learn how small molecules interact with other small molecules, proteins, RNA and DNA. They discover new chemical structures, reactions and mechanisms; enzyme inhibitors, agonists and antagonists; and molecules that mimic the structures and functions of bioactive protein surfaces.

Our biologists use these novel compounds to elucidate functions of human proteins and cells, and apply them to treat animal models of human diseases. They study mechanisms of protein and cell activation, biological processes, disease development and drug action.

Scientists within our laboratory combine their expertise across these fields to gain insights into human physiology and disease pathology, and develop skills in biochemistry, pharmacology, virology, immunology, oncology or neurobiology. They are working to discover new drugs and treatments for: viral and parasite infections, such as HIV, dengue fever and malaria; inflammatory diseases, such as arthritis and inflammatory bowel disease; metabolic and cardiovascular diseases resulting from obesity and type 2 diabetes; cancers; and neurological diseases, such as Alzheimer's and stroke.

### Next steps

Compounds showing efficacy and safety in rodent models of human diseases provide evidence of proof of concept, helping to validate the viability of drug targets or drug candidates. Our next steps are to evaluate these compounds and their analogues in preclinical and safety trials towards future clinical development.



## PROTEIN STRUCTURE IN DRUG AND INSECTICIDE DESIGN

Professor David Craik

Peptides and proteins play a vital role in almost every cellular process in living organisms. Our research discovers and determines the structural information of peptides and proteins to design drugs to more effectively treat human disease and develop natural protein-based insecticides to protect Australian food and fibre crops.

We use protein engineering to modify proteins by 'grafting' new biologically active peptide sequences onto them. We also stabilise proteins through cyclisation, a process where the head and tail ends of the protein chain are joined together to make a circular protein. Circular proteins are exceptionally stable and we have modelled our protein engineering studies on naturally occurring proteins known as cyclotides that we discovered in plants.

We undertake fieldwork in Australia and overseas for the collection of plant species so we can explore the diversity and evolution of the cyclotide family of plant proteins. We have chemically re-engineered cyclotides under development for the treatment of multiple sclerosis, cardiovascular disease, cancer and chronic pain.

We also study the structures of a range of toxins from cone snails, spiders and snakes and use this information to understand their mode of action against ion channels and other receptors involved in the pain pathway.

During the past 12 months we have discovered novel gene architectures for naturally occurring cyclic proteins; we discovered a large number of new cyclotides from plant families that are widely used in human nutrition; and we demonstrated that natural cyclotides can be adapted or reengineered for pharmaceutical applications.

### Next steps

Our next step are to develop improved methods of making peptide-based drugs by drawing on our expertise in chemistry, biology, biosynthesis, distribution, evolution and applications of cyclotides. This will include developing new ways of making them chemically in the laboratory, as well as exploring the possibility of using plants as factories for making peptide-based pharmaceuticals.



## ALGAL BIOFUELS AND PROTEIN STRUCTURAL BIOLOGY

Professor Ben Hankamer

One of the biggest global challenges facing our society today is the race to discover cleaner, more affordable and sustainable energy sources. Currently, most of the world's clean energy technologies are used to produce electricity. However, 80 per cent of the global energy demand is used in the form of fuel.

Our research is focused on developing single-celled green algae (microalgae) and advanced photobioreactor systems capable of capturing solar energy and converting it to chemical energy for clean fuel production. To do this, we collaborate with a range of experts across the fields of biology, engineering and economics, as we work together to develop high efficiency microalgae production systems.

There are many benefits expected from our research. Firstly, as microalgae technology can be located on non-arable land and use waste and saline water sources, it is increasingly recognised as a viable choice that can help to eliminate the 'food versus fuel' concerns of earlier biofuel systems.

Secondly, microalgae can produce a range of fuels, including: oil-based fuels, such as biodiesel and aviation fuels; methane; ethanol; and solar-driven hydrogen production from water.

The first step of all biofuel and bioproduct production is light capture. Given the importance of this step to process economics, a major focus of our team's work is on the structural biology of light capture, which guides the development of more efficient ways to capture solar energy and convert it on to larger scales.

### Next steps

Our next steps involve the targeted breeding of high efficiency strains of microalgae; the design and testing of advanced microalgae photobioreactors; and the analysis of pilot-scale production data of one of Australia's most sophisticated algal biofuels pilot plant, which IMB has developed in partnership with industry and the Queensland Government.

The pilot plant builds on our laboratory's research and the research of the Solar Biofuels Consortium ([www.solarbiofuels.org](http://www.solarbiofuels.org)), which was founded and is led by Professor Ben Hankamer. The pilot plant will help test the economic viability of using Queensland-grown algae to produce biofuels, advancing the state's position as a global leader and the Asia-Pacific hub for the biofuels industry.



## BIODISCOVERY: LEARNING FROM NATURE

Professor Rob Capon

Natural products are a hidden and almost limitless molecular resource that, with the right combination of expertise and technology, can be found in animals, plants and microbes.

Historically, knowledge of natural products fuelled a revolution in global science and commerce, leading to such well-known products as penicillin and aspirin and many more. Over time, modern societies have come to rely heavily on natural products, for example, as pharmaceuticals to treat infection, cancer, pain and other illness, and as agrochemicals to control disease and improve productivity in crops and livestock.

Our research explores Australian marine and microbial life to learn of and be inspired by their natural products, and to use this knowledge to inform and advance the development of valuable new products.

Together with a network of academic and industry collaborators, our scientists discover new natural products that can be used to treat an array of human diseases, including tuberculosis, malaria, Alzheimer's, cancer, pain and obesity, as well as intestinal parasites in commercial livestock, such as sheep, goats, and cows. We are also applying our skills to better understand the chemical ecology of the cane toad, to develop a means to chemically control this invasive pest that is poisoning many of Australia's native predator species, including quolls, lizards, snakes and crocodiles.

### Next steps

Our research is leading the discovery of natural products in Australia and is one of only a few marine and microbial biodiscovery laboratories in the world. Our next steps in infectious diseases will explore the multiple compounds that demonstrate promise, including a new class of anthelmintic we discovered that will soon undergo animal trials in sheep.

We will also explore a new class of kinase inhibitor with possible application in the treatment of Alzheimer's and related diseases. A promising inhibitor of P-glycoprotein has also proven capable of reversing multidrug resistance in human cancers and we will continue to investigate this further.

In pain, we have discovered lead compounds that are selective agonists of the mu opioid receptor (akin to morphine), and others that are isoform selective potentiators of the glycine gated chloride channel receptor, which both target different forms of pain.

Finally, in our cane toad research we will conduct extensive field trials for our chemical control traps.



## DRUGS AND DIAGNOSTICS FOR SUPERBUGS, VIRUSES AND CANCER

Professor Matt Cooper

We believe we can more effectively treat patients by improving the way we diagnose disease. Our research is aimed at discovering new ways of detecting and treating viral and bacterial infections and cancer. We are designing and developing novel antibiotics active against drug-resistant bacteria, known as superbugs. The alarming growth of superbugs, coupled with the paucity of companies working in this area, gives impetus to this research and our efforts communicating these issues in the media.

We also work on tuberculosis and dengue fever, diseases responsible for millions of deaths in the developing world. Our research is leading to new ways to diagnose infections caused by bacteria and viruses, and a deeper understanding of the molecular mechanisms that lead to the evolution and spread of drug resistance.

Many of our researchers have significant experience in both academia and industry, with past projects leading to products on the market today. We collaborate with government agencies and pharmaceutical, biotechnology and medical device companies in Australia, Asia, UK and the US. We have a strong translational focus and aim to deliver innovative solutions for unmet medical needs in the community.

During the past 12 months, other focuses of our research have been the role of gut biota, which are the bacteria that live in our digestive system, along with antibiotics, and inflammation in the development of diseases such as asthma, chronic obstructive pulmonary disease and cancer. This basic research helps us to develop new methods to diagnose and more effectively treat patients affected by these complex and deadly diseases.

### Next steps

Our next steps are to develop new antibiotics and methods to fight deadly superbugs, and then translate this research into better diagnostics and treatments for patients. We engage in public policy initiatives and legislative debate to encourage antibiotic stewardship; we promote international initiatives in antibiotic discovery; and we raise public awareness of superbugs. We will continue to expand our pipeline for new antibiotics and methods to fight against life-threatening superbugs.



## ANTIBIOTIC DISCOVERY, PROTEIN STRUCTURE AND DRUG DESIGN

Professor Jenny Martin

Our research aims to understand the role of proteins in disease and to develop novel drugs targeting the proteins that cause disease. We investigate proteins and their inhibitors using a range of biophysical techniques including: protein crystallography; small-angle scattering; chemical cross-linking; mass spectrometry; and structure-based approaches for inhibitor design. The disease areas that our research targets include bacterial and viral infection, type 2 diabetes and inflammation.

Of particular interest to our research is bacterial disulfide bond (DSB) forming proteins, which are essential for virulence and are important targets for the development of antibacterial agents. We are developing a library of DSB protein structures from human pathogens as a resource for structure-based drug design.

We are targeting structures of the soluble protein DsbA and its integral membrane protein partner DsbB in a range of invasive pathogens affecting both humans and animals, including *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Vibrio cholerae*, and *Mycobacterium tuberculosis*.

We are also working in collaboration with other leading Australian researchers to develop inhibitors of these proteins using a multipronged approach, including fragment screening, in silico screening and peptidomimetic design. From these investigations, we hope to develop a new class of antibiotic that may be useful in treating infections caused by multidrug-resistant bacteria and combating the growing global threat of antimicrobial resistance.

### Next steps

Our next steps are to tackle challenging structural biology targets including integral membrane proteins and membrane protein complexes. By better understanding the structure of these proteins we can identify weak spots, which can then be targeted for drug design.



# DESIGN AND DISCOVERY OF BIOACTIVE PEPTIDES AND PROTEINS IN VENOMOUS FAUNA

Professor Paul Alewood

Our research focuses on identifying bioactive molecules from Australia's venomous animals that have the potential to create drugs that will play important roles in finding treatments for chronic pain, heart disease, inflammation, irritable bowel syndrome, and breast cancer.

Although toxins from these animals can have a devastating effect, molecules within them have been found to be useful in treating human disease. Specifically, we are interested in the discovery and total synthesis of potent and selective peptides (toxins) from venomous animals; the chemical synthesis of proteins and bioactive peptides; the development of new synthetic and analytical chemistry; and protein structure and function.

A major focus of our research is determining the structure-function relationships of natural and designed molecules. Current research in our laboratory includes the discovery, isolation and characterisation of toxins from snakes, spiders, cone snails, platypus, ticks and scorpions; mimetics of calcium-binding inflammatory proteins from the S100 class; the chemical engineering of disulfide-rich peptides and proteases and uncovering new pain pathways in chronic pain.

## Next steps

Our next steps are to underpin our research base through a centre of excellence where outcomes will include: the identification of new toxin families and their potential function; a greater understanding of the molecular evolution of venoms; new methods to accelerate de novo (from the beginning) sequence determination and posttranslational modification of toxins; and new chemistry to accelerate regioselective control of toxin folding.

We also hope to discover fast and efficient chemistry application to deliver chemically-modified toxin libraries; novel expression approaches to deliver fully folded toxins; new fast nuclear magnetic resonance (NMR) methods to determine 3D structures of toxin families; novel cell-based molecular pharmacology to uncover toxin receptors; and tissue-based pharmacology to identify novel functionality, pharmacological tools, drug and insecticide leads.



# PHARMACOLOGY OF MARINE TOXINS

Professor Richard Lewis

Peptides are small proteins that can be used in research or for developing new therapeutics. Much of our research focuses on the conotoxins, small peptides from predatory marine snails, many of which have potential in pain management.

These mini-proteins act selectively at a wide range of ion channels, receptors and transporters found in the membranes of cells. This research starts with the discovery of new venom peptides, the synthesis of these peptides, studying their effects on tissues and receptors, cellular imaging of functional effects through to finally co-crystal structures and docking models revealing how the peptide binds to its target.

Several conotoxins discovered by our scientists have been taken into the clinic, including Xen2174 for severe pain. In addition, we are studying how another class of marine toxins, the ciguatoxins, produces the debilitating disease known as ciguatera.

During the past 12 months, we have discovered a new mechanism of peptide diversification. We have also discovered the neuronal basis of cold pain associated with ciguatera, and we have worked closely with industry partners to commercialise our novel findings.

## Next steps

Our next steps involve further characterising the analgesic venom peptides discovered in our pain relief research to determine target specificity and efficacy in a range of animal models of acute and chronic pain. If successful, these molecules will be considered for preclinical development as the first step towards their eventual clinical use and potential commercialisation.



## BUGS AND DRUGS

Professor Glenn King

Our research harnesses the chemistry of venoms from arthropod predators, such as spiders, scorpions and centipedes, to develop novel pharmaceuticals to treat chronic pain and stroke. Stroke is the second leading cause of death worldwide. In addition, it causes an extremely high incidence of disability in surviving victims due to the brain damage suffered during stroke. Likewise, chronic pain is a huge medical problem that affects one in five adults. There are few drugs available for treating chronic pain, and many of these have limited efficacy and dose-limiting side effects.

Animal venoms are a rich source of stable natural peptides that potently modulate the activity of a wide range of neuronal ion channels and receptors. We have the largest collection of arthropod venoms in the world, a high-throughput pipeline for venoms-based drug discovery, protocols for rapid protein expression and structure determination, and links to key laboratories for testing the efficacy of lead molecules in rodent models of pain and stroke. We are using these world-class resources to move us closer to achieving our aim of developing novel analgesics for pain relief and novel neuroprotective agents for treating stroke victims.

An equally important focus of our research is on helping to safeguard Australia's agricultural crops and reduce the spread of disease from insect pests by discovering new environmentally friendly insecticides. Currently, arthropod pests destroy one-third of the world's food supply and spread pernicious diseases such as dengue and malaria. Our work is finding better, safer ways to control disease-spreading pests and protect crops.

### Next steps

We have discovered a number of small peptides that potently and selectively modulate the activity of neuronal ion channels that play key roles in pain and stroke. Our next steps are to test the therapeutic potential of these peptides in rodent models of pain and stroke. It is hoped that some of these peptides will progress to clinical trials against a variety of human conditions such as cancer pain, postoperative pain, neuropathic pain, and stroke.



## COMBINATORIAL CHEMISTRY AND MOLECULAR DESIGN

Associate Professor

Mark Smythe

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

Our projects are multidisciplinary and focus on achieving medical outcomes. Several of them involve partnerships with industry. They range from technology development and early drug discovery to preclinical candidate selection. Using a combination of mathematics, software development, drug design, medicinal chemistry and phage display, we are developing new approaches to treat asthma, leukaemia and inflammatory bowel disease.

In addition, we have designed and synthesised a new spin label to accurately determine distances in biological systems, capitalising on rapid advances in biological techniques. Determining distance is a vital step in understanding a molecule's structure, which is integrally link to its function.

In 2012 we continued to pursue our most advanced drug discovery projects towards the clinic, and initiated another two drug discovery programs.

### Next steps

Several of these drug discovery programs are in late-stage preclinical development. The next steps involve optimising various parameters of the drug candidate, for example, affinity, efficacy, half life, and solubility, and testing select compounds in various disease models to select the best candidates for investigational new drug (IND) enabling studies. This provides preclinical validation of the drug discovery methodologies being developed, which will have broader implications to other disease states.





## Division Head

Professor Mark Ragan

## Laboratory Heads

Dr Tim Bailey, Dr Lachlan Coin, Professor Sean Grimmond, Dr Nick Hamilton and Dr Ryan Taft

Researchers Senel Idrisoglu (left), Ehsan Nourbakhsh (centre) and Dr Tim Bruxner (right)

# RESEARCH HIGHLIGHTS

## GENOMICS AND COMPUTATIONAL BIOLOGY

### Division overview

Scientists in IMB's Genomics and Computational Biology Division study the structure and organisation of genomes, the regulation of genes and the localisation and function of gene products. They do this by conducting high-throughput sequencing, imaging, computation and bioinformatics.

Their research applies approaches based on mathematics, statistics, computer science and bioinformatics to understand the molecular basis of mammalian and vertebrate biology at full genome scale, specifically in the areas of comparative functional genomics, small regulatory RNAs, and computational modelling of genetic and cellular regulatory networks.

During 2012, the Division supported research in the following areas:

- › computational systems biology
- › medical and population genomics
- › RNA regulation, epigenetics and inherited disease
- › modelling, visualisation and classification of bioimaging
- › pattern recognition and modelling in computational biology.

The Division hosts the ARC Centre of Excellence in Bioinformatics, Queensland Centre for Medical Genomics, and QFAB Bioinformatics. It also actively participates in the teaching and learning activities of UQ's School of Chemistry and Molecular Biosciences, School of Information Technology and Electrical Engineering, and School of Mathematics and Physics. In 2012, it successfully organised the annual Winter School in Mathematical and Computational Biology, which attracted more than 300 students, postdoctoral researchers and other professionals working in fields ranging from engineering to chemical and medical sciences.

Many leading technologies are used to help the Division advance discovery in these fields, with advanced on-site facilities for large-scale DNA sequencing, computing and data management.

Major funders of the Division include the NHMRC, ARC, Queensland Government, US National Institutes of Health, J.S. McDonnell Foundation, and industry partners.

### Featured publications

#### Pancreatic cancer genomes reveal aberrations in axon guidance pathway genes.

Biankin AV, **Waddell N**, **Kassahn KS**, Gingras MC, Muthuswamy LB, Johns AL, **Miller DK**, **Wilson PJ**, **Patch AM**, Wu J, Chang DK, Cowley MJ, **Gardiner BB**, **Song S**, **Harliwong I**, **Idrisoglu S**, **Nourse C**, **Nourbakhsh E**, **Manning S**, **Wani S**, **Gongora M**, Pajic M, Scarlett CJ, Gill AJ, Pinho AV, Rooman I, **Anderson M**, **Holmes O**, **Leonard C**, **Taylor D**, **Wood S**, **Xu Q**, **Nones K**, **Fink JL**, **Christ A**, **Bruxner T**, **Cloonan N**, Kolle G, **Newell F**, Pinese M, Mead RS, Humphris JL, Kaplan W, Jones MD, Colvin EK, Nagrial AM, Humphrey ES, Chou A, Chin VT, Chantrill LA, Mawson A, Samra JS, Kench JG, Lovell JA, Daly RJ, Merrett ND, Toon C, Epari K, Nguyen NQ, Barbour A, Zeps N; Australian Pancreatic Cancer Genome Initiative, Kakkar N, Zhao F, Wu YQ, Wang M, Muzny DM, Fisher WE, Brunicardi FC, Hodges SE, Reid JG, Drummond J, Chang K, Han Y, Lewis LR, Dinh H, Buhay CJ, Beck T, Timms L, Sam M, Begley K, Brown A, Pai D, Panchal A, Buchner N, De Borja R, Denroche RE, Yung CK, Serra S, Onetto N, Mukhopadhyay D, Tsao MS, Shaw PA, Petersen GM, Gallinger S, Hruban RH, Maitra A, Iacobuzio-Donahue CA, Schulick RD, Wolfgang CL, Morgan RA, Lawlor RT, Capelli P, Corbo V, Scardoni M, Tortora G, Tempero MA, Mann KM, Jenkins NA, Perez-Mancera PA, Adams DJ, Largaespada DA, Wessels LF, Rust AG, Stein LD, Tuveson DA, Copeland NG, Musgrove EA, Scarpa A, Eshleman JR, Hudson TJ, Sutherland RL, Wheeler DA, **Pearson JV**, McPherson JD, Gibbs RA, **Grimmond SM**. (15 November 2012) *Nature*, 491 7424: 399-405.

Pancreatic cancer is a lethal malignancy with few effective therapies. In this paper the authors performed exome sequencing and copy number analysis to define genomic aberrations in a prospectively accrued clinical cohort of early sporadic pancreatic ductal adenocarcinoma. They also defined 16 significantly mutated genes.

#### Sleeping Beauty mutagenesis reveals cooperating mutations and pathways in pancreatic adenocarcinoma.

Mann KM, Ward JM, Yew CC, Kovoichich A, Dawson DW, Black MA, Brett BT, Sheetz TE, Dupuy AJ; Australian Pancreatic Cancer Genome Initiative, Chang DK, Biankin AV, **Waddell N**, **Kassahn KS**, **Grimmond SM**, Rust AG, Adams DJ, Jenkins NA, Copeland NG. (17 April 2012) *Proceedings of the National Academy of Sciences of the United States of America*, 109 16: 5934-5941.

The identification of molecular cancer drivers is critical for further understanding pancreatic cancer. The authors of this paper conducted a mutagenic screen using Sleeping Beauty (SB) in mice to identify new candidate cancer genes, and used statistical methods to identify loci commonly mutated by SB in these tumours.

# COMPUTATIONAL SYSTEMS BIOLOGY

Professor Mark Ragan

DIVISION HEAD

The structure, function and fate of living cells are determined by complex networks of interactions among biomolecules. These networks cannot be observed directly, but must be reverse-engineered from genome-scale data. Our research develops and applies approaches based on mathematics, statistics, computer science and bioinformatics to infer and analyse these networks from individual samples or patients.

We are particularly interested in understanding how networks of gene regulation differ between normal and cancerous states. We collaborate with biologists and clinicians on projects investigating breast cancer, ovarian cancer, pancreatic cancer and prostate cancer. Likewise, the spread of drug resistance and virulence among infectious-disease bacteria can be drawn as a graph and studied mathematically. Using high-performance computers, we identify features of these networks that help us understand and predict properties of cells, organisms and communities.

Our research in computational systems biology of mammalian cells will extend the power of genome-scale sequencing, including personal genomics, to help understand normal developmental processes and to design systems-level intervention in chronic disease and cancer.

## Next steps

Our next steps are to develop more powerful computational methods to study networks of gene regulation and protein interaction in cells, based on genome-scale datasets from single individuals. This will enable us to predict how individuals are likely to differ in susceptibility to both disease and in response to therapies.



# POPULATION GENOMICS

Dr Lachlan Coin

During the first decade of the 21st century, sequencing of a single reference genome from multiple animal and plant species provided a tremendous amount of information about eukaryotic genome structure, function and evolution. Now, in the second decade, technological developments allow affordable 'population sequencing' of thousands of genomes per species. Moreover, it is now possible to sequence not just the genome, but also the epigenome and transcriptome of different cell populations at different points in time, enabling use of this technology to profile important physiological processes.

Our research focuses on integrative population genomics, where we develop and apply statistical approaches to extract information from high-throughput population sequence data. Of particular interest to our research is mapping the impact of structural variation on disease risk. We have developed population modelling approaches to improve detection and genotyping of indels, copy number variation (CNV), and tandem repeat variation.

We apply these tools to understand the genetic basis of common diseases including: metabolic disease, such as obesity and type 2 diabetes; autoimmune diseases, such as psoriasis, rheumatoid arthritis and systemic lupus erythematosus; and susceptibility to infectious disease. We have previously identified rare deletions and duplications associated with extreme obesity and also common deletions associated with obesity and variation in lipid levels.

Our group uses integrative genomics approaches to profile the genome, transcriptome and proteome from the acute to convalescent stage of disease in order to identify rapid cheap biomarkers for both early stage disease diagnosis and prognosis and also to understand biological pathways that are active during disease. Using this approach, we have recently identified transcriptomic and proteomic signatures that can distinguish active tuberculosis infection from other disease in HIV-positive individuals in Africa.

## Next steps

We are currently using integrative genomics approaches to investigate the effect of host-pathogen interactions on susceptibility and severity of meningococcal infection in children. Of particular interest is the interaction between genetic variability in the human complement factor-H and the pathogen factor H binding proteins.

Development of biomarkers of early stage disease development remains an ongoing interest of our lab. We are currently investigating use of high-throughput sequencing to profile CNV from tumour DNA found at low concentrations in blood plasma.

We will also continue to investigate the phenotypic effects of structural variation, with a particular focus on variants that have been difficult to detect, such as repeat variation. This research is currently focused on identifying further genetic causes of extreme paediatric obesity.



## QUEENSLAND CENTRE FOR MEDICAL GENOMICS

Professor Sean Grimmond

One in two Australians will develop cancer before the age of 85 and one in five will die from the disease, making cancer an important national health priority area. Our research at the Queensland Centre for Medical Genomics (QCMG) aims to discover the process for how normal cells transform into cancer cells, one patient at a time. From this information, we can then help to choose drugs and treatments to treat each individual, not just their cancer type.

To achieve this, we survey genomic and gene activity information, as well as how non-genetic factors influence physical traits using high-throughput genomic sequencing and microarrays. The combined data sets are then integrated to enable us to define the molecular networks controlling biological processes, such as cell division and specialisation, and disease states, including cancers of the pancreas, prostate, bowel, brain, ovary and breast. This systems-wide approach will provide the means to identify key genes driving specific physical traits and enable us to model the different layers of control guiding biological states.

We are continuing to survey gene activity in specific biological states using high-throughput sequencing approach (RNAseq) in an effort to put newly discovered gene products into a functional context. We are actively engaged in RNAseq studies to create a human and mouse tissue gene activity atlas, studying gene activity complexity in stem cells and we are surveying gene activity during the cell cycle.

During the past 12 months, we led an international team of more than 100 researchers working as part of the International Cancer Genome Consortium to conduct the most comprehensive investigation to date into the genetic sequencing of pancreatic cancer, which garnered significant international media attention. We also established new experimental models by using mouse models of pancreatic cancer to identify new key drivers in cancer initiation and tumour progression.

### Next steps

As modern technology increases the volume of patient data available, the need to automate both laboratory and informatics pipelines becomes more critical.

Our next steps will focus on finding new ways to automate and sort these large and important data sets. By better understanding the molecular signature of each individual patient we can make more informed decisions about effective treatment solutions, which has the potential to offer patients a better quality of life and hopefully fewer side effects of treatment.



## RARE CHILDHOOD DISEASES

Dr Ryan Taft

Our research seeks to answer pressing biological and medical questions using our fundamental knowledge of the genome and how it operates. For example, our work helps to directly identify and diagnose patients with rare genetic diseases, which currently affect more than 1.5 million Australians, with at least 400,000 of these patients fewer than 15 years of age. This research is also assisting with the development of tailored therapeutics and treatments for children diagnosed with rare diseases, including as leukodystrophies and Prader-Willi syndrome.

During the past 12 months, we have expanded our work in personalised medicine. We sequenced the genomes of a three-year-old boy with a leukodystrophy to identify the candidate disease likely to have caused the disease; we solved the case of a little girl with Leigh syndrome; and we found the mutation responsible for a leukodystrophy called H-ABC. We also identified the mutation causing a young boy's epilepsy, which allowed us to target the mutation using the best drug to for the job.

In parallel with this research, we are actively rethinking how the genome operates by studying the long-ignored 98 per cent of our DNA that isn't genes, which has sometimes been referred to as 'junk' DNA. Using state-of-the-art bioinformatics and laboratory approaches, we are able to study this biological dark matter and the vast amounts of RNA produces. Our work has resulted in a number of important findings, including four classes of very small RNAs that can act as regulators of gene activity.

### Next steps

Our immediate next steps include getting our high-throughput sequencing approaches into the clinic, and to begin to tackle difficult clinical cases with a combination of genome sequencing, RNA sequencing and even more subtle genomic interrogations.

Our long-term aim is to use our increasing knowledge of the genome itself and the RNAs that regulate it to completely understand, diagnose, and treat a range of inherited and acquired illnesses.





## MODELLING, VISUALISATION AND CLASSIFICATION OF BIOIMAGING

Dr Nick Hamilton

Modern scientific methods that allow researchers to rapidly perform millions of tests are leading to massive bioimage sets in need of new methods of analysis. Scientists can now produce 3D time-lapse footage of live cells and organs that show the interactions and dynamics of the systems. For example, it is now possible to observe live in 3D as individual Salmonella bacteria invade a cell. Our research develops the methodologies, tools and mathematical models to realise the benefit of these rich advanced new data sources in areas such as drug and genomic discovery.

Our laboratory has two key streams of research in the analysis of multidimensional bioimaging. The first is in developing methods to automatically extract key information that describes the biological systems being observed. The second is in building predictive mathematical models of the cellular and organ level systems. We hope to use these models to predict the behaviour of these systems under a range of conditions, be they health, disease or drug action.

Currently we are applying these methods to answer some of the most pressing questions in modern biology, including: 'What are the factors affecting the growth of nephrons, the fundamental filtering unit in the human kidney?'; 'How does the lymphatic system develop?'; and 'How do macrophages, the front line of the human immune system, fight bacteria and infection?'

### Next steps

Our next steps include building models of cell proliferation in developing and diseased kidneys. By understanding the mechanisms driving or inhibiting growth we can develop drugs to prolong development of nephrons in diseased kidneys and help improve kidney function.

By better understanding the lymphatic system and modelling how it develops it will be possible to predict and develop treatments for the many disease processes such as lymphoedema, obesity and inflammation associated with the lymphatic system.

As well as developing new knowledge in fundamental cell biology, our research into the immune response of cells will enable better understanding of how drug internalisation works and molecular approaches to blocking the invasion of cells by pathogens.



## PATTERN RECOGNITION AND MODELLING IN COMPUTATIONAL BIOLOGY

Dr Tim Bailey

Modern biological experiments produce massive amounts of data and require sophisticated computer software to extract knowledge from this endless information. Our laboratory develops specialised software for analysing the results of experiments that sequence DNA and RNA, the information storage workhorses of the cell. It is impossible for biologists to make sense of this type of experiment without the aid of computers, and we have been developing the software to help them do this for more than 20 years.

Our research provides scientists with a detailed look at how the information stored in the chromosomes is converted to action by the cell. The first step in this process (transcription) is itself controlled by earlier events, all driven by DNA, RNA and proteins. By surveying these three types of molecules, mapping where they go in the cell and how they interact with each other, our research will allow us to understand how a single cell develops into a complex organism – growing, dividing and changing into other kinds of cells.

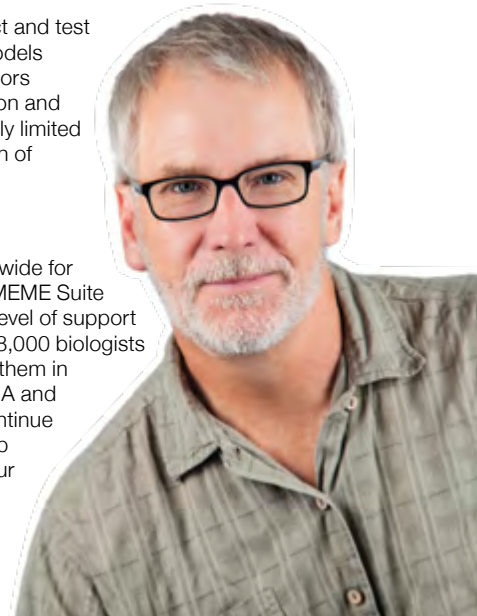
Our research focuses on three main areas of cell biology. Firstly, we study the regulation of transcription, by which the information in genes is transcribed into a format that can be transported around the cell. This is the initial process through which the information in genes influences physical changes in the body. Secondly, we study the organisation and stability of proteins in the cell nucleus, the control centre of the cell. Thirdly, we study the formation of triple-stranded DNA. By studying transcription, subcellular protein organisation and protein stability, we focus on three key steps in gene expression. Our work on triple-stranded DNA is partly motivated by recent evidence that suggests that these too may play a role in gene expression. Knowing how gene expression is regulated is essential to understanding cellular processes such as reproduction and metabolism.

During the past 12 months, we collaborated with internal and external scientists to unravel the roles of key regulators of development. This work studied the molecular program controlling the development of three types of cells: red blood cells, neurons, and lung cells. We developed and published a number of computational methods for studying the regulation of transcription, and also published on modelling the import and location of proteins in the cell nucleus. We also continued our development of a method for testing triple-helix formation in vitro.

### Next steps

Our next steps are to construct and test new types of mathematical models to try and pinpoint the key factors responsible for turning genes on and off, and expand on the currently limited understanding of the regulation of transcription.

Our laboratory is known worldwide for the quality of the web-based MEME Suite software we develop and the level of support we provide to the more than 18,000 biologists who use it each year to assist them in their work to analyse DNA, RNA and protein sequences. We will continue to develop this program to help meet the changing needs of our research clients.





## Division Head

Professor Alpha Yap

## Laboratory Heads

Professor Kirill Alexandrov, Dr Brett Collins, Professor Rob Parton, Professor Jennifer Stow, Professor Mike Waters and Associate Professor Rohan Teasdale

Professor Alpha Yap and lab members meet to discuss an upcoming paper

# RESEARCH HIGHLIGHTS

## MOLECULAR CELL BIOLOGY

### Division overview

IMB's Molecular Cell Biology Division seeks to elucidate the molecular workings of the cell, the building blocks of our bodies. This is fundamental for a full understanding of how our bodies function and as a foundation to investigate the cellular basis of disease.

IMB scientists are tackling key issues in cell biology, investigating the mechanisms responsible for how cells develop, function and interact with one another. Laboratories within the Division regularly work alongside collaborators from other research disciplines too, where a multidisciplinary approach is necessary to tackle fundamental problems or build new technologies.

During 2012, the Division supported research in the following areas:

- ▶ cadherin cell-cell adhesion and tissue organisation in health and disease
- ▶ molecular engineering: better tools, better science, better life
- ▶ molecular trafficking
- ▶ role of the cell surface in health and disease
- ▶ protein trafficking in human disease
- ▶ role of growth hormone in human development
- ▶ endosomal dynamics and pathogen invasion.

Many leading technologies are used to help the Division advance discovery in these fields, with advanced on-site facilities for quantitative optical microscopy, live-cell imaging, single-molecular protein interaction analysis and protein structure determination.

Notably, this Division is home to the Australian Microscopy and Microanalysis Research Facility, which allows for the application of cryo-electronic microscopy, cellular tomography, advanced visualisation and high-performance computing, and oversees the Australian Cancer Research Foundation's Cancer Biology Imaging Facility and Dynamic Imaging Facility.

Major funders of the Division include the NHMRC, ARC, Queensland Government, the US National Institute of Health, Australian Cancer Research Foundation (ACRF), and industry partners.

### Featured publications

#### Constitutive formation of caveolae in a bacterium.

Walser, Piers, **Ariotti, Nicholas, Howes, Mark, Ferguson, Charles, Webb, Richard, Schwudke, Dominik, Leneva, Natalya**, Cho, Kwang-Jin, Cooper, Leanne, **Rae, James**, Floetenmeyer, Matthias, Oorschot, Viola M. J., Skoglund, Ulf, Simons, Kai, Hancock, John F. and **Parton, Robert G.** (17 August 2012) *Cell*, 150 4: 752-763.

Caveolin plays an essential role in the formation of characteristic surface pits, called caveolae, which cover the surface of many animal cells. However, the fundamental principles of caveola formation are only slowly emerging. This paper showed that caveolin expression in a prokaryotic host lacking any intracellular membrane system drives the formation of cytoplasmic vesicles containing polymeric caveolin.

#### Centralspindlin and $\alpha$ -catenin regulate Rho signalling at the epithelial zonula adherens.

Ratheesh, Aparna, **Gomez, Guillermo A., Priya, Rashmi, Verma, Suzie**, Kovacs, Eva M., Jiang, Kai, Brown, Nicholas H., Akhmanova, Anna, Stehbens, Samantha J. and **Yap, Alpha S.** (August 2012) *Nature Cell Biology*, 14 8: 818-828.

The biological impact of Rho depends critically on the precise subcellular localisation of its active, GTP-loaded form. This can be determined by the balance between molecules that promote nucleotide exchange or GTP hydrolysis. However, how these activities may be coordinated is poorly understood. This paper reported a molecular pathway that achieves exactly this coordination at the epithelial zonula adherens. It also identified an extramitotic activity of the centralspindlin complex, better understood as a cytokinetic regulator, which localises to the interphase zonula adherens by interacting with the cadherin-associated protein,  $\alpha$ -catenin.

# CADHERIN CELL-CELL ADHESION AND TISSUE ORGANISATION IN HEALTH AND DISEASE

Professor Alpha Yap

DIVISION HEAD

Cells are the building blocks of our bodies. Interactions between different cells are important to shape our developing bodies and maintain the healthy organisation of our tissues. Importantly, those interactions are disturbed in many diseases, including cancer and inflammation.

My laboratory studies one set of cell-cell interactions, those that occur when cells attach to one another. We focus on the cadherin family of cell-cell adhesion receptors. These critically determine the ability of cells to recognise one another and organise into coherent tissues. The importance of these receptors is emphasised by the fact that loss of cadherin function promotes cancer progression in epithelial tissues such as the breast and colon, which are the commonest forms of human cancers.

Cadherin dysfunction also contributes to the breakdown of epithelial barriers during inflammation, notably in chronic disease of the intestine. By understanding the basic biological mechanisms of cadherin-mediated cell recognition, we aim to provide vital insights into the basis of development and common human diseases.

Currently we focus on understanding how cadherins cooperate with the actin cytoskeleton, the cellular structure that allows the cells to move and which has long been believed to be central to cadherin function.

Our research indicates multiple regulators are coordinated in cadherin adhesion to maintain the integrity of cell-cell junctions. This carries the challenge of understanding how these many proteins are coordinated to work together at the right time and place in the cell. A significant breakthrough came with our recent discoveries, published in the scientific journal *Nature Cell Biology*, that these cell signals and effectors function in modules that make specific contributions to junction integrity.

## Next steps

Much of our current work is focused on understanding the links between the cellular mechanisms and physical effects in the control of cell-cell interactions. We believe that the mechanical perspective (mechanobiology) this provides will give us an important new perspective from which to analyse the cell biology of these interactions. Furthermore, we have increasing evidence that aberrant regulation of mechanical regulation at junctions participates in disturbing tissue architecture in disease, notably during cancer.



# MOLECULAR ENGINEERING: BETTER TOOLS, BETTER SCIENCE, BETTER LIFE

Professor Kirill Alexandrov

Human civilisation is built on exploiting and manipulating biological systems, from the most simple to the most complex. While domestication, cultivation and the breeding of living systems laid the foundations for contemporary industries, the introduction of molecular biology has, as we know it, transformed medicine, agriculture and industry.

Animal cloning, sequencing and synthesis of complete genomes demonstrated the technical capacity of modern biotechnology to modify and replicate living organisms. The next step in this development is the knowledge-based design of biological systems. While the classical engineering-driven designs of devices is based on the first principles of physics and mathematics, the lack of quantitative descriptions of living system makes their redesign an empirical and unpredictable process.

Our research is focused on filling this technological gap by developing new methods for rapid in vitro synthesis and engineering of proteins and protein-based machines to help develop treatments for cancer, blindness, thrombosis and excessive bleeding. These methods are vital in biotechnology, as the ability to produce and analyse proteins determines the expense and speed of the discovery and creation of new vaccines, drugs and diagnostic methods. We combine this technology with molecule spectroscopy to quantitatively analyse protein dynamics and protein-protein interactions.

During the past 12 months, through our work to combine these technologies, we have developed synthetic protein signal transduction and amplification cascade based on proteases for the use in organism engineering and in vitro diagnostics. We have also developed a novel cell-free protein expression system based on the single-celled organism known as *Leishmania tarentolae*. By using this technology, we have successfully converted large sets of genes into proteins within hours.

## Next steps

Our next steps will be to further develop our protease-based biosensors for use in human diagnostics, and pursue partnerships with industry to help make them commercially accessible. We will also continue developing novel engineering technology based on biophysically guided directed evolution. We expect that having developed this technology we will be able to engineer novel enzymes and protein-based machines with multiple industrial uses. Our current focus is on developing enzymes for use in animal feedstock.



# MEMBRANE TRAFFICKING AT ATOMIC RESOLUTION

Dr Brett Collins

The body has tens of trillions of cells, and each of these cells contains tens of thousands of different tiny machines called proteins. When these proteins are not working as they should, the result is often a disease such as cancer, Alzheimer's, Parkinson's, or even inflammation. We are investigating how these proteins work together so we can understand how they allow our cells to function correctly, and what we might do to fix them when things go wrong.

Our research investigates several related families of proteins with important roles in controlling cellular membrane trafficking, with a particular emphasis on a key sub-cellular structure called the endosome. We combine different approaches to understand the function of endosome-associated proteins and to determine how their dysfunction contributes to disease, right down to the atomic level.

Many endosomal proteins control the formation of cellular membrane structures, which are selective regions of the endosome that package and transport 'cargo' around the body in a process called protein trafficking, which is essential for normal cellular function. Of particular interest to our laboratory is the amyloid precursor protein (APP), which when broken down forms amyloid peptides that are believed to be a major cause of Alzheimer's disease, and cell adhesion receptors which are targets for anti-inflammatory therapies.

During the past 12 months we have discovered how a protein family called SNX-FERM molecules interact with a host of different receptors, including the APP receptor central to Alzheimer's and the P-selectin receptor required for inflammatory cell adhesion to the blood vessel wall.

## Next steps

Our next steps will be determining high-resolution structures and mapping the blueprints of the protein machinery that performs many important biological functions, such as regulating endosome trafficking, which helps transport receptors, lipids and regulatory proteins.

We are also beginning to dissect the molecular basis for caveolae formation, specialised structures within the plasma membrane. We hope to use this new structural information to design new compounds that inhibit trafficking machinery and regulatory molecules, which we can use to develop chemical tools for biology research and as leads for new therapeutic drugs.



# ROLE OF THE CELL SURFACE IN HEALTH AND DISEASE

Professor Rob Parton

Each of the cells that make up our organs is enclosed in a plasma membrane, a complex sheet made up of fats and proteins, that plays a crucial role in detecting growth signals or taking nutrients up into the cell. At the same time, the plasma membrane protects the cell against unwanted invaders.

The properties of the plasma membrane rely on its specialisation into regions of specific function. Our research focuses on caveolae, a specialised domains of the cell surface with a distinct structure and functions. Caveolae have been implicated in regulation of cell growth and in maintaining the balance of fats in the cell. Defective caveolae in human patients are associated with cancer, lipodystrophies (lack of fat tissue), muscular dystrophy, and cardiovascular disease.

To study caveolae function, we are studying cells and animals that lack caveolae or have defective caveolae. We have discovered new proteins needed for caveolar formation (cavins) and explored their function. From this, we have shown that caveolae can respond to forces on the plasma membrane by releasing signals into the cell. This allows the cell to detect and respond to stresses on the cell surface. We are investigating if the loss of this specialised detection system is responsible for causing some forms of muscular dystrophy.

We are also developing novel drug encapsulation systems with potential therapeutic applications for targeted drug delivery.

## Next steps

Our next steps include optimising drug loading and drug delivery with our novel system. We are also working towards a detailed structural analysis of caveolae and of their key components. Using cells, zebrafish and mice, we hope to clarify the precise function of caveolae in vertebrate muscle and elucidate how defective caveolae cause disease.



## PROTEIN TRAFFICKING IN HUMAN DISEASE

Professor Jennifer Stow

Proteins are 'trafficked' or moved around within our cells and then released as a means of communication between cells. This process is fundamental to many diseases ranging from infection to cancer. Our laboratory aims to piece together the trafficking highways and regulators in cells of our immune system and major organs. Understanding this trafficking network will allow us to manipulate cells in disease, improving our use of existing drugs and identifying targets for developing new drugs.

A major focus of our research is investigating how white blood cells make and release chemical messengers called cytokines, which mount an immune response by recruit other cells to sites of infection. These cytokines are critical for fighting off infectious bacteria and other microbes. But when it comes to cytokines, too much is not a good thing. Excessive release of cytokines causes inflammatory diseases like rheumatoid arthritis, inflammatory bowel disease and diabetes. Our laboratory is identifying the genes and proteins that can be targeted to enhance cytokines in infection and reduce them in inflammatory disease.

We also study how immune cells eat or 'phagocytose' bacteria, normally digesting and killing these microbes. However, some bacteria can avoid being killed after being phagocytosed and instead they grow inside our cells, causing diseases ranging from food poisoning and typhoid fever to respiratory infections.

As part of a national research program, we are working to investigate and document the many bacterial and host cell genes that allow some bacteria to escape our immune systems. We are learning from the bacteria about how to manipulate our own cells. This research aims to develop new vaccines, antibiotics and other treatments to increase our ability to avoid or fight infectious diseases.

### Next steps

Our next steps include studying protein trafficking in living cells using new high-resolution microscopy to investigate host-bacterial interactions during phagocytosis. We will also be testing some of our new anti-cytokine drug targets in early stage screening to determine whether they can effectively control inflammation in disease models of sepsis and infection.



## ROLE OF GROWTH HORMONE IN HUMAN DEVELOPMENT

Professor Mike Waters

Growth hormone affects all of us throughout our lives and regulates our cognitive ability. In childhood and adolescence it causes us to grow and determines our final height. In adulthood, it regulates body composition – the distribution of muscle, bones, organs and fat. Finally, in old age, at least in rodents, it regulates our lifespan. Our research studies the molecular means used by growth hormone to achieve these changes using a variety of approaches.

The growth hormone receptor determines the degree of the cell response to growth hormone. Through various techniques, we have developed a physical mechanistic understanding of how the growth hormone receptor is activated by the cell, the first such model for the 30 receptors in this cytokine receptor class. This study has led us to create growth hormone receptors that are permanently activated, and these are being used to promote the growth of fish in aquaculture in China.

We also recently described a growth hormone receptor initiated signalling pathway that is essential for expression of a powerful immune tolerance molecule that may improve the success of human liver and kidney transplants. We have also been investigating the use of growth hormone therapy as a potential treatment for hepatic steatosis (fatty liver) and cirrhosis (scarring of the liver).

Our scientists have found that growth hormone acts in normally fed mice to burn fat, so as to maintain a normal amount of fat. This changes the view of fat as a simple storage organ that supplies lipid for muscle to burn, to a view where the fat regulates its own level both by controlling appetite and by burning itself.

Finally, the striking resistance of growth hormone-deficient and growth hormone-receptor mutant mice and humans with defective growth hormone receptors to cancer has led us to elucidate the pathways involved, and to seek to develop small molecule (drug) growth hormone antagonists of therapeutic value in cancer treatment. We have evidence that the erroneous synthesis of growth hormone within cells can promote cancers where an initial mutation or insult is present. However, growth hormone acting externally is prevented from doing this by a set of opposing factors, which means it is a safe therapeutic.

### Next steps

Our next steps involve expanding the generality of the growth hormone receptor activation model to related significant cytokine receptors to assist with the development of antagonists and agonists of clinical value.

We will also conduct a clinical trial that extends our fat burning findings with the aim to fully uncover the mechanism of growth hormone action in 'browning' of white fat, which encourages tissue to burn fat rather than store it. We will also conduct further studies in the role of growth hormone in chronic liver disease, dementia, short stature, gigantism, stem cell research, prostate cancer and lung cancer.



# ENDOSOMAL DYNAMICS AND PATHOGEN INVASION

Associate Professor  
Rohan Teasdale

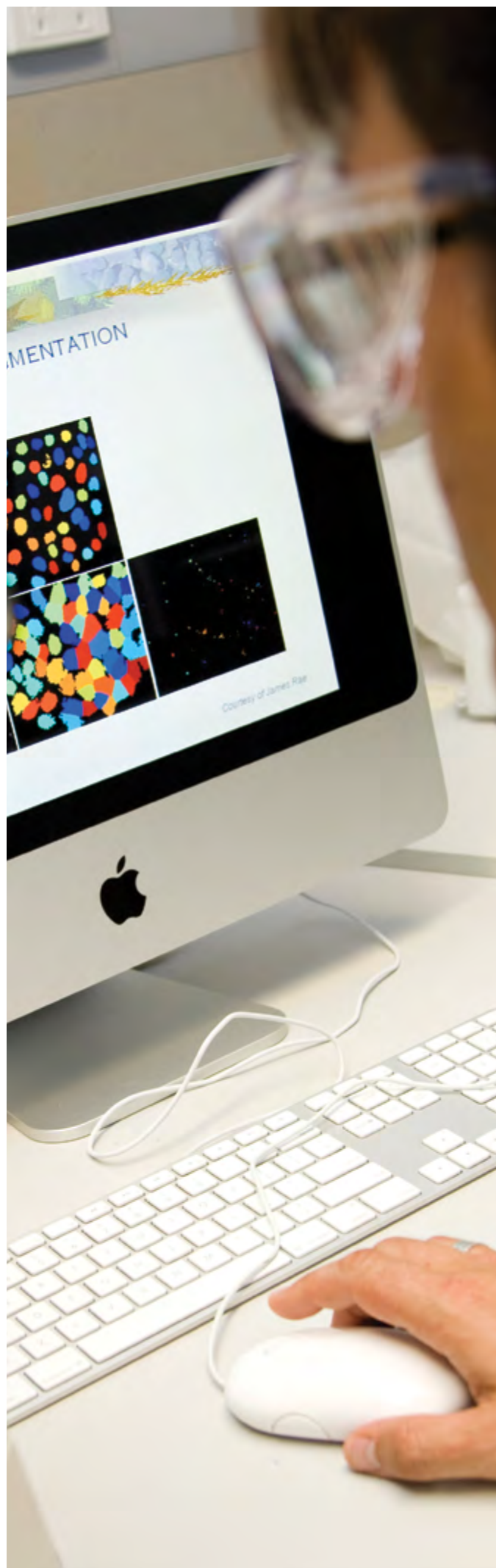
The endosomal/lysosomal system of mammalian cells is a highly dynamic organelle, and the trafficking pathways within the endosomal system are fundamental for a wide variety of key cellular processes. Our laboratory is developing cellular and computational approaches to identify novel mammalian proteins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

The regulated movement of membrane receptors and ligands between the cell surface and intracellular compartments is vital to many cellular operations, including communication between cells and their environment. Macropinocytosis is a regulated form of endocytosis that mediates the non-selective uptake of extracellular material, such as proteins. Numerous infectious pathogens exploit macropinocytosis to invade the host. Characterisation of pathogen entry pathways is essential for understanding infectious diseases but has also proven to be a powerful tool for gaining insight into normal cellular processes. We are currently investigating the molecular details of these pathways and how they are modulated in response to infection with *Salmonella*, a leading cause of human gastroenteritis.

A major focus of our research is the characterisation of the mammalian endosomal protein complex called the retromer, which is a central regulator of early endosome protein trafficking. Retromer has recently been implicated in the progressive neurological disorders such as Alzheimer's and Parkinson's diseases. We are currently examining the known cellular biochemical properties of retromer to determine the molecular mechanisms underlying these disease states.

## Next steps

Next steps for our research include determining the deficiencies in the membrane trafficking properties of retromer encoding the disease causing mutations. We will also work to determine the contribution of the hosts membrane transport pathways have to the formation of the Chlamydia Inclusion. Furthermore, we hope to define the host proteins whose function is modulated by *Salmonella* effectors during the early invasion stage.





## Division Head

Professor Peter Koopman

## Laboratory Heads

Dr Mat Francois, Dr Ben Hogan, Professor Melissa Little, Professor George Muscat, Associate Professor Rick Sturm, Associate Professor Matt Sweet, Professor Brandon Wainwright and Associate Professor Carol Wicking

Dr Alex Combes using the ACRF imaging facilities

# RESEARCH HIGHLIGHTS

## MOLECULAR GENETICS AND DEVELOPMENT

### Division overview

Some of the most serious diseases facing society today are known to have a genetic component, and for many of these, disease susceptibility is determined during fetal life. Research conducted in IMB's Molecular Genetics and Development Division generates important insights into gene structure, function and interaction, clues to the causes of genetic diseases, including cancer, and new molecular approaches to the diagnosis and treatment of these diseases.

IMB scientists within the Division focus on how proper gene function contributes to adulthood wellbeing, how genes regulate the optimal development of the embryo, and how errors in these genetic processes can cause disease. They examine gene function at the molecular level, but also in the living cells of entire organisms.

Laboratories within the Division collaborate closely with other research groups internally and around the world, drawing on expertise in bioinformatics, cell biology and chemistry to apply common skillsets and approaches to a broad range of biological problems.

During 2012, the Division supported research in the following areas:

- › kidney development, damage, repair and regeneration
- › cardiovascular and lymphatic vessel development and disease
- › genetics of human dysmorphism syndromes
- › pigmentation and skin cancer
- › disorders of sex development, infertility and testicular cancer
- › neural development and brain cancer
- › nuclear hormone receptors and metabolic disease
- › infection and innate immunity.

Advanced technologies are applied to these research programs, with world-class on-site facilities for microarray and high-throughput genome and exome sequencing; protein visualisation including immunofluorescence and confocal imaging methods; and gain- and loss-of-function gene analyses in mice and zebrafish.

Major funding sources include the Australian Cancer Research Foundation (ACRF), NHMRC, ARC, Queensland Government, the US National Institute of Health and industry partners.

### Featured publications

**Conservation and divergence in Toll-like receptor 4-regulated gene expression in primary human versus mouse macrophages.**

**Schroder, Kate**, Irvine, Katharine M., Taylor, Martin S., **Bokil, Nilesh J.**, **Le Cao, Kim-Anh**, **Masterman, Kelly-Anne**, Labzin, Larisa I., Semple, Colin A., Kapetanovic, Ronan, Fairbairn, Lynsey, Akalin, Altuna, Faulkner, Geoffrey J., Baillie, John Kenneth, **Gongora, Milena**, Daub, Carsten O., Kawaji, Hideya, McLachlan, Geoffrey J., Goldman, Nick, **Grimmond, Sean M.**, Carninci, Piero, Suzuki, Harukazu, Hayashizaki, Yoshihide, Lenhard, Boris, Hume, David A. and **Sweet, Matthew J.** (24 February 2012) *Proceedings of the National Academy of Sciences of the USA*, 10916: E944-E953.

The immune system is under strong evolutionary pressure, which leads to substantial differences in immune responses between species. This limits the capacity to translate immunological research breakthroughs from animal models, such as the mouse, through to the clinic. This paper identified widespread divergence in human versus mouse innate immune responses, as well as the mechanisms responsible. The findings help us to understand the limitations of the mouse as a model for immune-related diseases, and may also guide new therapeutic approaches for infectious and inflammatory diseases.

**Genetic ablation of SOX 18 function suppresses tumour lymphangiogenesis and metastasis of melanoma in mice.**

**Duong, Tam**, Proulx, Steven T., Luicani, Paola, Leroux, Jean-Christophe, Detmar, Michael, **Koopman, Peter** and **Francois, Mathias** (20 April 2012) *Cancer Research*, 72 12: 3105-3114.

For cancers involving solid tumours, it is usually not the primary tumour but the secondary tumours (metastases) that are lethal. Metastases are mostly spread through the body by the network of lymphatic vessels, which are specialised for absorbing and transporting cells and fluids through the body. We show here that mice lacking the function of Sox18, a gene we previously discovered that promotes lymphatic vessel growth, show dramatically reduced tumour metastasis. This study paves the way for designing drugs to block lymphatic vessel function, suppress tumour metastasis, and help prevent cancer deaths.

# DISORDERS OF SEX DEVELOPMENT, INFERTILITY AND TESTICULAR CANCER

Professor Peter Koopman

DIVISION HEAD

Our research focuses on genes that regulate sex development - whether an embryo develops as a male or a female - and finding how problems with these genes can cause intersex, infertility and testicular cancer.

We are studying SRY, the Y-chromosome maleness gene, and how it controls the genetic and cellular events leading to testis development and male sex determination. We also use molecular genetics tools to identify other sex development genes and to study how these affect sex development, using transgenic and gene-knockout mice to answer questions about gene function. Ultimately, we hope this research will help us to better understand the causes of human disorders of sex development.

We are also interested in how germ cells – the embryonic precursor cells that become sperm in males or eggs in females – receive molecular signals from the testis or ovary in order to choose the corresponding path of sperm or egg development. We have discovered several signalling proteins that direct this decision and are discovering how these signals act. This work is helping us understand the causes of infertility and of germ cell tumours such as testicular cancer, since inappropriate signalling to germ cells during fetal stages is thought to be the genetic basis of these disorders. More broadly, the study of embryo development provides insight into mechanisms of disease and cancer, and provides a molecular and cellular basis for diagnostic and therapeutic approaches, including stem cell therapies.

## Next steps

Understanding the genetic causes of disorders of sex development (DSD) provides a basis for accurate diagnosis, prognosis and clinical management of children with these conditions. An important aim is to connect scientists, patients and doctors involved with DSD so as to demystify these conditions and provide effective personalised treatments.

We will also use our recent laboratory discoveries as a basis for developing new molecular diagnostics for testicular cancer and possibly also new drugs that target gonadal cancers.



# KIDNEY DEVELOPMENT, DAMAGE, REPAIR AND REGENERATION

Professor Melissa Little

Chronic kidney disease affects more than 4000 Australian adults each year, costing the Australian health system in excess of \$2 billion per year. Once a patient has reached end-stage renal failure, chronic kidney disease can only be treated with dialysis or transplantation. This, coupled with the rising rate of chronic kidney disease, is creating an urgent need for scientists to develop novel therapeutic treatments to improve quality of life for patients affected by the disease.

Our laboratory is known internationally for defining the genes involved in normal kidney development and integrating this information with an understanding of how the adult kidney responds to damage. We hope to develop novel approaches to the diagnosis and treatment of both acute and chronic kidney disease and encourage the kidneys to heal themselves.

The risk of kidney failure during our lives is linked to what happens during the development of our kidneys. We have now shown that a mild change in the amount of oxygen available during development is enough to affect eventual kidney structure and function and that this depends upon the timing, severity and duration of the insult. We have also been able to visualise the developing kidney across time to such a high degree of resolution that we can now build mathematical models predicting the outcome in a given circumstance. This will improve our understanding of how variation in kidney development comes about and possibly how we might be able to alter this.

## Next steps

Having shown that number of nephrons, the 'filters' of the kidney, is influenced by the oxygen tension of the embryo during development, our next steps will look further at how environment and genetics interact to affect the predisposition of the adult kidney to disease later in life. We will also advance our mathematical modelling of kidney development in the mouse to see if we can predict the outcomes of certain insults or even predict how we might improve organ growth.

We will continue our work with kidney stem cells, investigating approaches for the recreation of nephron progenitors from adult cells or embryonic stem cells using all available technologies in the stem cell field. And we will begin to investigate bioengineering options for using these cells for nephrotoxicity screening or even the bioprinting of replacement organs. Having reached nephron progenitor, we will also try to develop methods for selectively encouraging these cells to differentiate further into a number of specific kidney cell types.





# MOLECULAR GENETICS AND VASCULAR DEVELOPMENT

Dr Ben Hogan

Our vascular system is comprised of two vital and interconnected networks: a network of blood vessels responsible for distributing blood cells, oxygen, hormones and essential nutrients around our bodies; and a network of lymphatic vessels responsible for carrying lymphatic fluid around the body and draining lymph waste and excess fluid.

However, when the function and development of either of these two networks is affected, so too is our health, with abnormal vascular performance associated with a range of cardiovascular diseases, including vascular malformations, stroke, macular degeneration, lymphoedema, inflammation, and the spread of cancer (known as metastasis).

Despite the importance of this network of vessels, much remains to be discovered about the development and function of both the blood and lymphatic vascular systems. Our research investigates how blood and lymphatic vessels form from pre-existing vessels with a current focus on the formation of new lymphatic vessels in a process called lymphangiogenesis.

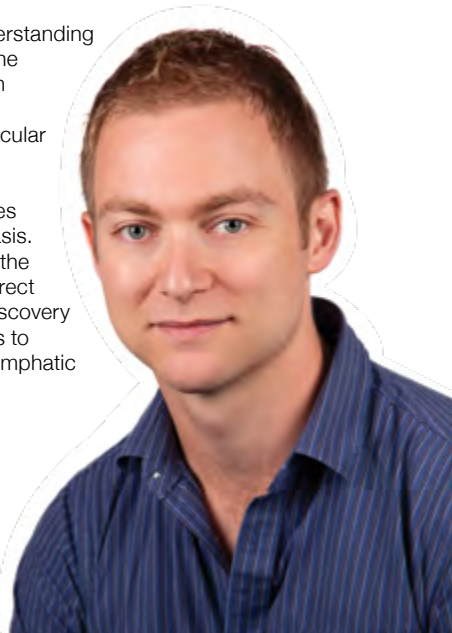
Our work aims to discover new genes and molecular pathways that regulate vascular growth during the development of the embryo. To do this, we use the zebrafish embryo as a model biological system as it is similar to mammalian models and humans, and offers a unique combination of direct imaging techniques, embryological tools and genetic tools for the study of developmental processes.

We have used genetic screening to identify unique zebrafish mutants – zebrafish that have had their genetic information altered via a physical or chemical agent – which fail to form lymphatic vessels. This has led us to discover important new genes and pathways that are needed for healthy lymphatic development and function. The ongoing study of these genes in mammals, and their role in health and disease, will directly inform research from basic developmental biology through to drug discovery and design.

## Next steps

Our next steps will be to scale-up our genetic approaches using high-throughput mutant discovery and characterisation aided by whole-genome resolution genetic mapping. This approach promises to identify the comprehensive system of genes and pathways involved in lymphatic development in vertebrates.

By gaining a better understanding of the genes that form the vascular system, we can directly inform human geneticists studying vascular disorders and provide a base for focused drug design targeting diseases such as cancer metastasis. We are also developing the zebrafish as a tool for direct small molecule (drug) discovery approaches to find ways to manipulate blood and lymphatic vessel growth.



# TRANSCRIPTIONAL REGULATION OF BLOOD AND LYMPHATIC VESSELS

Dr Mat Francois

Lymphatic vessels are a vital component of the vascular system and are essential for immune surveillance and maintaining fluid balance. In the adult, aberrant formation of lymphatic vessels is associated with a wide range of diseases that include chronic inflammatory disorders, such as rheumatoid arthritis, cancer metastasis and lymphoedema.

Under these pathological conditions, the developmental programs that drive lymphangiogenesis become dysregulated. Therefore, understanding the molecular basis that governs normal lymphatic vessel development in the embryo is a prerequisite to further identify novel target genes and develop potential new therapeutic avenues to prevent aberrant development in adults.

Our research identifies and characterises key genetic pathways influencing lymphatic vascular development in the mouse embryo. We are using preclinical mouse models of cancer or lymphoedema in order to validate the central role of developmental programs that are reactivated in these diseases. This work will help us to develop a new class of compounds that will enable the pharmacological management of the lymphatic network, with the view to explore vascular development and establish the basis for drug development.

The experimental strategies we have developed to perform this translational research program rely on a range of tests and involve close collaborations with other IMB scientists and international research groups with experts in zebrafish biology, medicinal chemistry and live imaging.

During the past 12 months we have used genetics to demonstrate the key developmental gene Sox18 is a molecular target that can be addressed to pharmaceutically modulate the growth of the vasculature and help to limit tumour metastasis.

## Next steps

Our next steps include developing a pipeline of assays to identify and characterise small molecules able to block transcription factor activity. By better understanding the molecular mechanisms that drive the transcriptional modulation of lymphatic vessel outgrowth, we can discover novel therapeutic avenues to more effectively treat cancer.



# NUCLEAR HORMONE RECEPTORS AND METABOLIC DISEASE

Professor George Muscat

Nuclear hormone receptors (NRs) are proteins that translate endocrine, metabolic and pathophysiological signals into gene regulation. Our research utilises transgenic mouse models and focuses on understanding the molecular role of NRs (coregulators) and how they control metabolism in muscle, fat and liver in the context of obesity and type 2 diabetes.

Epidemiological evidence points to associations between metabolic disease and cancer. Along these lines we collaboratively examine the molecular role of NRs in breast cancer. We use mouse models and human cohort studies to gain insights into obesity, type 2 diabetes and cancer, which we can then use to better understand human health and disease.

We have previously shown that mice with decreased and dysfunctional expression of an NR called Ror alpha are resistant to (high fat) diet-induced obesity. Our studies during the past 12 months pursued this finding further and by exploring the regulation of glucose metabolism, we identified the important role Ror $\alpha$  plays in controlling insulin sensitivity and glucose tolerance in skeletal muscle.

In addition, our work has produced transgenic mouse lines with muscle-specific expression of an activated form of the nuclear receptor NOR-1. These investigations have demonstrated that NOR-1 signalling controls skeletal muscle reprogramming and exercise capacity. Also, the insights obtained from the studies in lean, obese and diabetic murine models are helping our team to profile the expression of the NRs, NR-associated cofactors and metabolic genes in overweight and obese children before and after introducing a nutrition and lifestyle program. This will enable the translation of this basic research into outcomes to improve childhood and human health.

## Next steps

Our next steps are to examine how Ror $\alpha$  regulates fat content, and whether Nor-1 mediates resistance to diet induced obesity and insulin resistance. We hope to therapeutically exploit these pharmacologic NR targets for the growing health epidemics of obesity, type 2 diabetes and cancer.

In our work to help develop new drugs and diagnostics for breast cancer and identify new targets that will help reduce the risk of metastasis, we will direct our activities towards producing mammary-specific Nur77 and PRMT6 mice to validate the role of Nur77 and this epigenetic factor on the onset/incidence of breast cancer, respectively.

Our laboratory has fostered cooperative multidisciplinary teams to help translate our expertise in these areas into outcomes for the community. This includes the Obesity Research Centre, directed by Professor George Muscat, and a national consortium to study breast cancer. These initiatives will provide a range of opportunities for the training and development of students and postdoctoral fellows.



# MELANOGENIX AND SKIN CANCER

Associate Professor  
Rick Sturm

The skin is the human body's largest organ and is constantly working to protect itself by adapting to a range of internal and external factors, such as chemicals, temperature and ultraviolet radiation (UVR). Our research investigates variations in the genes and melanocyte cell processes that produce pigment and determine an individual's skin type, hair colour and eye colour and how this affects their sensitivity to sun exposure. We are studying how melanocytes develop into specialised cells within the skin, and how the interaction of melanocytes with keratinocytes after UVR exposure modifies the tanning response, causing our skin to darken to varying degrees.

Knowing the genetic basis of ultraviolet-sensitive skin types will allow us to better understand the changes that occur in skin pathology to improve public health and awareness campaigns for the prevention and early detection of skin cancers, especially within those Australians who are genetically most at risk of being diagnosed with the disease in their lifetime.

Of major interest to our laboratory is the role of the protein melanocortin-1 receptor (MC1R), which is active on the surface of melanocyte cells and plays a role in stimulating melanin production. MC1R gene variants are common in the Australian population and these determine a person's skin phototype and response of the skin to UV damage.

We are investigating genetic associations of known and previously unknown candidate genes with skin and hair colour to develop a full appreciation of how differences in these physical traits come about. In collaborative efforts we are also studying genes involved in freckling, mole shape, size and colour in the hope of discovering new ways to genetically screen for, diagnose and treat melanoma in at-risk Australians.

## Next steps

We know fair skinned individuals are more susceptible to sun damage, however, the relationship between sun exposure, skin colour and skin cancer formation is less clear. A major regulator of the response of skin to UV light is the MC1R protein expressed by the cells that make the melanin pigment involved in the tanning response. It is essential to understand the biology and complex interactions of this receptor that directs tanning and susceptibility to skin cancer.

Our next steps are to work in partnership with our collaborators to conduct a clinical trial with 1200 phenotyped volunteers for melanoma risk factors that will undergo a detailed assessment of mole count, size, colour, distribution and provide DNA stocks suitable for genetic association analysis, with the findings to aid in future genetic risk prediction.



## DEVELOPMENTAL GENES AND HUMAN DISEASE

Associate Professor  
Carol Wicking

Defects arising from abnormal embryonic development are a major cause of infant mortality and childhood disability. Ciliopathies form a class of genetic disease that arise in the developing embryo as a result of dysfunction of the primary cilium, a recently recognised cellular organelle with a pivotal role in developmental signalling. These diseases are characterised by a variable set of features, including extra fingers and toes (polydactyly), kidney disease, obesity, retinal degeneration, and skeletal, craniofacial, heart and brain anomalies.

My laboratory has been focused on analysis of mouse and cell-based models of human ciliopathies, with a particular focus on those characterised by skeletal abnormalities. The mouse models we work on have primarily arisen through random forward genetic screening approaches and have provided insight into the function of the primary cilium and the underlying mechanism of disease. In addition, we have used engineered mouse models of the Hedgehog developmental signalling pathway to study the craniofacial defects associated with ciliopathies, providing insight into common defects such as cleft lip and palate.

More recently we have begun to search for additional genes involved in the skeletal ciliopathies using a gene discovery approach in human patient cohorts. This work involves collaboration with clinical geneticists and genomics researchers both nationally and internationally, and uses state-of-the-art next generation sequencing approaches. This collaborative network enables us to cover the full gamut of ciliopathy research, from gene discovery in patient cohorts to functional studies in animal and cell-based models.

### Next steps

Through our network of clinical geneticists and genomic scientists, we will continue to discover new genes and mutations in ciliopathies, and use functional studies to uncover the mechanism of action at a whole organism and cellular level. Our research has the potential to influence diagnosis, screening and management of skeletal ciliopathies, and in the longer term may contribute to therapeutic approaches for ciliopathy associated abnormalities.



## TISSUE REPAIR AND CANCER

Professor Brandon Wainwright

Skin cancer is a major public health issue in Australia, with the treatment of non-melanoma skin cancer costing our community more than \$264 million each year. Moreover, brain tumours remain the most common cause of cancer related death in children and of these, medulloblastoma is the most commonly diagnosed.

Our laboratory has made great progress in understanding the genetic pathways behind the most common form of skin cancer in Australia, Basal Cell Carcinoma (BCC), and medulloblastoma, a type of brain tumour that occurs predominantly in children.

Having mapped and isolated the Naevoid Basal Cell Carcinoma Syndrome (NBCCS) gene called Patched, which is the driver for a medical condition where affected individuals have a predisposition for developing BCC and medulloblastoma, we were able to identify the Patched gene as a controller of a molecular signalling pathway called the Hedgehog pathway.

The Hedgehog pathway is a set of genetic mutations that contribute to the development of a wide range of tumour types, including lung, pancreatic and ovarian cancer. By examining this pathway and how it interacts with other genetic pathways, our scientists have gained a better understanding of the normal development of the skin and cerebellum, a part of the brain that controls motor functions.

By manipulating the strength of the Hedgehog pathway we believe stem cell populations can be expanded or can be induced to become cancerous.

During the past 12 months, we examined the Hedgehog pathway and how it interacts with other genetic pathways to gain a better understanding of the normal development of the skin and cerebellum and the tumours derived from those organs. We also began to use small molecule drugs to examine novel treatments for both medulloblastoma and BCCs of the skin. Translating our research findings in both tumour types will have a significant impact on improving the health of all Australians affected by these diseases.

### Next steps

Next steps for our skin cancer research include proving that the cells generated by manipulating the Hedgehog genetic pathway are true stem cells and can repair and regenerate skin after insults such as wounds or burns. By better understanding the relationship between stem cells and skin cancer we will be better positioned to prevent and treat this disease and the findings will likely also provide a paradigm for other cancer types.

Next steps for our medulloblastoma research include proving that we can block tumour growth by manipulating a number of genetic pathways we have linked to the Hedgehog signalling pathway. We hope this will open up a wider range of therapeutic approaches than those currently available for children affected by this disease.



# INFECTION AND INNATE IMMUNITY

Associate Professor  
Matt Sweet

Our bodies have an innate immune system that protects us from harmful microbes, acting as an alarm system for the human body and helping to initiate repair when damage occurs. But some agents that cause infectious diseases are able to overcome this defence system.

Macrophages are a remarkably dynamic type of white blood cell that are important for innate immune responses. These cells are able to directly destroy microbes and also trigger inflammation to prevent infections spreading. However, many important human pathogens, such as HIV and tuberculosis, actually live within macrophages to avoid the immune response. Our research investigates how macrophages destroy microbes and how important pathogens subvert these responses to survive within macrophages.

During the past 12 months, we discovered that macrophages utilise zinc to kill microbes. Moreover, we discovered that *Salmonella Typhimurium*, which is a bacterium that causes severe gastrointestinal disease leading to high mortality rates around the world, evades this response. We also found that a bacterium that causes urinary tract infections is able to kill macrophages and we hope these findings may ultimately lead to new strategies to treat infectious diseases caused by bacteria.

In addition to providing protection against infectious diseases, the innate immune system can trigger inappropriate inflammation, which contributes to many serious acute and chronic inflammatory diseases such as septic shock, atherosclerosis and rheumatoid arthritis. Our laboratory also studies the genes and pathways leading to inappropriate inflammatory responses in macrophages. In 2012, we discovered proteins that promote excessive macrophage inflammatory responses. We are working to discover inhibitors that block the activity of these proteins as they may provide new avenues for anti-inflammatory drugs.

## Next steps

Our next steps include more precisely determining the molecular mechanisms by which macrophages utilise zinc as part of their anti-bacterial response, and how *Salmonella* evades this response.

We will also work to characterise the molecular mechanisms by which strains of bacteria causing urinary tract infections kill macrophages, and determining the relevance of this process to disease severity.

Functionally screening novel human genes for involvement in macrophage antimicrobial pathways will also be a priority, as by doing so we should identify new pathways that are important for control of infectious disease.

Furthermore, we will determine the mechanisms by which specific human proteins promote macrophage-mediated inflammation. By doing so, we may be able to develop new strategies for the treatment of inflammation-related diseases such as septic shock, rheumatoid arthritis and inflammatory bowel disease.



IMB's zebrafish facility

**Joint appointments and affiliates foster research collaborations between IMB and other institutes and schools at The University of Queensland and around the world. They are actively involved in sharing resources and facilities, supervising students and supporting IMB initiatives.**

# JOINT APPOINTMENTS AND AFFILIATES

## UQ joint appointment

Professor Philip Hugenholtz  
*School of Chemistry and Molecular Biosciences*

## Honorary and adjunct appointments

Dr Peter Beattie  
*Former Premier of Queensland*

Professor Frances Brodsky  
*University of California (US)*

Professor Kevin Burrage  
*QUT / Oxford University (UK)*

Dr Nathan Cowieson  
*Australian Synchrotron (Vic)*

Professor John Funder  
*Prince Henry's Institute (Vic)*

Professor Frank Gannon  
*Queensland Institute of Medical Research*

Professor Yoshihide Hayashizaki  
*RIKEN (Japan)*

Professor David Hume  
*The Roslin Institute (Edinburgh)*

Dr Gary Leong  
*Mater Children's Hospital (Qld)*

Professor Sangkot Marzuki AM  
*Eijkman Institute for Molecular Biology (Indonesia)*

Professor John Mattick AO  
*Garvan Institute (Sydney)*

Dr Grant Montgomery  
*Queensland Institute of Medical Research*

Professor Nicos Nicola  
*Walter and Eliza Hall Institute of Medical Research (Vic)*

Mr Ken Roberts  
*Former Managing Director of Wellcome Australasia Limited*

Dr Greg Smith  
*SciVentures Investments Pty Ltd (Vic)*

Professor Peter Turnbull  
*Chairman of QFAB Bioinformatics (Qld)*

Professor Peter Visscher  
*Queensland Brain Institute*

Dr Dagmar Wilhelm  
*Monash University (Vic)*

## UQ affiliates

Dr Mikael Boden  
*School of Chemistry and Molecular Biosciences*

Professor Matthew Brown  
*Diamantina Institute*

Dr Richard Clark  
*School of Biomedical Sciences*

Dr Norelle Daly  
*IMB / James Cook University*

Dr Marcel Dinger  
*Diamantina Institute*

Professor Ian Frazer  
*Translational Research Institute*

Associate Professor Stuart Kellie  
*School of Chemistry and Molecular Biosciences*

Professor Bostjan Kobe  
*School of Chemistry and Molecular Biosciences*

Professor Alan Mark  
*School of Chemistry and Molecular Biosciences*

Associate Professor Frederic Meunier  
*Queensland Brain Institute*

Dr Mehdi Mobli  
*Centre for Advanced Imaging*

Dr David Pennisi  
*School of Biomedical Sciences*

Dr Johan Rosengren  
*School of Biomedical Sciences*

Associate Professor Joseph Rothnagel  
*School of Chemistry and Molecular Biosciences*

Dr Kate Stacey  
*School of Chemistry and Molecular Biosciences*

Associate Professor Peter Thorn  
*School of Biomedical Sciences*

Professor Istvan Toth  
*School of Chemistry and Molecular Biosciences*

Associate Professor Christine Wells  
*Australian Institute for Bioengineering and Nanotechnology*

Professor Paul Young  
*School of Chemistry and Molecular Biosciences*

Professor Nicholas Fisk  
*Faculty of Health Sciences*

Dr Alison Pettit  
*UQ Centre for Clinical Research*

Dr Liza Raggatt  
*UQ Centre for Clinical Research*



Members of the 2012 SIMBA executive committee, IMB's student association

# PERFORMANCE HIGHLIGHTS

## Research training

Our research scientists in training make an important contribution to our work and achievements. IMB's postgraduate program is designed to give students a strong start to their careers by surrounding them with the best researchers, facilities, and support services. As active members of our laboratory teams, students are encouraged to expand their skillsets, seek answers to the hard questions, explore their scientific potential, and make the most of student life at UQ.

2012 was a year of sustained effort and focus for IMB's postgraduate office, specifically within the areas of international student recruitment and future student engagement. We also provided extensive support to our 86 continuing students and 42 new students as we introduced the UQ Career Advantage PhD program to help current PhD students to accelerate career development.

### Recruitment highlights:

- › initiated student recruitment campaigns in China, Europe, South East Asia and Brazil
- › welcomed 42 new PhD and MPhil students, 75 per cent of whom are international students, from 20 different countries, including Peru, Serbia, Macedonia and Venezuela
- › supported all commencing PhD and MPhil students to secure full scholarships for their studies prior to commencing.

### Engagement highlights:

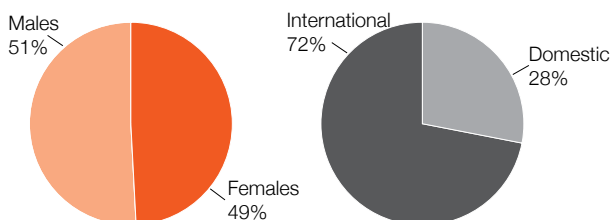
- › awarded 17 promising second and third year students the opportunity to work in our laboratories for eight hours per week during semester through IMB's Undergraduate Research Scholarship Scheme
- › awarded 28 summer students the opportunity to undertake projects at IMB during the 2011/2012 summer semester
- › hosted 30 international visiting students, primarily from Europe, who joined IMB laboratories as occupational trainees
- › hosted 20 Honours students throughout the year who completed their research at IMB
- › welcomed two secondary school students from Brisbane Boys College to complete a project as part of their assessment
- › participated in IMB's community engagement activities during UQ's Research Week, Market Day and Open Day

- › coordinated the IMB Science Ambassadors program, which saw our 25 IMB Student Ambassadors engage with hundreds of future students and community members at 15 events throughout the year, including tours of the Institute, meet and greet sessions and recruitment events
- › hosted student support workshops in a range of professional development areas, including advanced statistics, communications, commercialisation, stress management and career planning
- › supported IMB's student association (SIMBA) to bring staff and students together for social and networking opportunities.

### Performance highlights:

- › conferred 30 PhD and MPhil students
- › congratulated IMB graduate Dr Martin Smith on becoming UQ's 10,000th PhD graduate
- › congratulated Dr Johanna Barclay for being awarded scientific journal *Endocrinology's* Student Award for Outstanding Publication in 2011 (awarded June 2012)
- › congratulated 2012 graduate, Dr Praveer Gupta (Fairlie Lab), who was part of the team awarded a Biotech Ignition Grant (BIG) by the Government of India's Biotechnology Industry Research Assistance Council to establish a small biotech company
- › commended Tam Duong (Francois Lab) for winning best poster presentation at the 14th International EMBL PhD Symposium
- › congratulated Yu Leng Phua (Little Lab) who was selected from more than 5000 applicants to present his abstract at the American Society of Nephrology Kidney Week 2012 conference
- › commended 2011 graduating Honours student Hilary Martin who was awarded the Amgen Australia Award for research excellence
- › congratulated student Wilko Duprez who won the People's Choice Award at UQ's 3 Minute Thesis (3MT) competition.

## Postgraduate student profile





Dr Martin Smith was announced as UQ's 10,000th PhD conferral



IMB PhD students attending UQ's December graduation ceremony

# LEARNING / DISCOVERY / ENGAGEMENT

## PhD conferrals

NAME	SUPERVISOR	DEGREE	THESIS TITLE	DESTINATION
Kalyani Akondi	Alewood	PhD	Characterisation and SAR studies of novel and selected $\alpha$ - and $\mu$ - conotoxins	India
Pierre Cattenoz	Mattick	PhD	Characterisation of Alu element expression and A-to-I RNA editing in human and mouse	Institut de Génétique et de Biologie Moléculaire et Cellulaire, France
Lai Yue (Angeline) Chan	Craik	PhD	Engineering and discovery of bioactive disulfide-rich peptides	Craik Lab, Institute for Molecular Bioscience
Michael Clark	Mattick	PhD	Transcriptional complexity and post-transcriptional regulation of long noncoding RNAs	Taft Lab, Institute for Molecular Bioscience
Lena Constantin	Wainwright	PhD	The role of Dicer in cerebellar development and Hedgehog-mediated medulloblastoma	Wainwright Lab, Institute for Molecular Bioscience
Marianne Diaz	Muscat/Leong	PhD	Ski-dependent regulation of metabolism in skeletal muscle and adipose tissue: implications for obesity and type 2 diabetes	Cook Medical Australia, Brisbane
Tram Anh Do	Fairlie	MPhil	Short helix-constrained peptides as RSV fusion inhibitors and vaccine candidates	Fairlie Lab, Institute for Molecular Bioscience
Leith Fremlin	Capon	PhD	Technology and biodiscovery: using modern technologies and methods to tackle the challenges of biodiscovery	Bruker Daltonics, New South Wales
Praveer Gupta	Fairlie	PhD	Towards HDAC selective inhibitors	PAHL Nanotherapeutics, India
Hui Ping (Rhonda) Kan	Wainwright	PhD	The role of nMyc and cMyc in skin development and in Hedgehog pathway induced tumorigenesis	Brisbane-based biotechnology company
Darren Korbie	Mattick	PhD	The identification and characterisation of novel RNAs in the mouse transcriptome	UQ's Australian Institute for Bioengineering and Nanotechnology
Oleksiy Kovtun	Alexandrov	PhD	All in vitro platform for rapid protein engineering and analysis based on Leishmania tarentolae	Collins Lab, Institute for Molecular Bioscience
Christina Kulis	Smythe	PhD	Substrate-based design of SHP-1 inhibitors	Smythe Lab, Institute for Molecular Bioscience
Lindsey McFarlane	Wilhelm	PhD	Investigating the mechanisms of small non-coding RNA-directed gene regulation in teleost fish	Adelaide
Robert McLeay	Bailey	PhD	Predicting tissue-specific transcription factor binding and gene expression in silico	DoseMe Pty Ltd, Brisbane
Vicki Metzis	Wicking	PhD	The role of Patched-1 in mammalian facial dysmorphogenesis	Wicking Lab, Institute for Molecular Bioscience
Carolin Offenhöuser	Stow	PhD	SNARE-mediated secretion and late endosomes in macrophages	Queensland Institute of Medical Research, Brisbane
Basar Oku	Craik	PhD	Novel cyclotide genes and their processing mechanisms	Brisbane
Sandy Pineda Gonzalez	King	PhD	Probing the chemical diversity of venom from the Australian funnel-web spider Hadronyche infensa	King Lab, Institute for Molecular Bioscience
Fabien Plisson	Capon	PhD	Bioassay-guided and computer-aided investigation of marine-derived kinase inhibitors: applications to control neurodegenerative disorders	Fairlie Lab, Institute for Molecular Bioscience
Aaron Poth	Craik	PhD	Proteomics as a tool for rapid detection and characterisation of cyclic peptides: a path to discoveries in cyclotide biosynthesis and evolution	Craik Lab, Institute for Molecular Bioscience
Changjin Shin	Ragan	PhD	Diversity of mammalian interactome in different biological contexts	SK Telecom, South Korea
Ranee Singh	Fairlie	PhD	Molecular pharmacology of C3aR modulators	Khon Kaen University, Thailand
Elizabeth Skippington	Ragan	PhD	Lateral genetic transfer: bias, barriers and the construction of genetic exchange communities	University of Indiana, USA
Martin Smith	Mattick	PhD	Revising the evolutionary imprint of RNA structure in mammalian genomes	Garvan Institute, Sydney
Phillippa Smith	Craik	PhD	PEPLINK: a fragment-based method for screening peptides as drug leads	Office of the Chief Scientist, Canberra
Rathi Thiagarajan	Grimmond	PhD	A transcriptome atlas of the developing mouse urogenital system	University of California, San Diego, USA
Soumini Vijayarathy	Capon	PhD	Synthesis and stereochemical studies towards bioactive marine scaffolds	CSIRO - Plant Industry Division, Brisbane
Simone Vink	Alewood	PhD	Investigation of novel bioactive peptides from Australian venomous animals	Protagonist Therapeutics Inc., Brisbane
Winnie Waudo	Hankamer	PhD	Developing metabolic fingerprinting strategies to decipher algal hydrogen production	Melbourne-based power company



# PERFORMANCE HIGHLIGHTS

## Grants

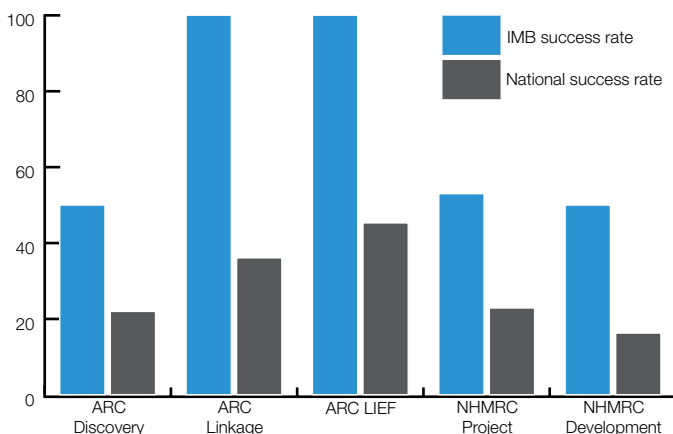
Competitive grant funding represented more than 60 per cent of IMB's total income in 2012, reflecting the high quality and scientific importance of our research.

During the past 12 months, we performed exceptionally well in major competitive grant rounds offered by the Australian Research Council (ARC), National Health and Medical Research Council (NHMRC) and Queensland Government. IMB achieved well above national average success rates, recording 28 per cent higher than the national average success rate for ARC Discovery Project grants, and 30.1 per cent higher than the national average success rate for NHMRC Project grants.

### In 2012, funding commenced for the following grants:

- › 10 ARC Discovery Project grants totalling \$3,740,000
- › 4 ARC Linkage grants totalling \$1,351,000
- › 2 ARC Linkage Infrastructure, Equipment and Facilities (LIEF) grants totalling \$527,000
- › 17 NHMRC Project grants totalling \$8,978,815
- › 1 NHMRC Development grant totalling \$417,340.

## Competitive grant success rates



## Fellowships

IMB Fellows are supported by a range of competitive fellowship schemes awarded by the ARC, NHMRC, UQ and Queensland Government.

Thanks to the support of these organisations, our Fellows are able to undertake research that is recognised as some of the best in their respective fields, and that has the potential to benefit global scientific progress and improve the health of all Australians.

### Total competitive fellowships held in 2012:

- › 2 ARC Australian Laureate Fellows and Federation Fellows
- › 2 ARC Future Fellows and Queen Elizabeth II Fellows
- › 4 ARC Discovery Early Career Researcher Awards (DECRA) Fellows and Australian Postdoctoral Fellows
- › 2 NHMRC Australia Fellows
- › 10 NHMRC Research Fellows
- › 1 NHMRC Career Development Fellow
- › 9 NHMRC Early Career Fellows.

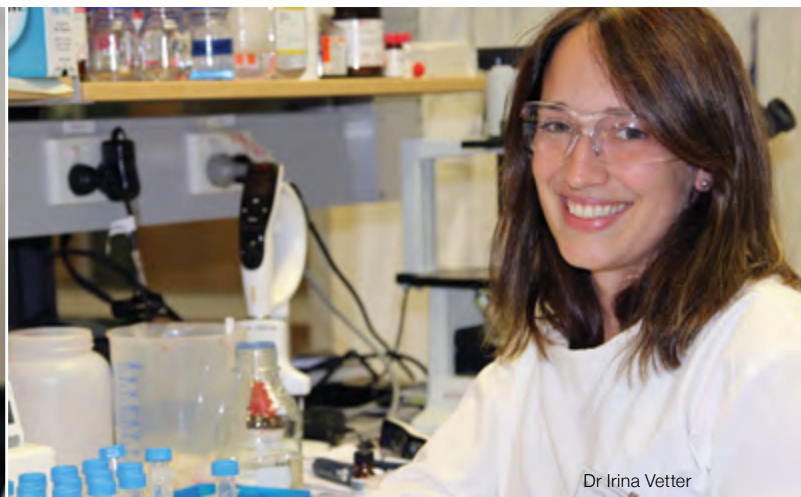
### Fellowships commencing in 2012:

- › 4 ARC Future Fellows totalling \$2,696,012
- › 3 ARC Discovery Early Career Researcher Award (DECRA) Fellows totalling \$1,125,000
- › 5 NHMRC Research Fellows totalling \$3,790,170
- › 2 NHMRC Early Career Fellows totalling \$646,224.





Dr Ryan Taft



Dr Irina Vetter

# LEARNING / DISCOVERY / ENGAGEMENT

## Awards

Our researchers do great science every day, and awards play an important role in publicly acknowledging our scientific excellence within the research community and beyond.

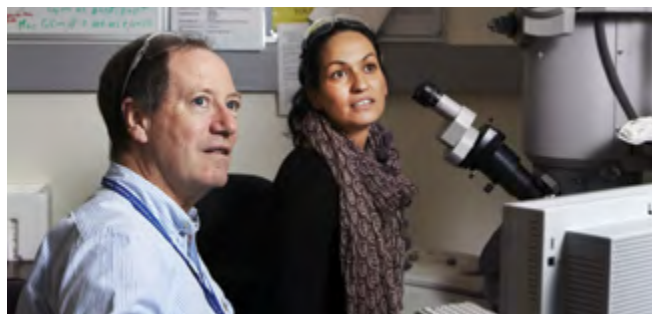
In 2012 we were fortunate to celebrate many achievements as our research staff were awarded for their sustained effort and commitment to pursuing research that matters.

### 2012 IMB award highlights included:

- ▶ Professor David Craik received the prestigious Josef Rudinger Memorial Lecture Award from the European Peptide Society for his on going contributions to the field of peptide chemistry.
- ▶ Dr Josh Mylne won the 2012 Peter Goldacre Award from the Australian Society of Plant Scientist for his unusual finding that the drug-like protein, SFT1, begins life buried in a sunflower seed protein.
- ▶ Dr Ryan Taft was awarded an \$85,000 grant to identify the genes that underlie rare paediatric brain disorders as part of the UQ Foundation Research Excellence Awards.
- ▶ Dr Irina Vetter was awarded a \$75,000 Ramaciotti Foundation grant for outstanding biomedical research in understanding the fundamental molecular basis of sensory perception.
- ▶ Professor Richard Lewis' cone snail research was selected to feature in NHMRC's *Ten of the Best Research Projects 2011* (announced in February 2012).
- ▶ Professor Brandon Wainwright's skin cancer and brain tumour research was selected to feature in NHMRC's *Ten of the Best Research Projects 2012*.
- ▶ Dr Andrea Burgarcic won a UQ Teaching and Learning Week Award for her active participation in developing innovative research based teaching activities.
- ▶ Professor Rob Capon received a highly commended in the 2012 UniQuest Trailblazer competition for his entry 'Ecological solution for an ecological disaster.' IMB PhD student Ms Anh Do also participated in the competition and was awarded the Pitching Excellence Award for her entry 'Easy subcutaneous injection for rodents'.



Professor David Craik (centre) received the Josef Rudinger Memorial Lecture Award at the 32nd European Peptide Symposium. *Image credit: European Peptide Society*



Professor Brandon Wainwright's (left) research was selected as NHMRC's *Ten of the Best Research Projects 2012*. *Image credit: NHMRC and James Braund*



Professor Richard Lewis' (centre) research was selected as NHMRC's *Ten of the Best Research Projects 2011* (announced February 2012). *Image credit: NHMRC*



IMB's UniQuest team (L-R): Dr Stephen Earl, Dr Rachel De las Heras, Dr Mark Ashton and Dr Amanda Smith

# PERFORMANCE HIGHLIGHTS

## Commercialisation

During the past decade, IMB has worked to develop a strong discovery pipeline, with the goal of ensuring our research has the potential to provide social and environmental benefits to the community through commercialisation. This year commenced with the transfer of the Institute's commercialisation functions from IMBcom Pty Ltd to UniQuest Pty Ltd.

UniQuest is one of Australia's leading research commercialisation companies, specialising in global technology transfer and facilitating access for all business sectors to world-class university expertise, intellectual property and facilities. Established by UQ in 1983, the company has since grown into a highly regarded and successful self-funded enterprise that provides the critical mass of cross disciplinary skills required to translate IMB's intellectual property and expertise in to commercial outcomes.

During the first half of 2012 work was undertaken to transfer IMB's commercialisation activities to UniQuest. This included the management of IMB's intellectual property (IP) portfolio, start-up companies and the transfer of three key members of the IMBcom staff under the leadership of Dr Mark Ashton, UniQuest's Manager of Innovation and Commercial Development.

During the second half of the year, UniQuest carried out a review of IMB's IP portfolio and expanded IMB's engagement initiatives, representing the Institute at a number of key meetings with industry representatives, including Elanco, Janssen, Pfizer, Agilent, BioProton and the Fraunhofer Research Institute. International events such as BIO2012, BioPartnering Future Europe and AusBiotech also proved valuable opportunities to expand IMB's global industry engagement.

Much of UniQuest's work during the past 12 months has been to strengthen the internal collaboration between the commercialisation team and IMB's 32 laboratories, seeking opportunities to increase industry engagement and package selected research capabilities and IP for presentation to potential investors or licencing partners.

To further support this, we seek to educate the Institute's postgraduate and early career researchers about how they can use technology transfer to ensure their research has an impact beyond their lab bench. One way this was achieved in 2012 was through UniQuest's two commercialisation workshops, which provided researchers with the opportunity to receive expert advice and guidance from professionals working in the pharmaceutical, biotechnology, investment, intellectual property and research sectors.

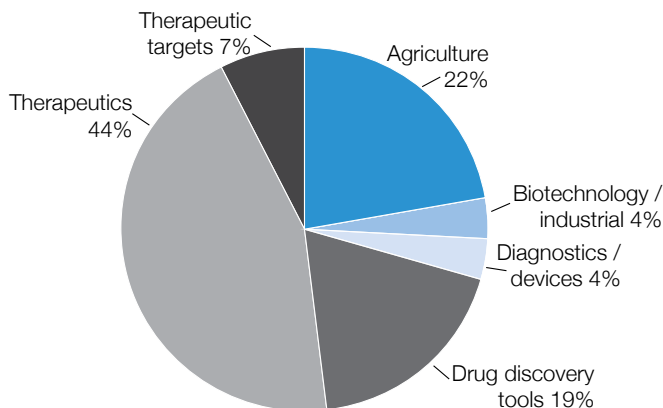
In 2012, UniQuest helped secure the following agreements for IMB research: a collaboration with international pharmaceutical company Janssen to discover new pain therapies; a research and development contract with US biotechnology company Viral Genetics to collaborate on an innovative biofuel production system and an expansion of our metabolic disease research collaboration with Pfizer.

Other significant research and development agreements were secured with Adenium, KBR, TPI and SYNthesis; and ARC linkage agreements were signed with BioProton, Australian Red Cross, and BioAustralis. Additionally, the IMB start-up company Protagonist Therapeutics Inc. was successful in negotiating a new collaboration agreement with Danish biotechnology company Zealand Pharma, and an expansion of an existing agreement with Ironwood Pharmaceuticals in the US.

The intellectual property portfolio of IMB was further strengthened in 2012 with the filing of seven new provisional patent applications and the granting of three patents in key jurisdictions.

UniQuest will continue to work alongside IMB's research teams to pursue commercial opportunities in the areas of human therapeutics, including new treatments for inflammation, pain, metabolic disorders, infection and cancer; in agriculture, including insecticides, pesticides and agents for the control of cane toads; and in biotechnology, including microalgae based biofuels and hydrogen production.

## Patent portfolio by research area





Artworks from IMB artist-in-residence Joannah Underhill's *Envisaging the Invisible* collection

# LEARNING / DISCOVERY / ENGAGEMENT

## Scientific publications

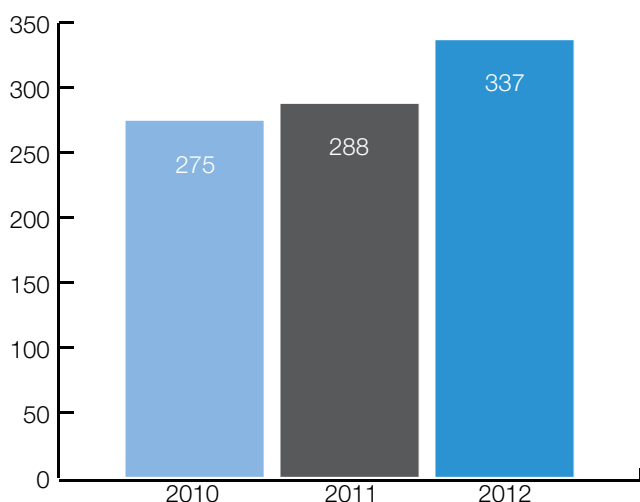
The impact and expertise of IMB's research is evident in the high number of publications our staff and students have contributed to during the past 12 months.

IMB researchers publish with the primary purpose of sharing their discoveries in leading scientific journals for the benefit of their peers around the world. Their findings expand our understanding of the world around us and add value to other research being conducted within their focus areas.

In 2012, we published 337 peer reviewed journal articles and 382 total publications, including books, book chapters and conference papers. This included 30 high impact peer reviewed publications in journals with an impact factor greater than 10.

IMB researchers were published in a number of leading scientific journals in 2012, including: *Nature Reviews Molecular Cell Biology*; *Nature*; *Cell*; *Science*; *Nature Biotechnology*; *Nature Chemistry*; *Nature Cell Biology*; *Developmental Cell*; *Angewandte Chemie - International Edition*; *Acta Crystallographica Section D-Biological Crystallography*; *Hepatology*; *Journal of Cell Biology*; *EMBO Journal*; *Plant Cell*; *PLOS Genetics*; and *Diabetes*.

## Total peer reviewed publications



## Occupational health and safety

IMB's occupational health and safety (OH&S) program is a crucial component of its day-to-day operations.

In 2012, IMB passed all mandatory compliance audits for the Department of Agriculture, Fisheries and Forestry (DAFF) Biosecurity and the Office of Gene Technology Regulator (OGTR).

The Institute also introduced new policies and procedures to reflect changes made to the Queensland Work Health and Safety legislation in regards to chemical manifest requirements and carcinogen handling and storage, among others. In partnership with UQ, IMB helped to develop a University-wide guideline for users of restricted and prohibited carcinogens listed in the new legislation and assisted several IMB groups using these materials to apply for the relevant approvals.

Reviews were also undertaken for IMB's chemical purchasing and inventory system, and the X-ray and unsealed radiation safety and protection plans. As a result, changes were made to improve accountability and traceability of chemicals purchased. Moreover, renovations and restructuring of the Institute's X-ray facility were carried out and the facility recertified for use.

During the past 12 months, IMB and industry partners developed the Solar Biofuels Research Centre at UQ's Pinjarra Hills site. In addition to maintaining IMB's compliance with all regulatory requirements in 2013, expanding and refining safety systems at this centre will remain a key focus for IMB's OH&S team as the centre develops further in the year to come.

### OH&S highlights included:

- › inducted 307 visitors, staff and students into IMB
- › inducted 192 external contractors into the Queensland Bioscience Precinct
- › trained more than 40 new fire wardens
- › achieved all stipulated UQ OH&S objectives for 2012, including an average 97 per cent compliance with UQ general workplace safety training, and an average 96 per cent for UQ fire safety online training
- › subsidised the purchase of 25 pairs of prescription safety glasses for personnel working in IMB laboratories.



IMB's 2012 Toshiya Yamada Memorial Lecture (L-R): Linda Yamada, Professor Konrad Basler and Professor Brandon Wainwright



Professor Sean Grimmond shares his pancreatic cancer research breakthrough on TODAY (Nine Network)



# PERFORMANCE HIGHLIGHTS

## Scientific engagement

IMB's researchers play an active role within Australia's scientific and medical research communities here and abroad. Their contributions keep the Institute at the forefront of scientific advancement, sharing our progress on the global stage and welcoming new opportunities to collaborate with expert colleagues around the world.

During the past 12 months, our researchers have made the following contributions to, and were acknowledged for their achievements by the scientific and medical research communities.

### Appointment highlights:

- › Professor Melissa Little was appointed to the NHMRC McKeon Review expert panel, which is responsible for recommending a 10-year strategic health and medical research plan for the nation.
- › Professor Peter Koopman was appointed to the Council of the Australian Academy of Science.
- › Professor Peter Koopman was appointed editor-in-chief of scientific journal *Sexual Development*.
- › Professor Alpha Yap was appointed to the editorial board of scientific journal *Developmental Cell*.
- › Associate Professor Rick Sturm was elected to the steering committee of the International Society for Melanoma Research.
- › Associate Professor Rohan Teasdale was appointed to the committee of the Australian Phenomics Network.
- › Professor Rob Capon was appointed to UQ's Research Higher Degree Committee, and was elected as the representative for all UQ institutes on the UQ Academic Board and its respective standing committees.
- › Associate Professor Carol Wicking was appointed to the ANZ Trustees Queensland expert scientific and medical advisory panel.

### Presentation and event highlights:

- › Professor Brandon Wainwright participated in an expert panel discussion at the 17 August launch of NHMRC's *Ten of the Best Research Projects 2012*, which featured his skin cancer and brain tumour research.
- › Professor Melissa Little was the distinguished speaker at the Harvard Stem Cell Institute's Kidney Program Think Tank in October.

- › Professor Jennifer Stow organised and co-chaired the 12th Hunter Meeting in March, Australia's premier cellular biology meeting.
- › Professor Brandon Wainwright presented a guest lecture on 17 September at the University of Witwatersrand's Medical School in Johannesburg as part of his role as a member of the University's Sydney Brenner Institute for Molecular Bioscience Scientific Advisory Committee.
- › Dr Ryan Taft was the invited speaker for the UQ Research Week Engagement Dinner held at the Brisbane Convention Centre on 20 September.
- › IMB senior researchers delivered 196 lectures to UQ undergraduate students.
- › IMB hosted the annual Toshiya Yamada Memorial Lecture on 13 November, presented this year by Professor Konrad Basler on the topic of 'β-caterin mediated transcription'. The lecture is held in memory of former IMB member Dr Toshiya Yamada and was attended by the Yamada family and all IMB staff and students.
- › IMB hosted more than 40 guest speakers during the year as part of IMB's Friday Seminar Series.
- › IMB registered 310 participants and hosted 11 guest speakers and many industry partners as part of this year's Division of Chemistry and Structural Biology symposium on 6-9 November, which focused on the Australian biotech industry.
- › IMB's early career researchers (ECR) organised and hosted the 3rd Brisbane ECR poster symposium held on 20 November, which attracted 72 posters and 150 participants from institutes across southeast Queensland.
- › Dr Nick Hamilton and Lanna Wong organised the 2012 Winter School in Mathematical and Computational Biology, an event hosted annually by IMB. Held from 2-6 July, the event attracted 30 expert speakers and 310 participants from 56 Australian and international institutions.
- › Professor Jenny Martin spoke on the past and future of women in biochemistry at the International Union of Biochemistry and Molecular Biology's (IUBMB) 22nd congress held in Spain in September.
- › Professor David Craik was chair of the 2nd International Conference on Circular Proteins in October.



Launch of Joannah Underhill's collection at Brisbane's Gallery of Modern Art



IMB artist-in-residence Joannah Underhill and Dr Nick Hamilton

# LEARNING / DISCOVERY / ENGAGEMENT

## Donor engagement

The impact of IMB's research stretches far beyond the laboratory walls. As IMB welcomes more visitors into our laboratories, we are also taking our world-class science out into the community – to surround them in it, engage them with it and inspire them by it.

In 2012, we continued to explore the nexus of art and science in our collaboration with IMB's artist-in-residence Joannah Underhill. As Mike Bruce reported in *U on Sunday* magazine (2 December 2012):

"As artist Joannah Underhill was undergoing chemotherapy, she grew curious about what was happening to her body. So she asked her doctors about the physical reactions the treatment was causing in her cells.

"They (the doctors) had no idea," Underhill, 34, explains. "I needed to visualise it. I thought 'How can I visualise and support this process if I can't see what's happening?' I wanted to understand exactly what chemotherapy was doing to a cell, how it targets, infiltrates and operates on it."

After conducting some research herself, Joannah contacted IMB's Dr Nick Hamilton to see if he would be willing to help her analyse her cells under a microscope. Over several months, she studied, sketched and brought her inspirations to life creating more than twenty original artworks.

This pioneering collection was launched with a reception entitled 'Envisaging the invisible: a sub-cellular life' at Brisbane's Gallery of Modern Art on 30 August. More than 140 members of the community joined us to celebrate the exploration, including The Hon. Ros Bates MP, Minister for Science, Information Technology, Innovation and the Arts.

Later in the year, the collection was also exhibited at the Royal Brisbane and Women's Hospital and the Mount Tamborine Art Gallery. A special public reception at IMB and final exhibit was held in October, which was attended by 150 guests. Ms Underhill also allowed us to produce prints of three of her original artworks to sell as a fundraising initiative in support of our research.

In the same month, IMB researchers and students participated in Brisbane's first pancreatic cancer walk hosted by the Avner Nahmani Pancreatic Cancer Foundation. IMB, particularly the Queensland Centre for Medical Genomics directed by Professor Sean Grimmond, shares and is committed to the Avner Nahmani Pancreatic Cancer Foundation's vision of doubling the pancreatic cancer survival rate by

2020, and acknowledges the importance of community engagement in pursuing this mission. We were proud to join the more than 150 people who attended the inaugural walk at the Brisbane Botanical Gardens and we look forward to supporting this walk again in 2013.

We were fortunate to receive the continued support of our loyal donors in 2012, all of whom share our vision to improve quality of life for all through scientific research.

Notably, we acknowledge the support of UQ alumnus Dr Rosamond Siemon, whose generous annual donation brings us one step closer to IMB's first fully endowed research scholarship. The Dr Rosamond Siemon Scholarship currently supports PhD student Barbara Maier in IMB's Kidney Research Laboratory, led by Professor Melissa Little. The Laboratory investigates the molecular basis of kidney development, disease and repair in the hope of finding a treatment for chronic kidney disease. Along with training the next generation of kidney researchers, IMB's Kidney Research Laboratory is finding more ways to give back to their community, including hosting a fundraising BBQ in support of Kidney Health Australia.

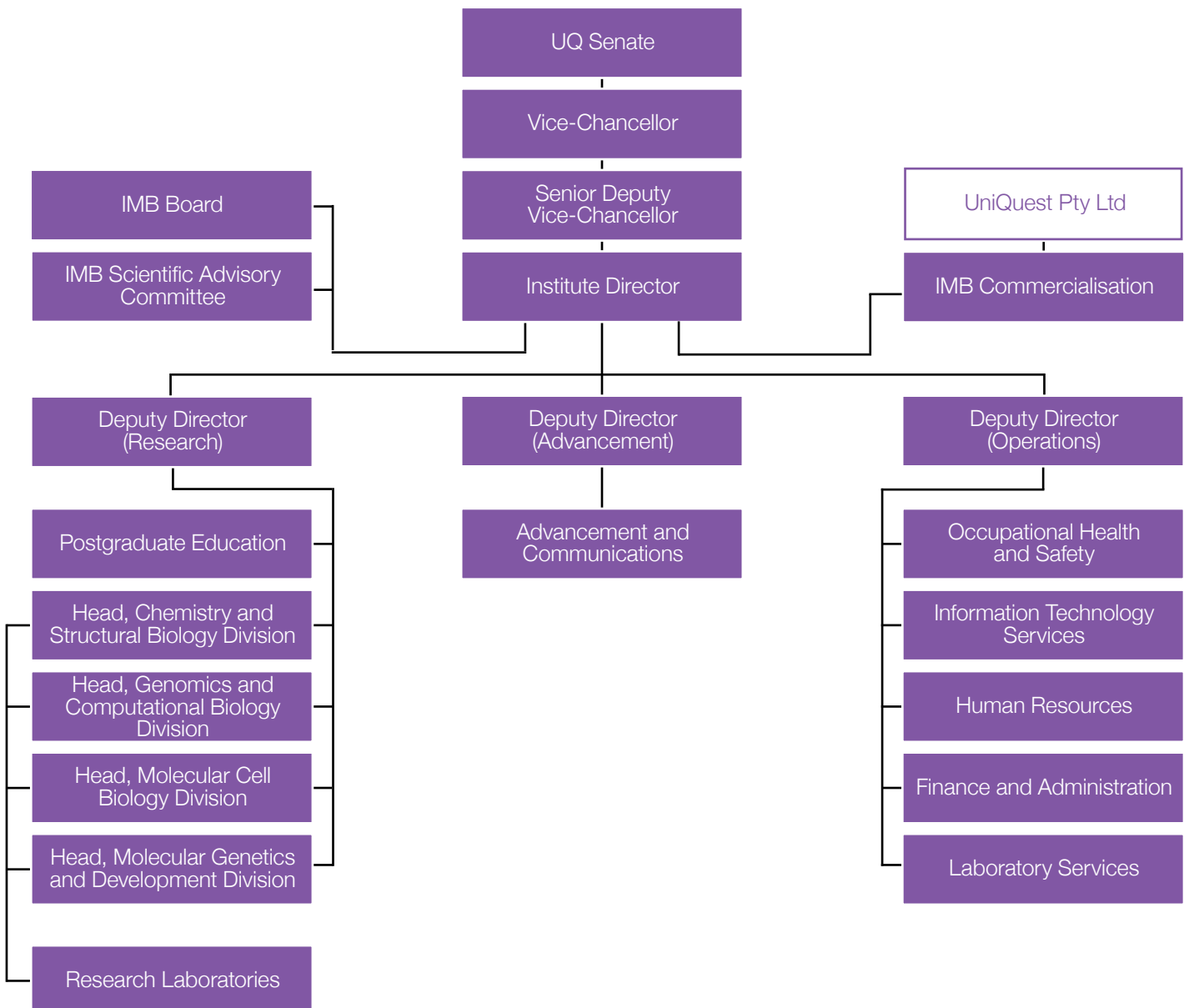
Finally, I would like to thank each of our valued donors and supporters for the vital role they play in our shared success. Thanks to you, we have been able to connect many more people with our research, and we look forward to continuing to expand our efforts in this area in the year ahead.



IMB's Kidney Research Laboratory, led by Professor Melissa Little



# ORGANISATIONAL CHART





IMB's Workshop and Maintenance team



IMB support staff collected donations for the 2012 Salvos Christmas Appeal

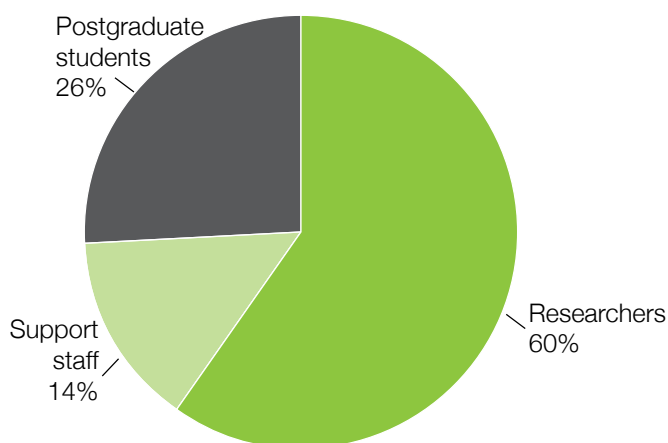
# SUPPORT STAFF

## Staff engagement

In 2012, 298 researchers, 72 support staff and 128 students worked tirelessly to advance IMB's research efforts. With staff and students from more than 40 countries around the world, our people form a diverse and talented team working to build a healthier and more prosperous future for our community.

As part of the wider UQ community, IMB staff had access to a wide range of benefits, including flexible working arrangements, wellbeing and support programs, and learning and development schemes. Staff were also supported and protected by both IMB and the University's effective management policies, practices and systems.

## Staff profile



## Support staff

**Administration support:** Sue Allen, Margarette Elsmore, Lucinda Essery\*, Jenny Greder\*, Susannah Hawtin, Gail Howard, Patricia Howarth, Desla Shand

**Finance:** Scott Aldridge\*, Robyn Craik, *Angela Gardner (Manager)*, Louise Hendriks, Thi Lu, Rosanna Quinlivan, Sanjay Sundarlal

**Grants officer:** Michelle Foley

**Infrastructure support:** *Chris Barnett (Manager)*, Jill Bradley, Karl Byriel, Christine Fraser, John Griffin, Michael Hanzal-Bayer, Jacky Hung, Alun Jones, Ian Lane, Angela Lawton\*, Miki Miyagi, Darren Paul, Jodie Robinson\*, James Springfield, Anne Tobin

**Workshop and maintenance:** Gary Carlross, Rene Croisier, Jason Hurst, Leigh Rose, John Srnka, *Mick Thwaite (Manager)*, Mark Ziza

**Stores:** Bob Allen, Jeremy Mead, *Barry Pitt (Manager)*

**Central sterilising facility:** Marie Campbell, Sol Koppmann, José Martinez, Linda Molloy\*, *Dawn Walsh (Manager)*

**Safety manager:** Paul Lovelock

**Human resources:** Natasha Crocker\*, Joanne French\*, Caraine Gomez, Liza Leibbrandt, *Felicity Ray (Manager)*

**Information technology:** Derek Benson, Damien Beverley, Matthew Bryant, Christian De Marco, *Brett Dunsmore (Manager)*, Calvin Evans, *Rowan Gronlund\* (Manager)*, Chris Hunt, Nelson Marques, Scott Martin, Lance Rathbone, Yves St-Onge, Jimmy Wu

**Advancement and communications:** Bronwyn Adams, June Cullen, Emma Lee\*, Gemma Ward

**Postgraduate office:** Amanda Carozzi, Olga Chaourova, Robyn Evans, Cody Mudgway

**IMBcom (to March 2012):** Ujjwal Dua, Paul Ellender, Deborah Ferguson, *Peter Isdale (CEO)*, Erin Kefford, Fiona McMillian, Christine Morrison, Lyn Rosen, Amanda Smith, Karen Soxsmith, Carla Toland, Heidi Widberg

**UniQuest (from March 2012):** *Mark Ashton (Manager)*, Rachel De las Heras, Stephen Earl, Amanda Smith, Charlie Widberg\*

**QFAB Bioinformatics:** *Jeremy Barker (CEO)*, Cheong Chan, Pierre-Alain Chaumeil, Xin-Yi Chua, Mark Crowe, Mathilde Desselle, Alain-Dominique Gorse, Anne Kunert, Roxane Legaie, Leo McHugh, Jeremy Parsons, Margaret Puls, Nicholas Rhodes, Cas Simons, Angeline Stelling, Sarah Williams

\* 2012 departing support staff



IMB's Grimmond Lab participated in the Avner Nahmani Pancreatic Cancer Foundation's 'Put Your Foot Down' fundraising walk during Pancreatic Cancer Awareness Month

# RESEARCH STAFF

## Research staff

**Alewood Lab:** *Paul Alewood (Lab Head)*, Andreas Brust, Zoltan Dekan, Thomas Durek, Aihua Jin

**Alexandrov Lab:** *Kirill Alexandrov (Lab Head)*, Christina Bollenbach, Dejan Gagoski, Yann Gambin, Nichole Giles, Zhong Guo, Regine Hartmann, Wayne Johnston, WooRam Jung, Sergey Mureev, Masuda Nabi, Marinna Nilsson, Mark Polinkovsky, Rachel Quin, Veronika Schreiber, Emma Sierecki, Clinton Simpson, Viktor Stein, Zakir Tnimov

**Bailey Lab:** *Tim Bailey (Lab Head)*, James Johnson, Mathieu Lajoie

**Capon Lab:** *Rob Capon (Lab Head)*, Andrew Piggott, Jill Robb, Angela Salim, Soumini Vijayasarathy, Xue Xiao

**Coin Lab:** *Lachlan Coin (Lab Head)*, Qin Song

**Collins Lab:** *Brett Collins (Lab Head)*, Priscilla Goh, Oleksiy Kovtun, Suzanne Norwood, Ru-Ting Tay

**Cooper Lab:** Bernd Becker, Mark Blaskovich, Domingos Boucas da Silva, Tanya Bradford, Mark Butler, Fuen Chong, *Matthew Cooper (Lab Head)*, David Edwards, Frank Fontaine, Scott Fry, Reena Halai, Karl Hansford, Johnny Huang, Gayathri Jayaraman, Tomislav Karoli, Angela Kavanagh, Karl-Fredrik Lindahl, Sreeman Mamidyala, Craig Muldoon, Ruby Pelingon, Jan Pinder, Rajaratnam Premraj, Soumya Ramu, Max Ranall, Andrea Ranzoni, Avril Robertson, Emma Sierecki, Chris Steel, Jason Steen, Ernest Tee, David Thomson, Daniel Watterson, Zyta Ziora, Johannes Zuegg

**Craik Lab:** Muharrem Akcan, Amy Argyros, Lai Chan, Aurelie Chanson, Olivier Cheneval, Daniel Clayton, Barbara Colless, Ashley Cooper, *David Craik (Lab Head)*, Norelle Daly, Shabli Diwan, Katherine Ewen, Sarah Flenley, Ingrid Hamernig, Peta Harvey, Yen-Hua Huang, Husen Jia, Quentin Kaas, Mani Kuchibhotla, Soohyun Kwon, Thi Thu Thao Le, Han Lee, Jeffrey Mak, Emma Miles, Susan Northfield, Aaron Poth, Anjaneya Ravipati, Tina Schroeder, Philip Sunderland, Joakim Swedberg, Sonia Troeira Henriques, Carmen van der Merwe, Shannon Waldron, Phillip Walsh, Conan Wang, David Wilson

**Fairlie Lab:** Kalyana Akondi, Nilesh Bokil, Adam Cotterell, Aline Dantas de Araujo, Johnathan Faber, *David Fairlie (Lab Head)*, Lyn Fairlie, Praveer Gupta, Timothy Hill, Huy Ngoc Hoang, Abishek Iyer, Woan Kok, James Lim, Ligong Liu, Rink-Jan Lohman, Andrew Lucke, Fabien Plisson, Robert Reid, Martin Stoermer, Jacky Suen, Mei-Kwan Yau

**Francois Lab:** Cameron Curtis, *Mathias Francois (Lab Head)*, Melanie Murrell, Jeroen Overman, Renae Skoczylas, Vy Truong Thuy

**Grimmond Lab:** Matthew Anderson, Timothy Bruxner, Angelika Christ, Nicole Cloonan, Jody (Lynne) Fink, Marie Gauthier, *Sean Grimmond (Lab Head)*, Deborah Gwynne, Ivon Harliwong, Shiv Hiriyur Nagaraj, John Holland, Oliver Holmes, Senel Idrisoglu, Karin Kassahn, Conrad Leonard, Suzanne Manning, David Miller, Felicity Newell, Katia Nones, Ehsan Nourbakhsh, Craig Nourse, Ann-Marie Patch, John Pearson, Jason Steen, Anita Steptoe, Darrin Taylor, Nick Waddell, Shivangi Wani, Peter Wilson, Scott Wood, Qinying Xu

**Hamilton Lab:** Oliver Cairncross, Nicholas Condon, Matthew Dean, *Nick Hamilton (Lab Head)*, Seetha Karunaratne, Timothy Lamberton, James Lefevre, Daniel Marshall

**Hankamer Lab:** Lou Brillault, Naomi Epstein, *Ben Hankamer (Lab Head)*, Michael Landsberg, Melanie Oey, Khairul Radzun, Ian Ross, Amalia Rothnagel, Evan Stephens, Eugene Zhang

**Hogan Lab:** Neil Bower, Emmanuelle Frampton, *Ben Hogan (Lab Head)*, Katarzyna Koltowska, Anne Lagendijk, Ludovic Le Guen, Christine Neyt, Scott Paterson

**IMB Fellows:** Josh Mylne, Kate Schroder, Kelly Smith

**King Lab:** Richard Allen, Raveendra Anangi, Rikki Andersen, Fernanda Caldas Cardoso, Yanni Chin, Evelyne Deplazes, Sing Er, Margaret Hardy, Volker Herzig, Maria Ikonopoulou, *Glenn King (Lab Head)*, Julie Klint, Linlin Ma, Mohammadmehdi Mobli, David Morgenstern, Joseph O'Neill, Sandy Pineda Gonzalez, Lachlan Rash, Natalie Saez, Sebastian Senff, Brit Winnen, Emily Wong

**Koopman Lab:** Josephine Bowles, Simon Cridland, Tara-Lynne Davidson, Barbara Feenstra, Chun-Wei Feng, Jessica Ineson, *Peter Koopman (Lab Head)*, Kim Miles, Ee Ng, Alex Quinn, Cassidy Spiller, Terje Svingen, Liang Zhao

**Lewis Lab:** Asa Andersson, Fernanda Caldas Cardoso, Andrew Deuis, Sebastien Dutertre, Valentin Dutertre, Tamarind Hamwood, Marco Inserra, *Richard Lewis (Lab Head)*, Thea Monks, Blessy Paul, Lotten Ragnarsson-McGrath, Jennifer Smith, Irina Vetter, Ching-I Wang

**Little Lab:** Alexander Combes, Pei Er, Kylie Georgas, Melissa Johnstone, Adler Ju, Joan Li, *Melissa Little (Lab Head)*, Nick Martel, Norseha Mohamed Suhaimi, Calida Neal, Bree Rumballe, Minoru Takasato, Jessica Vanslambrouch, Lorine Wilkinson





Participants at IMB's Chemistry and Structural Biology Division Symposium



Participants at IMB's Early Career Researchers retreat

**Martin Lab:** Julia Archbold, Prabhakar Bachu, Kai-En Chen, Michelle Christie, Maria Greenup, Shu-Hong Hu, David Jacques, Russell Jarrott, Gordon King, Premkumar Lakshmanane, *Jenny Martin (Lab Head)*, Roisin McMahon, Patricia Walden, Andrew Whitten

**Mattick Lab:** Guy Barry, Michael Clark, *John Mattick (Lab Head)*

**Muscat Lab:** Dennis Dowhan, Natalie Eriksson, Rebecca Fitzsimmons, Joel Goode, Akira Ichino, Wai Lau, *George Muscat (Lab Head)*, Michael Pearen, Shu-Ching Wang

**O'Neill Lab (based in Cairns):** Abbey Belcher, Frederico Carvalho Muzzi, Martin Durkan, Sarah Flenley, Adrian Gover, Antoinette James, Brian Montgomery, *Scott O'Neill (Lab Head)*, Andrew Turley

**Parton Lab:** Nicholas Ariotti, Michele Bastiani, Doris Berchtold, Gregory Bourne, Charles Ferguson, Manuel Fernandez Rojo, Tom Hall, Rachel Hancock, Mark Howes, Harriet Lo, Robert Luetterforst, Nick Martel, Kerrie-Ann McMahon, Susan Nixon, Satomi Okano, *Robert Parton (Lab Head)*, Maaïke Pols, James Rae, Nicole Schieber

**Ragan Lab:** Graham Cameron, Cheong Chan, Melissa Davis, Elham Gharazi, Gavin Graham, Gerald Hartig, Josha Inglis, Kim-Anh Le Cao, Stefan Maetschke, Grischa Meyer, Chanyarat Paungfoo-Lonhienne, *Mark Ragan (Lab Head)*, Anne Senabouth, Sriganesh Srihari, Alexander Varlakov, Kerri Wait, Lanna Wong

**Smythe Lab:** Christina Kulis, Ramya Mandyam, Jaimee McMahon, Eva Mowe, Craig Murphy, Sonya Scott, *Mark Smythe (Lab Head)*, Simone Vink, Jie Zhang

**Stow Lab:** Darren Brown, Nicholas Condon, Tatiana Khromykh, Nathan King, Natalie Lansdaal, Lin Luo, Brad Marsh, Massimo Micaroni, Amanda Stanley, *Jennifer Stow (Lab Head)*, Yue Tang, Zewen Tuong, Juliana Venturato, Adam Wall, Xuan Wong, Fiona Wylie, Changyu Yeo

**Sturm Lab:** Stephen Ainger, Adam Dinsdale, Matthew Harrison, Kasturee Jagirdar, Katie Lee, Wen Lim, Darren Smit, Elizabeth (Caroline) Sturm, *Rick Sturm (Lab Head)*, Shu Wong, Chuan-Hsin Kelvin Yin

**Sweet Lab:** Steven Broomfield, Melinda Greenfield, Daniel Hohenhaus, Gregory Kelly, Kelly-Anne Masterman, Ayanthi Richards, Kolja Schaale, Melanie Shakespear, *Matt Sweet (Lab Head)*, Flor Vasquez Sotomayor

**Taft Lab:** Gregory Baillie, Christine Ender, Ke-lin Ru, Cas Simons, *Ryan Taft (Lab Head)*

**Teasdale Lab:** Hadiya Agada, Andrea Bugarcic, Markus Kerr, Genevieve Kinna, Brian Lee, David Liebl, *Rohan Teasdale (Lab Head)*, Zhe Yang

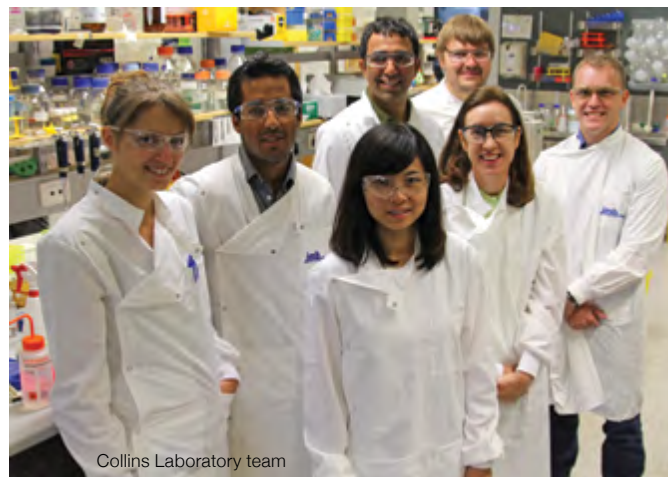
**Wainwright Lab:** Christelle Adolphe, Lena Constantin, Richa Dave, Laura Genovesi, Paul Joosa, Elaine Julian, Alex Koon, Elizabeth O'Brien, Jonathan Robson, *Brandon Wainwright (Lab Head)*, Han-Chung Yee

**Waters Lab:** Andrew Brooks, Tania Brooks, Narelle Manzie, Tran Thao, Kathryn Tunny, *Michael Waters (Lab Head)*

**Wicking Lab:** Huijun Chen, Andrew Courtney, Jessica de Angelis, Begona Heras, Geraldine Kaeslin, Vicki Metzis, Maria Rondon, *Carol Wicking (Lab Head)*

**Wilhelm Lab:** Bettina Martin, James Palmer, *Dagmar Wilhelm (Lab Head)*

**Yap Lab:** Hayley Cox, Rashmi Priya, Srikanth Budnar, Guillermo Gomez, Siew Han, Magdalene Michael, Rukhmani Verma, *Alpha Yap (Lab Head)*



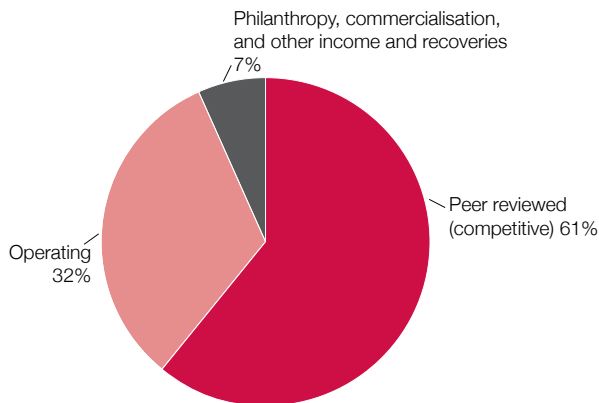
Collins Laboratory team

In 2012, IMB recorded a \$4,719,000 or 15.3 per cent year-on-year increase in total income. This was mainly due to improved peer reviewed (competitive) grant performance, which increased by \$3,670,000.

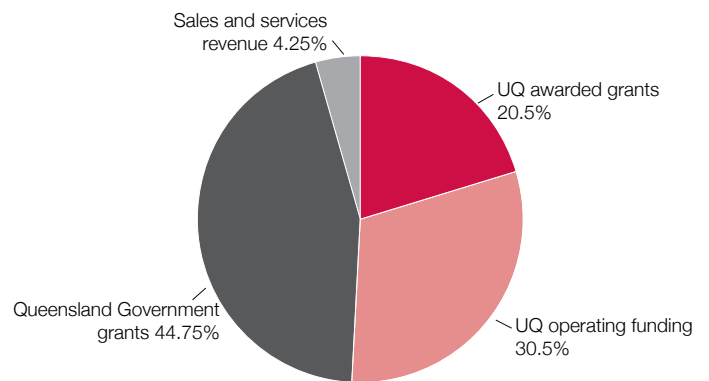
During the past 12 months we continued to invest in our staff, with a particular focus on expanding our research teams. As a result, we saw our operating expenditure rise by 26.34 per cent in 2012.

# FINANCIAL PERFORMANCE

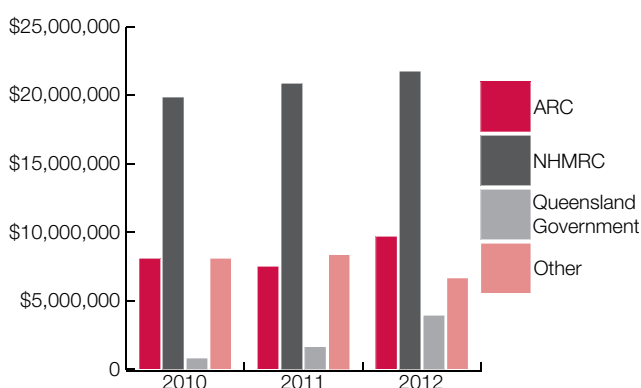
## 2012 total income



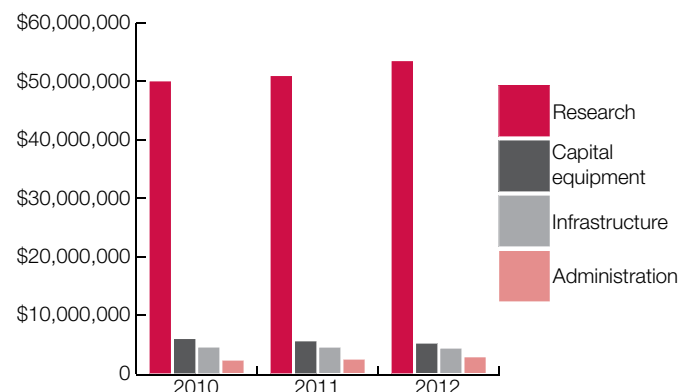
## 2012 operating (core) income



## Competitive grant income



## Distribution of expenditure





# INCOME STATEMENT

<b>INCOME</b>	<b>2010</b>	<b>2011</b>	<b>2012</b>
<b>PEER REVIEWED (COMPETITIVE) INCOME</b>	<b>\$'000</b>	<b>\$'000</b>	<b>\$'000</b>
ARC grants	8,086	7,500	9,702
NHMRC grants	19,865	20,866	21,753
Queensland Government grants	826	1,663	3,946
Other peer reviewed grants - domestic	7,381*	5,577*	4,207
Other peer reviewed grants - international	713	2,794	2,462
<b>OPERATING INCOME</b>			
UQ awarded grants	4,137	4,769	4,580
UQ operating funding	6,321	6,539	6,812
Queensland Government operating grant	10,000	10,000	10,000
Sales and services revenue	1,556	1,278	957
<b>OTHER INCOME</b>			
Philanthropy	307*	133*	168
Commercialisation	2,269*	2,884*	3,525
Other income and recoveries	1,004*	670*	782
<b>TOTAL INCOME</b>	<b>62,465</b>	<b>64,674</b>	<b>68,893</b>
<b>EXPENDITURE</b>	<b>2010</b>	<b>2011</b>	<b>2012</b>
<b>REMUNERATION EXPENDITURE</b>	<b>\$'000</b>	<b>\$'000</b>	<b>\$'000</b>
Researchers	29,890	31,206	34,598
Infrastructure	2,656	2,752	3,016
Administrative	1,865	2,002	2,414
<b>RESEARCH EXPENDITURE</b>			
Research services	17,027	16,371	15,525
Commercialisation	1,200	1,200	600
Research higher degree support	1,253	1,384	1,387
UQ internal collaborations and agreements	683	810	1,413
<b>OPERATING EXPENDITURE</b>			
Capital equipment	5,928	5,530	5,104
Information technology	745	674	529
Administration and support	330	359	382
Infrastructure and development	1,071	1,010	733
<b>TOTAL EXPENDITURE</b>	<b>62,649</b>	<b>63,298</b>	<b>65,701</b>
<b>NET INCOME</b>	<b>(184)</b>	<b>1,375</b>	<b>(3,192)</b>

## CORRECTION TO 2011 ANNUAL REPORT FINANCIALS

We wish to advise some 2010 and 2011 income funding allocations published in IMB's 2011 annual report financials (page 41) were incorrectly reported. The affected 2010 and 2011 allocations have been corrected in this income statement and can be identified by an asterisk (\*). These allocation errors did not change the total income figures for 2010 or 2011.



PhD student Marga Gual Soler

# SCIENTIFIC PUBLICATIONS

## High impact publications (IF>10)

Ratheesh, Aparna and Yap, Alpha S. (2012) A bigger picture: classical cadherins and the dynamic actin cytoskeleton. *Nature Reviews Molecular Cell Biology*, 13 10: 673-679. **IF: 39.123**

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“Although there is currently no cure, achieving a **diagnosis** gives us **hope**. It is the vital **first step** to one day developing a **treatment** for Massimo.”

- Stephen, Massimo's Dad

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# IMB

At just three years of age, Massimo was diagnosed with Leukodystrophy, a set of rare brain disorders.

IMB Laboratory Head Dr Ryan Taft used a method called whole genome sequencing to examine the genetic differences between the genomes of Massimo and his parents, and identified the gene responsible for Massimo's illness.

*Dr Taft hopes to use these findings to help other families affected by these rare diseases, but he can't do it without your support.*



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