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2013 ANNUAL REPORT

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COVER ARTWORK

Quantify and Observe by Joannah Underhill

This artwork is a celebration of the scientific research process. It is inspired by the roles science, technology, mathematics and observation play in understanding molecular structures and models, and playfully hints at the diversity of sub-cellular life and the unlimited complexity of how cells interact.

It is based on the idea that in order to learn and understand, we first need to observe our subject in the most objective way possible. It also reminds us to keep in mind the basic structures of what we are observing, while simultaneously keeping an eye on the bigger picture.

Quantify and Observe forms part of Brisbane artist Joannah Underhill's IMB artist-in-residency collection, Envisaging the Invisible.

You can read more about Ms Underhill's collaboration with IMB, and view her full collection, at jounderhill.com

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

ACKNOWLEDGEMENTS

This report was published by IMB Communications in May 2014 and is an accurate record of IMB's achievements from 1 January–31 December 2013.

To enquire about this report, please email communications@imb.uq.edu.au.





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VICE-CHANCELLOR AND PRESIDENT'S MESSAGE

The quality, energy and productivity of the University's research community grew to new levels in 2013.

Our life sciences institutes including our first and largest institute, the Institute for Molecular Bioscience (IMB), played an integral part in our ongoing success.



Strengthening UQ's global position

The University continued its surge in global rankings, improving in all four major international university rankings in 2013.

By December, UQ sat at 63 in the Times Higher Education World University Rankings (up from 65); at 43 in the QS World University Rankings (up from 46); at 67 in the Performance Ranking of Scientific Papers for World Universities (up from 72); and at 85 in the Academic Ranking of World Universities (up from 90).

IMB and its fellow UQ life sciences institutes can be proud to have contributed to UQ being ranked in the top 25 in the world —and second in Australia—for biological sciences. The University ascended 16 places for biological sciences since last year's QS World University Subject Rankings, a considerable achievement.

These solid positions in the world rankings demonstrate a strong foundation on which we are further building our capacity for scientific innovation. Moreover, it testifies to the relevance and impact of our research in solving the challenges faced by people throughout our shared global environment.

Partnering with industry

The culture of collaboration and innovation at IMB has attracted the support of public and private organisations nationally and internationally.

During the year, IMB had active collaborations with three of the top five pharmaceutical companies globally; worked closely with leading companies in the agriculture, biofuels and reagents sectors; and initiated new, or extended existing partnerships with Alchemia, Elanco, Janssen, Phylogica and Innovate Ag.

These partnerships have provided a clear pathway for translating the institute's research into practical applications of value to the community.

The broad range of industry investment and commitment testifies to the life-

changing outcomes of IMB's biomedical and biotechnology research. Furthermore, the institute continued to demonstrate its innovative research through the management of an intellectual property portfolio of 25 patents, ranging from drug discovery tools to therapeutics and agriculture.

In April, I had the pleasure of celebrating a key milestone for one of IMB's longterm industry collaborations, welcoming Queensland Premier, Campbell Newman, and Minister for Science, IT, Innovation and the Arts, Ian Walker, to the official opening of UQ's \$3.5 million Solar Biofuels Research Centre.

Professor Ben Hankamer developed this leading-edge facility with the Queensland Government, KBR Inc., Neste Oil Corp., Cement Australia Pty Ltd, Siemens, Bielefeld University and the Karlsruhe Institute of Technology in Germany. This exemplary partnership forms part of a spectrum of discovery under the UQ Energy initiative, which is helping Queensland pursue its scientific and economic potential in pioneering sustainable, clean energy solutions.

Leading from the front

Scientific leadership remains a key priority for the University, and 2013 delivered many opportunities for UQ to nurture, support and celebrate its amazing depth of talent.

In March, five UQ scientists were among the 20 new Australian Academy of Science (AAS) Fellows named in 2013 for their outstanding contributions to science, joining the existing 19 UQ scientists admitted to the academy as fellows since 1988. IMB's Professor David Craik was one of the new fellows announced, in recognition of his discovery of a novel class of proteins known as cyclotides, whose circular shape makes them ultra-stable and therefore an ideal base for therapeutic drugs.

In November, two IMB research projects were recognised as some of the best in the country by the National Health and Medical Research Council (NHMRC). Cell biologist Professor Rob Parton was awarded the topranked NHMRC Project grant out of 3500 applications nationwide in 2012 for his work to study a cellular pathway that appears to play a crucial role in cell migration around the body, including the spread of cancer cells. And infectious disease expert Professor Matt Cooper was awarded the top-ranked NHMRC Development grant out of 102 applications nationwide in 2012 for his work to develop improved treatments for drugresistant tuberculosis.

I also want to congratulate Professor Melissa Little for her contributions to delivering the McKeon Review to the Australian Government in April, which details a 10-year strategic health and medical research plan for the nation.

The life sciences sector has an important role to play in improving the health of our people and prosperity of our state. Through its many productive partnerships and collaborations, IMB has proven itself to be a driving force in Queensland life sciences. I congratulate and thank Brandon and his dedicated team for their hard work in 2013, and I look forward to seeing the institute continue to expand its reach and impact, locally and globally.

Professor Peter Høj

Vice-Chancellor and President The University of Queensland

DIRECTOR'S MESSAGE

2013 was a year of great progress for IMB's staff and students, as we connected with our colleagues in industry, academia and clinics around the world to drive innovation in health and technology, and improve quality of life.



In May, we marked 10 years since the official opening of the \$105 million Queensland Bioscience Precinct (QBP)—the home of IMB. Ten years on, the QBP continues to be the cornerstone of one of the country's largest bioscience research precincts, housing a range of advanced technologies and facilities that allow IMB scientists to conduct comprehensive and multidisciplinary investigations.

Celebrating our leaders of today

The quality and relevance of our discoveries to the global community was reaffirmed during the year with IMB researchers publishing 354 scientific publications, and securing more than 58 per cent (\$36 million) of the institute's annual income (\$62 million) from competitive grant funding. We also secured five grants through the Australian Research Council's (ARC) Linkage program to work in partnership with industry to accelerate our basic research into practical applications of benefit to the community. I thank our industry partners for investing in our new and ongoing joint projects.

In 2013, Professor David Craik became the third IMB researcher to become a Fellow of the Australian Academy of Science (AAS); Professor Alpha Yap was awarded the Australia and New Zealand Society for Cell and Development Biology President's Medal; and Professor Glenn King received the Beckman Coulter Discovery Science Award from the Australian Society of Biochemistry and Molecular Biology.

Our rising research stars also achieved highly, with Dr Lachlan Coin and Dr Kate Schroder receiving UQ Foundation Research Excellence awards, and Dr Schroder and Dr Irina Vetter earning Tall Poppy awards for their outstanding research and community engagement activities aimed at inspiring young Australians about science.

Furthermore, Professor Melissa Little was part of the expert panel that delivered the McKeon Review, an independent review on the future of health and medical research (HMR) in Australia. Notably, the McKeon Review provided a welcomed reminder of the value of HMR, stating that every dollar invested in Australian HMR is estimated to deliver a return in health benefits of \$2.17. I would like to congratulate Professor Melissa Little for receiving IMB's first National Health and Medical Research Council (NHMRC)-European Union Collaborative Research grant; and Professor Matt Cooper, who will lead an international research team as part of his grant awarded by the Australia-India Strategic Research Fund. I would also like to congratulate Professors Rob Parton, Alpha Yap and Kirill Alexandrov, who were awarded a five-year NHMRC Program grant to investigate the cell surface at the molecular level; and Associate Professor Mark Smythe, whose IMB spin-out company, Protagonist Therapeutics, raised \$18 million from Series B private financing. The biotechnology company is developing oral drugs for diseases whose current treatments must be injected, providing a safer, and more effective, convenient, and affordable choice for patients and the healthcare system.

In April, we conducted an international recruitment process to find two new laboratory heads to join our leadership team. We received more than 100 applications, and following a competitive process we were fortunate to discover two outstanding candidates from within our own ranks, appointing immunity and inflammation expert Dr Kate Schroder, and heart development and disease expert Dr Kelly Smith, to establish and lead their own IMB labs.

Celebrating our leaders of tomorrow

This year we were training 121 research higher degree students and conferred a record 34 PhD students, who are now working in academic institutions such as the University of Oxford, leading life sciences organisations such as Lonza in the US, and government organisations such as CSIRO. We are also pleased to have been able to offer some of our alumni the opportunity to continue their research here at IMB and across UQ.

Our students demonstrated their motivation and scientific excellence in many ways during the year, including through their strong success in receiving prestigious awards and scholarships to advance their training and research projects.

Molecular cell biology PhD student Marga Gual Soler was selected from more than 10,000 applicants to undertake a threemonth traineeship with the United Nations in New York; and two of IMB's budding life scientists secured places in some of the world's top training courses in the US. PhD student Kathryn McClelland was one of only 23 participants accepted worldwide to join the Marine Biological Laboratory Embryology course in Woods Hole, Massachusetts. And PhD student Elanor Wainwright was one of only 14 participants accepted to join the Cold Spring Harbor Laboratory Mouse Development, Stem Cells and Cancer course in New York.

Celebrating our community

As always, our research was bolstered by community support. During the year, our researchers engaged with the community by hosting laboratory tours, public seminars, student information sessions and scientific conferences; contributing to online patient support and education resources, and health professional development sessions; and strengthened their relationships with the media to better inform Queenslanders about what we do, and why and how we do it.

A final remarkable achievement worthy of celebrating is Dr Ryan Taft's partnership with the Mission Massimo Foundation and an international team of collaborators, who together successfully diagnosed young Massimo's rare childhood disease. In the process, they also discovered a disease entirely new to medicine.

This report is a record of our collective achievements in 2013 and I commend and thank our staff, students, partners and supporters for helping to move us closer to realising our vision of being a life sciences institute with global impact. With your support, we can continue our work to transform the world through science.

Professor Brandon Wainwright

Director

Institute for Molecular Bioscience

ABOUT IMB

Our **mission** is to drive the bioeconomy and to create better health.

Our **vision** is to be a life sciences institute with global impact.

The University of Queensland's Institute for Molecular Bioscience (IMB), which is based at the Queensland Bioscience Precinct, is one of Asia-Pacific's leading life sciences research institutes.

Established in 2000 as UQ's first research institute, IMB is a multidisciplinary scientific research institute committed to improving quality of life by pursuing discoveries in medical genomics, drug discovery and biotechnology.

IMB's 500 researchers, postgraduate students and support staff work in partnership with their academic, industry and clinical colleagues around the world to advance knowledge in the institute's seven impact areas: cancer, pain, childhood diseases, infection and inflammation, diabetes and obesity, agriculture, and clean energy.

By investigating how we grow and develop at the genetic, molecular, cellular and organ levels, IMB researchers can better understand the development processes and pathways involved in human and animal health and disease.

The institute also has the technical capacity to translate its new knowledge into drugs, diagnostics and technologies to more effectively prevent, detect and treat disease; and pursue opportunities in a range of biotechnology applications for health, industry and the environment.



2013 SNAPSHOT





IMB uses annually:

100.000 petri dishes



4,300,000 pipette tips, which if laid end-to-end would stretch more than 172km

785,000 microfuge tubes



800,000 disposable safety gloves



IMB is home to:

5000 +

pieces of laboratorv glasswaré and plasticware, 300–400 of which are washed and sterilised daily

PETABYTE

of active disk storage, which is equivalent to the storage capacity of 223,000 DVDs



EXECUTIVE Committee



Professor Brandon Wainwright Director BSc (Hons) PhD (Adelaide)

Professor Wainwright was appointed Director of IMB in 2006. Previously, he was IMB's Deputy Director (Research). 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.

Professor Wainwright completed his undergraduate and postgraduate studies at The University of Adelaide, after which he secured a postdoctoral fellowship with St Mary's Hospital at Imperial College London. During his six years at Imperial 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 board of the Australian Genome Research Facility and a number of national and international scientific review committees.

Professor Jennifer Stow Deputy Director (Research) BSc (Hons) PhD (Monash)

Professor Stow was appointed as IMB's Deputy Director (Research) in 2008. Previously, she was 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 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.

Dr Ian Taylor

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

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, 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 late 1970s, he relocated to Australia to take up a position as a Research Fellow at the Ludwig Institute for Cancer Research, and a lecturer at the University of Sydney, before moving to Brisbane in 1984 to become the Queensland Institute of Medical Research's first Scientific Manager.

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

Ms Amanda Whelan Deputy Director (Advancement) BSc (Hons) MPA (Florida State)

Amanda Whelan was appointed as IMB's Deputy Director (Advancement) in 2011. In this role, she is responsible for managing the institute's philanthropic development, government relations and communications programs.

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



Professor David Fairlie Head, Chemistry and Structural Biology Division

BSc (Hons) (Adelaide), PhD (NSW)

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

Professor Fairlie completed his 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 Australian Research Council(ARC) Federation and Professorial fellowships and chief scientific officer and scientific director roles in leading scientific companies. He has also collaborated with some of the world's largest biopharmaceutical companies.

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

Professor Mark Ragan Head, Genomics and Computational Biology Division BA (Hons) (Chicago), PhD

(Dalhousie) Professor Ragan was appointed as the founding

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 vears 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 Director of the Australian Research Council (ARC) Centre of Excellence in Bioinformatics and a co-founder of QFAB Bioinformatics.

Professor Alpha Yap Head, Molecular Cell Biology Division MBBS PhD (Queensland), FRACP

Professor Yap was appointed as Head of IMB's Molecular Cell Biology Division in 2008. In this role, he leads a team of eight 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 National Health and Medical Research Council (NHMRC) Principal Research Fellow. He is an Associate Editor of scientific journal *Molecular Biology of the Cell* and a member of nine other editorial boards, including *Current Biology* and *Developmental Cell*. In 2013, he received the President's Medal of the Australia and New Zealand Society for Cell and Developmental Biology.

Professor Peter Koopman Head, Molecular Genetics and Development Division

and Development Division BA BSc (Hons) PhD (Melbourne)

Professor Koopman was appointed as 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 leading 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 sexdetermining 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.

Dr Mark Ashton

Senior Director, Commercial Engagement (Health), UniQuest BSc (Hons) PhD (Bath)

Dr Ashton was appointed as UniQuest's Manager, Innovation and Commercial Development (IMB) in 2012. Following a restructure of UniQuest in May 2013, Dr Ashton was promoted to Senior Director, Commercial Engagement (Health), where he is now responsible for strengthening UQ's healthcare pipeline and translating the university's research expertise and intellectual property into commercial outcomes.

Dr Ashton completed his undergraduate studies in chemistry, postgraduate studies in medicinal chemistry and postdoctoral studies in the discovery of new calcium channel antagonists. Before joining IMB, Dr Ashton was **Executive Vice President** (Business Development) of European-based biotech company, Evotec. Prior to this, he was President of the **Drug Discovery Operations** Division at Evotec.

Dr Ashton has worked within the biotech and pharmaceutical industries for almost 20 years, and serves as a director of Australian biotech companies Vaxxas Pty Ltd, Helmedix Pty Ltd and Dimerix Bioscience.

DISCOVERY

RESEARCH PRIORITIES

IMB's multidisciplinary research programs focus on advancing medical genomics, drug discovery and biotechnology to deliver outcomes that improve our health, industries and environment.



Medical genomics

Medical genomics allows patients to be diagnosed and treated on an individual level, based on the data extracted from their personal genetic code.

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 factors combined will ensure genomic knowledge continues to change the way medicine is practised.

Genomics has also proven its ability to improve the accuracy of diagnosis, reduce the cost of genetic testing and improve public health, specifically by targeting lifestyle advice to those whose genome sequences indicate they may be predisposed to certain diseases.

IMB's focus on medical genomics 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.



Drug discovery

Compounds with the potential to prevent or treat disease are everywhere, including in bacteria, plants and even the venom of spiders. But 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 many spin-out companies, which are leading the way in translating their discoveries into tangible health and economic outcomes for Australia.



Biotechnology

IMB differs from most, if not all, Australian biomedical institutes in that its investigative focus extends beyond disease. The institute's third research priority, 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 of them, to develop or improve products or processes of value to the community. This technology can be as simple as using 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 solve the challenges of supporting a growing global population. IMB researchers are working on projects with the potential to improve health and agriculture and provide alternative fuel sources, both now and into the future.

RESEARCH HIGHLIGHTS



Professor Sean Grimmond

Professor Brandon Wainwright

Professor George Muscat

Dr Eivind Undheim (King Lab)

Dr Irina Vetter (Lewis Lab)

Cancer

Revealing the genetic mutations in 30 common cancers

An international team, including scientists from IMB and the Garvan Institute of Medical Research, described the mutational processes that drive tumour development in 30 of the most common cancer types. The team analysed 7042 tumours and identified 21 distinct mutational signatures and the cancer types in which they occur. The study, published in leading scientific journal, Nature, allowed the team to pinpoint the root genetic cause of tumour development in common cancers and, in some cancers, to identify the biological process that damages the DNA and gives rise to the cancer. These findings could have potentially dramatic implications for early diagnosis, treatment, and particularly prevention in the future.

Pinpointing the genes behind brain tumours

Professor Brandon Wainwright led a team of researchers from Australia, Singapore, Canada, the UK, and the US to pinpoint 56 genes that could drive the formation of medulloblastoma, the most aggressive and frequent form of brain tumours found in children. The study, published in the *Proceedings of the National Academy of Sciences USA*, found these newly identified genes could provide potential targets for treatment. The team is now searching for existing drugs that may block these gene networks and act as viable and less invasive treatment alternatives for medulloblastoma.

New drug targets for breast cancer

Professor George Muscat led a team of 16 researchers from across Australia to identify new markers and treatment targets for women with breast cancer. The study, published in *Molecular Endocrinology*, compared the activity of a group of proteins called nuclear receptors (NRs) in 116 samples of normal breast tissue and tumours. The team found two NRs that are overactive in breast tumours, and five whose activity decreased as cell abnormality increased—all of which could serve as drug targets. The project also identified several NRs that act as markers, including four that are significant predictors of whether a patient who has been treated with tamoxifen will survive diseasefree.

Switching off the spread of breast cancer

Scientists from IMB and QIMR Berghofer Medical Research Institute identified a genetic 'switch' that indicates whether a woman's breast cancer will spread. Normally this particular ribonucleic acid (RNA) molecule acts like an 'emergency brake' in our genetic program, ensuring our cells continue to reproduce normally. But the team found this emergency brake fails in invasive, aggressive tumours, meaning its absence in cancer tests would be a clear marker that a tumour is likely to spread. They also found this microRNA to be missing in aggressive liver, stomach, brain and skin cancers, and potentially others, too.

Teaming up to treat aggressive breast cancer

As part of the Queensland Emory Development (QED) Alliance, Professor David Fairlie, in collaboration with researchers from QIMR Berghofer Medical Research Institute and US-based Emory University in Atlanta, Georgia, commenced work on a collaborative project that aims to develop a drug to treat a highly resistant form of breast cancer. The multidisciplinary team's expertise spans biochemistry and high-throughput screening (Emory University), preclinical models of triple-negative breast cancer (QIMR Berghofer), and medicinal chemistry and drug design (IMB). Together, they are investigating how to block a cancer pathway responsible for poor prognosis in about 20 per cent of breast cancer patients who are given existing cancer therapies.

Pain

Centipede venom could treat chronic pain

Professor Glenn King, together with researchers from UQ and the Chinese Academy of Sciences, discovered a molecule in centipede venom that has the potential to be developed into a painkiller as effective as morphine but without the side effects. The molecule they found blocks the Nav1.7 channel in pain-sensing nerves. It selectively targets this pain channel without impacting closely related channels that play critical roles in controlling the heart and muscles, making it a promising drug candidate for treating chronic pain and other conditions.

Using natural products to target pain pathways

Dr Irina Vetter and Professor Richard Lewis demonstrated for the first time how camphor —a crystal-like substance sourced from the camphor tree—affects nerve channels, including pain-sensing channels that determine how the body feels pain, in a study published in *The Journal of Neuroscience*.

A further study, which was published in leading scientific journal, *Pain*, revealed the crucial role that the Nav1.6 nerve channel plays in chemotherapy-induced pain, a finding that could help to improve quality of life for cancer patients receiving chemotherapy treatments. These discoveries were part of IMB's extensive research program into how natural products, such as cone snail venom, can be used to find new treatments for chronic pain, which affects one in five Australians.

In addition to their work with natural products, Professor Lewis and Dr Vetter are also collaborating with Australian-based biotech, Audeo Discovery Pty Ltd, to identify compounds active in pain pathways with the potential to become drug leads.











Dr Kate Schroder with the Hon. Ian Walker, Minister for Science Associate Professor Matt Sweet

Infection and inflammation

Tackling drug-resistant tuberculosis

Professor Matt Cooper led a team of infectious disease experts to develop new drug candidates to improve and hopefully replace current tuberculosis (TB) treatments, which consist of four drugs that must be taken for six to nine months to be effective. With many bacteria developing resistance to multiple TB drugs, new drugs are needed to reduce drug treatment time, improve patient cure rates, contain TB's spread and potentially save millions of lives.

Using zinc to starve lethal bacteria and stop infection

Professor Matt Cooper and a team of infectious disease researchers found how zinc can 'starve' one of the world's most deadly microbes by preventing its uptake of manganese, an essential metal microbes need to invade and cause disease in humans. The finding, published in Nature Chemical Biology, opens the way for further work to design antibacterial agents in the fight against Streptococcus pneumonia. These bacteria are responsible for more than one million deaths each year by causing pneumonia, meningitis, and other serious infectious diseases in humans.

Spin-out biotech secures funding for drug discovery

IMB spin-out biotech company, Protagonist Therapeutics, founded by Associate Professor Mark Smythe, raised \$18 million of venture capital funding to progress its drug discovery research into developing oral drugs for diseases whose current treatments must be injected, including inflammatory bowel diseases and other gastro-intestinal disorders. Oral treatments tend to be safer, more effective, more convenient, and more affordable for patients and the healthcare system in comparison to injectable

treatments. The company is headquartered at Menlo Park, California, US, and has discovery operations at IMB and Menlo Park.

Landmark discovery paves the way for a new class of low-cost medicines

Professor David Fairlie's lab has pioneered a much sought-after drug development technique that reduces large proteins to small molecules suitable for use as drugs. The result was a smaller, more bioavailable version of a powerful human inflammatory protein-complement protein C3a-that helps defend against disease. The finding, which was published in Nature Communications, could open up exciting new avenues for chemists to downsize valuable human proteins and obtain affordable new diagnostics and drugs for a range of diseases.

Inflammation research awarded

Dr Kate Schroder won a Tall Poppy award for her research into understanding the innate immune system, the body's front-line weapon against invading microbes. The body defends itself by mounting inflammatory responses, which underpin our ability to resist or fight infectious diseases. But these responses can be triggered inappropriately. Dr Schroder's research is helping to understand exactly how the body fights infection, and providing insight into the mechanisms behind the unhealthy inflammation that occurs in common diseases such as diabetes.

IMB researchers identify possible target for anti-inflammatory drugs

Associate Professor Matt Sweet led a team that identified histone deacetvlase 7 (HDAC7) as a protein that drives inflammatory responses in macrophages, cells that alert the body to signs of danger. When macrophages are activated inappropriately they can drive inflammatory diseases, meaning HDAC7 could represent a viable target for future anti-inflammatory drugs.

Obesity and diabetes

Drug lead shows promise as potential treatment for obesity

Professor David Fairlie led a team of Queensland researchers to discover a new anti-inflammatory compound that prevents rats on a high-fat, high-sugar diet from becoming obese, preventing many of the detrimental health effects associated with obesity. The work-published in one of the world's most cited biology journals, The FASEB Journal-provides strong evidence that drugs designed to treat inflammatory diseases may also be able to prevent and treat obesity, a finding the team hopes to pursue further in future clinical trials.

Making safer drugs to treat type 2 diabetes

Professor Matt Cooper and Dr Avril Robertson received funding from the Australia-India Strategic Research Fund to develop new molecules that modulate the body's immune response to treat inflammatory diseases, including type 2 diabetes. Current drugs on the market for type 2 diabetes can cause side effects: so safer, more effective drugs are urgently needed. Together with scientists at the Indian Institute of Chemical Technology, Hyderabad, and Trinity College Dublin, they will work to advance their findings towards new drug leads to help tackle diabetes. Diabetes is one of the fastest growing chronic diseases in Australia, and affects more than 63 million people in India.

RESEARCH HIGHLIGHTS



Dr Michael Pearen (Muscat Lab)

Dr Ryan Taft (second from right) with his team

Massimo Damiani

Mini-kidney in a dish

Melissa Little

Associate Professor Carol Wicking

Obesity and diabetes (continued)

Key protein determines exercise capacity and metabolism

Professor George Muscat, Dr Michael Pearen and Joel Goode demonstrated that when activated in skeletal muscle cells, the nuclear hormone receptor Nor-1 plays key roles in the body. These roles include regulating fat metabolism; increasing physical endurance; stimulating the growth of mitochondria, which produce the energy that powers nearly all cellular activity; decreasing the amount of fat stored in the body; and inducing resistance to diet-induced obesity and weight gain. The research team also identified that Nor-1 regulates the expression of genes in the body, including alpha actinin, which is a protein associated with polymorphisms in humans, and is linked to changes in exercise capacity, strength, and metabolism. These genes and cellular pathways could prove effective as future drug targets for type 2 diabetes and obesity.

Childhood diseases

Mystery disease solved by genetic experts

Dr Ryan Taft led a global team of researchers to identify the gene behind young Massimo Damiani's rare paediatric brain disorder. Dr Taft analysed the genome sequences of Massimo-who was diagnosed with leukodystrophy-and his parents using a method called whole-genome sequencing, and found that a mutation in the DARS gene was likely causing his disorder.

The research team then examined the genomes of nine other children from around the world who appeared to be suffering from the same disease, and the genomes of their parents, and confirmed that they all had the same mutations in the DARS gene. Their discovery was published in the American

Journal of Human Genetics (AJHG), where they named their newly discovered disease HBSL because it causes Hypomyelination in the Brain stem and Spinal cord leading to Leg spasticity.

The team also used genomics to identify the genetic mutation responsible for another leukodystrophy, H-ABC, which was published in the same issue of AJHG. Dr Taft's work made headlines around Australia and featured in an episode of ABC TV's Australian Story (Cracking the Code, aired 21/10/13), which was viewed by more than 1.2 million people.

Reprogramming cells to repair damaged kidneys

In a landmark discovery published in the Journal of the American Society of Nephrology, Professor Melissa Little reprogrammed adult tissue cells to act as stem cells to repair damaged kidneys.

The team identified six key genes that can prompt some types of adult kidney cells to regress to an earlier stage of development and act like the precursors to the cells of the nephron. Nephrons filter the blood as it passes through the kidneys, with damage to the nephrons causing kidney disease.

All nephrons are formed before birth and people with fewer nephrons are at higher risk of kidney disease. By forcing adult cells to act like early nephron cells, the research team has potentially found a way to trigger the growth of new filters and reduce the risk of disease progression.

Rates of kidney disease in Australia continue to increase, fuelled by an ageing population, increased rates of obesity and diabetes, and declining access to organs for transplantation.

Growing a kidney from stem cells

In a further bioengineering breakthrough, Professor Little and her lab grew a minikidney in a dish using stem cells, work

published in Nature Cell Biology. The team designed a protocol that prompts stem cells to form all the required cell types to 'selforganise' and create the complex structures that exist within an organ, in this case, the kidnev.

Peter Koopman

The discovery could lead to improved treatments for patients with kidney disease, and might also be a powerful tool to identify drug candidates that may be harmful to the kidney before these reach clinical trials.

Unravelling the secrets of maleness

Professor Peter Koopman, in collaboration with Japanese scientists, identified the key to becoming male is an enzyme that 'unravels' DNA to trigger male development of the embryo, a discovery that may give greater insight into intersex disorders. The fundamental discovery, published in leading journal, Science, built on the knowledge that a specific Y-chromosome gene known as SRY is responsible for 'switching on' maleness genes. Importantly, it also found that the DNA containing SRY needed to be unwound before the gene could become active.

Key genes discovered behind Jeune syndrome

Associate Professor Carol Wicking and colleagues from UQ's Diamantina Institute and Centre for Clinical Research, and University College London, identified two new genes behind Jeune syndrome, a devastating inherited disease in which severe bone deformities lead to profound breathing difficulties and can sometimes lead to respiratory failure soon after birth. The discovery, published in the American Journal of Human Genetics, will improve genetic counselling for families affected by this disease, and may ultimately help improve the treatment of features associated with this disease and the broader class of disorders known as ciliopathies.



Clean energy

Biofuels centre fuels renewable future

In April, Queensland Premier, The Hon Campbell Newman MP, opened IMB's Solar Biofuels Research Centre (SBRC), an advanced biofuels pilot plant designed to develop microalgae-based systems as a source of clean fuel.

The SBRC was developed in partnership with the Queensland Government, KBR Inc., Neste Oil Corp., Cement Australia Pty Ltd, Siemens, and Bielefeld University and the Karlsruhe Institute of Technology in Germany.

Researchers leading the \$3.5 million project are working alongside industry to develop economically viable and sustainable methods of producing biofuels and other bioproducts, such as animal feeds. Their ultimate aim is to develop sustainable biofuels that can compete with fossil fuels dollar for dollar.

Algae proves fresh for scientific discovery

Dr Evan Stephens from the Solar Biofuels Research Centre trialled native algae species in the hope of developing commercially viable fuels from algae. In collaboration with Professor Ben Hankamer and researchers from Germany's Bielefeld University and the Karlsruhe Institute of Technology, Dr Stephens identified fast-growing and hardy microscopic algae that could prove the key to cheaper and more efficient alternative fuel production. Dr Stephens shared this work with the community as a finalist in the national science communication competition, Fresh Science.

Agriculture

Harnessing bacteria as possible new bioinsecticide

A team of Australian and New Zealand researchers, led by Dr Michael Landsberg, investigated the workings of *Yersinia entomophaga*, a bacterium that kills a range of insect species, including the diamondback moth, which are known to cause major crop damage worldwide.

The team discovered a molecular assembly manual that bacterial and animal cells use to manufacture generic canisters and store toxic or sensitive molecules. The bacterium can release the toxins from their canister on demand, which kills the target insect. Their findings, published in *Nature*, could lead to a possible new bioinsecticide to control crop pests.

Spider venom targets insect pests

Professor Glenn King and Dr Maggie Hardy found a natural component of Australian tarantula venom that is more potent against certain insect pests than existing chemical insecticides. The orally active toxin known as OAIP-1 is lethal if eaten by the cotton bollworm or termites, and could be developed into an environmentally friendly insecticide.

The work, published in *PLOS ONE*, could help meet the urgent need for new insecticides, due to insects becoming resistant to existing products and others being deregistered because of possible risks to human health and the environment.

Biofertiliser boosts sustainable sugarcane farming

Professor Mark Ragan and Dr Chanyarat Paungfoo-Lonhienne, along with colleagues from IMB, UQ's School of Agriculture and Food Sciences, and UQ's Australian Centre for Ecogenomics, have identified a new species of bacterium that could reduce the need for nitrogen fertiliser in cane farming.

The study, conducted in partnership with the local sugar industry and published in *Microbial Biotechnology*, could help deliver the nutrients crops need with increased sustainability and at a lower cost.

The process the research team used identified both a potential biofertiliser for Queensland sugarcane, and a useful method for developing bacterial biofertilisers for different varieties of sugarcane around the world.

Industry collaborations boosted by funding

Two agricultural projects from IMB were boosted by funding from the Australian Research Council that will facilitate collaborations with industry partners.

Professor Rob Capon will team with Eli Lilly Australia to develop antiparasitic agents to safeguard Australian livestock, while Professor David Craik and Dr Aaron Poth will join Innovate Ag Pty Ltd in developing ecofriendly alternatives to manage crop pests.

RESEARCH PROGRAMS

CHEMISTRY AND STRUCTURAL BIOLOGY

PhD student Sheila Barbero (Fairlie Lab)

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

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 throughout 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. Our researchers are also working to develop more effective agricultural products and more efficient clean energy production systems.

During 2013, the division supported research in the following areas:

- > chemistry and human therapeutics
- > protein structure in drug and insecticide design
- > bio-inspired design of solar fuel systems
- > molecular biodiscovery: learning from nature
- > drugs and diagnostics for superbugs, viruses and cancer
- > antibiotic discovery, understanding insulin signalling and protein structure
- > design and discovery of bioactive peptides and proteins in venomous animals

> pharmacology of marine toxins

OCI

> 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 National Health and Medical Research Council, Australian Research Council, Queensland Government, US National Institutes of Health and industry partners.

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
- > Associate Professor Mark Smythe

PROFESSOR DAVID FAIRLIE CHEMISTRY AND HUMAN THERAPEUTICS



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, and 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 explain the 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, in some cases with industry partners, 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.

During the year, we pioneered a new method to downsize proteins to small molecules with protein-like functions and potencies. This discovery can help researchers discover affordable new medicines.

Our lab also shown that the presence of an inflammatory protein called PAR2 in abdominal fat tissue of humans and rats correlates with obesity. Drugs that bound to this inflammatory protein were able to prevent and treat diet-induced obesity in rats.

Furthermore, as part of the Queensland Emory Development Alliance, we began a formal collaboration with colleagues at QIMR Berghofer, Brisbane, and Emory University, Atlanta, US, to investigate how to block a pathway responsible for intractable forms of breast cancer, potentially leading to a new cancer therapy.

PROFESSOR DAVID CRAIK PROTEIN STRUCTURE IN DRUG AND INSECTICIDE DESIGN



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 reengineered 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 used a range of medicinal chemistry techniques to determine the structures of biologically active molecules and identify functional regions of these molecules to exploit in drug design and development. In particular, we have developed structure-activity relationships for a number of novel conotoxins with potential to be used as leads in drug design programs. We have also demonstrated that natural cyclotides can be adapted or re-engineered for pharmaceutical applications, and we have further defined structure-activity relationships for a class of mammalian host defence peptides called theta-defensins. This work has been reported in 34 refereed articles published during 2013, including commentaries in high-profile journals, *Angewandte Chemie International Edition* and *Nature Chemistry*.

PROFESSOR BEN HANKAMER BIO-INSPIRED DESIGN OF SOLAR FUEL SYSTEMS



One of the biggest global challenges facing society today is our need to develop more efficient and commercially viable renewable energy systems, which can improve energy security and reduce our dependence on fossil fuels. Our work aims to contribute to meeting this challenge, and we have turned to nature to help us do this.

Solar energy is by far the largest renewable energy source available to us—particularly in Australia—and has the potential to both meet and exceed future global energy demands. Our team is focused on developing solar fuel technologies that are able to tap into this huge solar energy resource and use it to produce a wide range of fuels, such as hydrogen, methane and oil-based fuels, including transport fuels.

The natural photosynthetic machinery of plants has evolved to capture solar energy and store it in the form of chemical energy (fuel). Plants that are very good at this are single-celled green algae (microalgae), which we use as a model natural fuel system and inspiration for developing next-generation bio-inspired artificial solar fuel technologies.

During 2013, our lab investigated the complex in vivo structure of the dynamic photosystems of plants through a multi-scale approach, using electron tomography (cellular structures), single particle analysis (macromolecular structures), and crystallographic data (atomic resolution structures). By merging these data sets, our aim is to produce a pseudo-atomic resolution model of these intricate and dynamic systems in their cellular context. This cellular 3D atlas will be used to guide and refine the design of higher efficiency algae-based and artificial solar energy systems that we hope will, in future, be able to contribute to meeting renewable fuel demand.

A major achievement for our lab in 2013 was launching our advanced Solar Biofuels Research Centre, located at UQ's Pinjarra Hills site in Brisbane. The centre, which was officially opened by Premier Campbell Newman in April, provides an advanced microalgae facility where our lab will design and test microalgaebased systems as a source of clean fuels, and develop new ways to optimise production systems. These systems are also of benefit for the production of high-value products such as vaccines.

PROFESSOR ROB CAPON

MOLECULAR BIODISCOVERY: LEARNING FROM NATURE



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. Modern societies have come to rely heavily on natural products, for example, as pharmaceuticals to treat infection, cancer, pain and other illnesses; and as agricultural chemicals to control disease and improve productivity in crops and livestock.

Our research is leading the discovery of Australian natural products, and is one of only a few laboratories in the world specialising in marine and microbial biodiversity. The knowledge that we discover informs our understanding of the role of chemicals in nature, and inspires the development of valuable new pharmaceuticals, agrochemicals and more.

Together, with a network of academic and industry collaborators, we are exploring the application of new natural products to treat an array of human diseases, including tuberculosis, malaria, Alzheimer's, cancer, pain and obesity; as well as agrochemical challenges, including parasitic infections in 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 control this invasive pest that is poisoning many of Australia's native predator species, including quolls, lizards, snakes and crocodiles.

During 2013, we patented a new environmentally sustainable cane toad control solution utilising natural toad pheromones, and a new class of anthelmintic effective against multidrug-resistant gastrointestinal nematode infections in sheep. Both discoveries have attracted significant industry interest, and we hope to progress these opportunities in the near future. We are also working on developing natural product-inspired treatments for pancreatic cancer, chronic inflammatory pain, tuberculosis and malaria.

PROFESSOR MATT COOPER

DRUGS AND DIAGNOSTICS FOR SUPERBUGS, VIRUSES AND CANCER

We believe we can more effectively treat patients by improving the way we understand and diagnose disease. Our research is aimed at discovering new ways of detecting and treating bacterial infections, inflammatory disease 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 work to inform the community of these important health issues through 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, the 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, we have gained a deeper understanding of the role of gut biota, which are the bacteria that live in our digestive system, and how this affects inflammation in the development of diseases such as asthma, chronic obstructive pulmonary disease, diabetes 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.

Furthermore, in partnership with more than 12 laboratories worldwide, we are designing and developing new molecules to target the interface between infection and our immune system's response that leads to acute and chronic inflammatory disease.



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

Of particular interest to our research is bacterial disulfide bond (Dsb) forming proteins, which are master regulators of virulence and key targets for the development of antibacterial agents that inhibit the ability of bacterial pathogens to cause disease. 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 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 multi-pronged approach, including fragment screening, in silico screening and peptidomimetic design. From these investigations, we are developing a new class of antibacterial that may be useful in treating infections caused by multidrug-resistant bacteria and combating the growing global threat of antimicrobial resistance.

Our lab also works on diabetes, focusing on proteins that help regulate blood glucose levels in response to insulin signalling. Through collaborations in Australia and the US we are also unravelling the dynamic interactions induced by insulin binding to muscle and fat cells. This research aims to identify what goes wrong in diabetes, and in the long term may lead to new therapeutics to treat this devastating disease.

PROFESSOR PAUL ALEWOOD



DESIGN AND DISCOVERY OF BIOACTIVE PEPTIDES AND PROTEINS IN VENOMOUS ANIMALS

Our research focuses on identifies and develops bioactive molecules from Australia's venomous animals that have the potential to create 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, and their development into therapeutic candidates to treat a range of diseases.

Recently, our lab has investigated druggable receptors in the gut, and ways to reduce protease degradation and disulfide bond rearrangements in drug candidates. Our lab recently described a mouse model of chronic abdominal pain where oxytocin receptors are significantly upregulated in nociceptors (pain receptors) without affecting normal tissue, which is an important advantage in drug development.

During the past 12 months, we developed novel chemical strategies to engineer non-reducible and more stable oxytocin analogues, which may be developed as treatments for irritable bowel syndrome. Chemoselective selenide macrocyclisation yielded stabilised analogues equipotent to native oxytocin. Ultra-high-field nuclear magnetic resonance structural analysis of native oxytocin and the seleno-oxytocin derivatives revealed that oxytocin has a pre-organised structure in solution, in marked contrast to earlier X-ray crystallography studies.

Finally, we showed that these seleno-oxytocin analogues potently inhibit colonic nociceptors both in vitro and in vivo in mice with chronic visceral hypersensitivity, which mostly affects the gut. This research has important implications for clinical use of oxytocin analogues and cysteine-rich peptides in general.

PROFESSOR RICHARD LEWIS PHARMACOLOGY OF MARINE TOXINS



Our research explores the mechanisms of how the body feels pain and uses this knowledge to develop new drugs to combat chronic pain. To do this, we study conotoxins, which are small peptides from predatory marine snails that are very active in pain pathways and could provide the basis for a new class of pain management drugs with fewer side effects.

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 called ciguatoxins produce the debilitating disease known as ciguatera.

During the past 12 months, we have discovered new mechanism of peptide diversification through processing and transcriptomic messiness; identified peripherally analgesic ω -conotoxins, which are being developed as a new pain treatment, and defined a key role of potassium channels in the activity of nerves associated with cold pain. In addition, we have worked closely with industry partners to develop our novel findings, supported with the award of two new ARC Linkage grants to investigate spider toxins and small molecule blockers of sodium channels in pain pathways.

"Translatable discovery research is essential in furthering our understanding of disease and developing better treatments to help improve quality of life and survival rates for those affected."

PROFESSOR GLENN KING **BUGS AND DRUGS**



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 approximately 15 per cent 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.

During 2013 we reported the first orally active insecticidal toxin isolated from spider venom, with potential for the control of insect pests. We also reported a novel peptide isolated from centipede venom that proved to be a more potent painkiller than morphine in a variety of rodent pain models.

ASSOCIATE PROFESSOR MARK SMYTHE

COMBINATORIAL CHEMISTRY AND MOLECULAR DESIGN

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.

In 2013, we have achieved efficacy in an in vivo model of iron disease; achieved desired selectivity profile for a potential pain therapeutic; optimised an anti-asthma candidate; and achieved compelling in vivo data for a once-a-week injectable anti-IL-6 antagonist.

We have several applied projects pursuing constrained peptides to modulate difficult or undruggable targets for inflammatory bowel disease. Specifically, we are pursuing clinically validated targets serviced by marketed antibody drugs that are currently available as injectable treatments. We plan to replace these treatments with orally delivered constrained peptide alternatives, which will deliver more effective, affordable and non-invasive 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 drug candidate selection. Using a combination of mathematics, software development, drug design, medicinal chemistry, pharmacology, structural biology and phage display, we are developing new approaches to treat asthma, leukaemia and inflammatory bowel disease. Moreover, in our structural biology studies, we are using Electron Paramagnetic Resonance (EPR) spectroscopy to study the structure and dynamics of proteins using a suite of new chemical probes.

We continue to purse late-stage preclinical optimisation for several drug candidates in diverse therapeutic areas such as asthma, pain, iron overload disorders, and inflammatory bowel disease.

"Arthropod pests, such as insects, ticks, and mites are responsible for destroying one-third of the world's food supply, as well as transmitting a diverse array of human and animal diseases.

We hope our work will go a long way in safeguarding agricultural crops and preventing the spread of disease here and around the world."

US biology graduate Cecilia Prator (pictured) joined IMB's King Lab in 2012–13 on a Fulbright Postgraduate Scholarship



RESEARCH PROGRAMS



Scientists in IMB's Genomics and Computational Biology Division apply approaches based on mathematics, statistics, computer science, and bioinformatics to unlock new knowledge from the endless information buried in biological big data.

These valuable insights help the division to understand the molecular structures, functions and regulation of genomes in mammals, vertebrates, bacteria and plants, which has applications in human health and environmental management.

Researchers within the division conduct high-throughput sequencing, bioimaging and modelling, computation, and bioinformatics to explore comparative functional genomics, small regulatory RNAs, genomic epidemiology, molecular systems biology and computational modelling of genetic and cellular regulatory networks.

During 2013, the division supported research in the following areas:

- > computational systems biology
- > population genomics

illumna

an Nourbakhsh (Grimmond Lab)

- > Queensland Centre for Medical Genomics (QCMG)
- > rare childhood diseases
- > modelling, visualisation and classification of bioimaging
- > pattern recognition and modelling in computational biology.

The division hosts the Australian Research Centre (ARC) Centre of Excellence in Bioinformatics and QCMG. Its researchers also actively participate in the teaching and learning activities of UQ's Schools of Chemistry and Molecular Biosciences, Information Technology and Electrical Engineering, and Mathematics and Physics. In 2013, division staff successfully organised the annual Winter School in Mathematical and Computational Biology, which attracted almost 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 on-site facilities for large-scale DNA sequencing, computing and data management.

Major funders of the division include the National Health and Medical Research Council, Australian Research Council, Queensland Government, US National Institutes of Health, James S. McDonnell Foundation, and industry partners.

Division Head

> Professor Mark Ragan

Laboratory Heads

- > Associate Professor Tim Bailey
- > Dr Lachlan Coin
- > Professor Sean Grimmond
- > Dr Nick Hamilton
- <u>)</u> Dr Ryan Taft

PROFESSOR MARK RAGAN COMPUTATIONAL SYSTEMS BIOLOGY



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 reverseengineered 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 data 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.

During the past 12 months, we developed and applied computational approaches to discover the backup systems that cells use to repair damage to their DNA. These backup pathways can differ between cancerous and normal cells, and we are applying these approaches to discover novel ways to target breast cancer cells with minimal risk to normal healthy cells.

The international Sea-quence Project aims to generate core genetic data from the Great Barrier Reef and coral reefs in the Red Sea. As part of this collaboration, we began to assemble and analyse genomes of *Symbiodinium*, the algal symbiont in corals. Our goal is to identify the gene systems and mechanisms that underpin and stabilise this symbiosis, to assist in improving coral health and managing reef ecosystems.

Finally, we extended our studies of bacterial genomes to the communities associated with roots of sugarcane. In partnership with fellow UQ scientists, we identified a new soil bacterium, which under controlled conditions, promotes the growth of sugarcane. We then sequenced the genome of this bacterium to investigate its potential to supply nitrogen compounds to sugarcane.

DR LACHLAN COIN POPULATION GENOMICS



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. In particular, we are interested in 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 team uses integrative genomics approaches to profile the genome, transcriptome and proteome from the acute to recovery 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 adults in Africa. Moreover, we have developed an accurate test for diagnosing tuberculosis in children, which we hope to translate into an affordable, point-ofcare diagnostic. Finally, we have also used transcriptional profiling of T cells—white blood cells that play a role in immunity—and their response to allergens to identify new pathways involved in allergies, and determine how we can potentially control these pathways to treat allergies.

PROFESSOR SEAN GRIMMOND QUEENSLAND CENTRE FOR MEDICAL GENOMICS



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 highthroughput 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.

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 surveys of the genetic damage accumulated by pancreatic and ovarian cancers. We have used these large datasets, or cancer atlases, to mine out the root causes of cancer formation in more than 300 tumours, and provide insights—which we have shared with the research community—into the variability of patient response to chemotherapy.

During the coming year as we complete these cancer atlases, we will start to investigate the commonalities of solid cancer initiation and progression. We will also move towards using genome-wide analyses to investigate how cancers progress from early lesions to invasive disease and how they evolve to overcome standard cancer therapies.

DR RYAN TAFT Rare Childhood Diseases



Our research seeks to answer pressing biological and medical questions using our cutting-edge 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 under the age of 15. This research is also assisting with the development of tailored therapeutics and treatments for children diagnosed with rare diseases, including leukodystrophies and Prader-Willi syndrome.

During the past two years, we have dramatically expanded our work in personalised medicine, and have now sequenced more than 100 families in the quest to discover the genetic causes behind rare disease mutations. Our successes include the cases of a four-yearold boy with a central nervous system disease that we solved by identifying a disease new to medicine; the discovery of the genetic mutation responsible for a disease called H-ABC, which affects brain development in childhood; and the resolution of more than 10 additional clinical cases that were thought to be unsolvable.

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 it produces. Our work has resulted in a number of important findings, including the fact that genes often code 'secret' layers of RNA information, which act to fine tune the human genetic machine.

DR NICK HAMILTON MODELLING, VISUALISATION AND CLASSIFICATION OF BIOIMAGING



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 timelapse 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 help scientists unlock valuable information from these rich and advanced new data sources in areas such as drug and genomic discovery. Our laboratory has two key streams of research in the analysis of multi-dimensional bioimaging. The first is in developing methods to automatically extract key information that describes biological systems. The second is in building predictive mathematical models at both cellular and organ levels. We hope to use these models to predict the behaviour of organs and cells under a range of conditions, including in health, disease and under drug action.

In 2013, in collaboration with other research teams, we developed new combined methods in imaging, quantification and mathematical modelling, which for the first time allowed the most comprehensive, multi-scaled analyses of a developing kidney. Moreover, using advanced 3D imaging technologies together with new mathematical algorithms, we proved for the first time that the cellular branching structure of the kidney follows a strict pattern of development over time.

We are also applying these methods to answer some of the most pressing questions in modern biology, such as 'What are the factors affecting the growth of nephrons, the fundamental filtering unit in the human kidney?' and 'What are the critical stages in kidney development, and can they be altered to treat disease?' Other subjects that we are now applying our research to with interdisciplinary collaborators include: 'How does the lymphatic system develop?'; 'How do macrophages, the front line of the human immune system, fight bacteria and infection?'; and 'How do cancer cells escape and spread from epithelial tissues?'

ASSOCIATE PROFESSOR TIM BAILEY



PATTERN RECOGNITION AND MODELLING IN COMPUTATIONAL BIOLOGY

Modern biological experiments produce massive amounts of data and require sophisticated computer software to extract knowledge from this endless information. Our laboratory develops specialised web-based software for analysing the results of experiments that sequence DNA and RNA, the information storage workhorses of the cell. We also develop software tools to help biologists design experiments for modifying DNA (genetic surgery) or for modifying the regulation of genes in predictable ways. Our most notable software is MEME Suite, which is used by nearly 18,000 biologists each year to analyse DNA, RNA and protein sequences. 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 in health and disease. 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 2013, our bioinformatics tools were cited more than 1000 times, and we developed and published two new tools for designing genome and regulatory surgery experiments that will help biologists pinpoint the key genes in disease and normal cellular growth. We explored the regulation of transcription in cortical, forebrain and lung development, and we also developed a bioinformatics tool for studying the 3D structures of human chromosomes, which will help us understand the role of chromatin architecture in the regulation of gene expression.

Our work also contributed to developing a method for studying the formation of spider toxins, which may have applications in pain research. We also contributed to a review of the RGG motif, a common feature of proteins that interact with RNA and DNA molecules, which is implicated in neurological and neuromuscular diseases and in cancer. Finally, we are currently analysing the regulation of genes by the KLF1 protein to understand its role in a form of hereditary anemia.



RESEARCH PROGRAMS



IMB's Molecular Cell Biology Division seeks to understand the molecular workings of the cell, the building blocks of our bodies. This is vital for a full understanding of how our bodies function, and serves 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, move and interact with one another. Laboratories within the division regularly work alongside collaborators from other research disciplines, where a multidisciplinary approach is necessary to solve fundamental problems or build new technologies.

During 2013, 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
- > membrane trafficking at atomic resolution
- > role of the cell surface in health and disease
- > protein trafficking and inflammation
- > role of growth hormone in human development
- > endosomal dynamics and pathogen invasion
- infection and innate immunity
- > inflammation and innate immunity.

Many leading technologies are used to help the division advance discoveries in these areas, with state-of-the-art, on-site facilities for quantitative optical microscopy, live cell imaging, single-molecule protein interaction analysis, and protein structure determination.

Notably, the division is closely allied with the Australian Microscopy and Microanalysis Research Facility, which allows for the application of cryo-electronic microscopy, cellular tomography, advanced visualisation and high-performance computing. Members of the division also oversee the Australian Cancer Research Foundation's Cancer Biology Imaging Facility.

Major funders of the division include the National Health and Medical Research Council, Australian Research Council, Queensland Government, National Breast Cancer Foundation, and industry partners.

Division Head

> Professor Alpha Yap

Laboratory Heads

- > Professor Kirill Alexandrov
- > Dr Brett Collins
- > Professor Rob Parton
- > Dr Kate Schroder
- > Associate Professor Matt Sweet
- > Professor Jenny Stow
- > Associate Professor Rohan Teasdale
- > Professor Mike Waters

PROFESSOR ALPHA YAP

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

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 common 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.

We focus on how cadherins regulate the cell cytoskeleton to control the mechanical forces they exert on one another. Our most recent work revealed that cells control the patterns of tension with which they pull on their neighbours. By maintaining these patterns, cells are able to form epithelial tissues, the layers of cells that cover and protect organs, including skin. However, these patterns are altered when potentially cancerous cells are pushed out from epithelial tissues by surrounding cells, which can lead to cancer metastasis. This process of cellular extrusion involves many elements, including cell signals and components of the cytoskeleton, which are regulated by cadherins to control cellular forces. All of these elements present multiple opportunities for cellcell interactions to be disturbed and promote disease.

PROFESSOR KIRILL ALEXANDROV



MOLECULAR ENGINEERING: BETTER TOOLS, BETTER SCIENCE, BETTER LIFE

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 systems 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. These methods are vital in biotechnology, as the ability to produce and analyse proteins determines the cost and speed of discovering and creating new vaccines, drugs and diagnostic methods. We combine this technology with molecule spectroscopy to quantitatively analyse protein dynamics and protein-protein interactions. We then use this technological platform to create novel diagnostics and treatments for cancer, thrombosis and excessive bleeding.

During the past 12 months, we have developed synthetic protein signal transduction and amplification cascades based on proteases for use in organism engineering and in vitro diagnostics. We have also developed a novel approach for synthesis of polypeptides with non-native and improved properties for use in human health and industrial applications.

Notably, we partnered with two Australian biotechnology companies to ensure the practical application and relevance of our research. Together with Phylogica, we are identifying unique peptide drug candidates with therapeutic potential, and with Bioproton—which recently expanded its Brisbane manufacturing facility—we are developing new technologies to help reduce the environmental impact and costs of creating high-quality animal feed enzyme supplements.

In 2013, we also established a collaborative relationship with UQ's Sustainable Minerals Institute, and launched an initiative aimed at developing next-generation mining technologies that enable bioextraction of minerals without the need for excavation. We are currently exploring and developing a number of concepts, and we are particularly interested in finding new methods for mining gold and copper from low-grade or otherwise uneconomic deposits.



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 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—the process of how material moves into and out of the cell, or is shared between different membrane-bound organelles. We have a particular emphasis on a key sub-cellular structure called the endosome and 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' for 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. We have also investigated the function of proteins that are mutated in Parkinson's disease, and we are working with other IMB researchers to explore the structures of protein molecules involved in cancer, lipodystrophy and muscular dystrophy.

PROFESSOR ROB PARTON ROLE OF THE CELL SURFACE IN HEALTH AND DISEASE



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. Our work aims to understand the plasma membrane and what goes wrong in disease.

The properties of the plasma membrane rely on its specialisation into regions of specific function. Our research particularly focuses on caveolae, small 'pockets' on the plasma membrane that form a specialised domain of the cell surface with a distinct structure and function. 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 caveola function, we are studying cells and animal models, namely mice and zebrafish, which lack caveolae or have defective caveolae. We know loss of caveola proteins prevents efficient liver regeneration after liver damage and we have now shown that the major pathways involved in this process are those that handle fats (lipids) in the liver.

Moreover, we discovered new scaffolding proteins called cavins that are responsible for caveola formation, and we explored their function. Our investigations revealed how caveolae can respond to forces on the plasma membrane in a process called mechanotransduction. During this process, caveolae are stretched, causing cavins to be released into the cell and allowing them to interact with cellular components. We showed that this also alters the organisation of lipids, crucial for signalling. We further demonstrated that the formation of caveolae by cavins plays an important role in cancer, as an imbalance in caveola proteins can lead to prostate cancer.

In addition to providing molecular insights into diseases such as prostate cancer and muscular dystrophy, we have continued work to optimise a unique novel drug delivery system that builds upon our fundamental research, which we hope will have therapeutic benefits in the future.

PROFESSOR JENNIFER STOW PROTEIN TRAFFICKING AND INFLAMMATION



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 'phagocytose', or eat bacteria, a process that normally results in these microbes being digested and killed. However, some bacteria can avoid dying 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.

Our recent discoveries include identifying new genes that control cell signaling and cytokine secretion in macrophages. We are also testing some existing drugs for new applications in treating inflammation and infection, and we have developed new methods for analysing immune responses and protein interactions.

PROFESSOR MIKE WATERS ROLE OF GROWTH HORMONE IN HUMAN DEVELOPMENT



The growth hormone receptor determines the degree of cellular response to growth hormone. Through sophisticated techniques, we have developed a detailed molecular 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. As the first fruit from this landmark discovery, we have created growth hormone receptors that are permanently activated. These are being used to promote hormone-free growth of fish in Chinese aquaculture, with the potential to be applied to other aquaculture species such as lobster.

We also recently described a growth hormone receptor-initiated signalling pathway that is essential for expression of a powerful immune tolerance molecule that we predict will improve the success of human liver and kidney transplants. We are currently trialling this molecule in animal models of liver regeneration. We have also demonstrated the use of growth hormone therapy as a treatment for hepatic steatosis (fatty liver) in animal models, and determined how this works.

We have found that growth hormone acts in normally fed mice to burn fat, so as to maintain a normal amount of fat. We find it does this by inducing a special type of fat-burning cell known as the beige cell. 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, and have identified a variant growth hormone receptor that promotes lung cancer by inhibiting receptor degradation. However, growth hormone acting externally is prevented from doing this by a set of opposing factors, which means it is a safe therapeutic.

ASSOCIATE PROFESSOR ROHAN TEASDALE

ENDOSOMAL DYNAMICS AND PATHOGEN INVASION



The movement of the thousands of distinct membrane proteins between the cell surface and intracellular

compartments represents a critical cellular process as it controls the organisation of cells in tissues and the communication between cells and their environment. The success of this process depends on the regulated sorting and trafficking of proteins within the highly dynamic intracellular endosomal compartments of the cell.

Defects in endosomal trafficking are linked to many human diseases including various neurodegenerative diseases, cancers and metabolic diseases. Our long-term research program is focused on the discovery and characterisation of novel endosome associated proteins and defining their molecular function in endosomal trafficking pathways.

For example, our prior basic research into the characterisation of retromer, which is a central regulator of early endosome protein trafficking, recently enabled us to provide the first molecular insights into how its function is modified in disease. Genetic mutations in retromer have recently been associated with progressive neurological diseases including Parkinson's disease. We have determined the molecular changes that occur in endosomal trafficking to cause these disease states.

Numerous infectious pathogens depend on their ability to manipulate endosome trafficking, specifically through hostpathogen interactions, to successfully invade the host. We are currently investigating the molecular details of these pathways and how they are modulated in response to infection with a number of pathogens including *Salmonella*, a leading cause of human gastroenteritis; chlamydia, a major sexually transmitted disease; and Group A *Streptococcus*, a common bacterial cause of human mortality through a range of conditions.

ASSOCIATE PROFESSOR MATT SWEET INFECTION AND INNATE IMMUNITY



Our bodies have an innate immune system that acts as an alarm system. This system senses danger in the form of infection and/or cell damage, and helps to initiate recovery and repair processes. Macrophages are remarkably dynamic white blood cells that are particularly important cellular components of the innate immune system. 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 lab studies the interactions between macrophages and specific human pathogens, with the goal of understanding how pathogens overcome macrophage functions. Such an understanding will help us to develop new approaches to combat infectious diseases.

Two bacterial pathogens that we are currently studying are *Salmonella*, which is a bacterium that causes severe gastrointestinal disease leading to high mortality rates around the world; and uropathogenic *E. coli* (UPEC), which is the major cause of urinary tract infections and is one of the most common infectious diseases.

In 2012 we found that macrophages use zinc to kill bacteria. During the past 12 months, we have built on our understanding of this molecular process, discovering multiple mechanisms that *Salmonella* uses to evade this particular macrophage response. Since zinc supplementation is used to treat severe diarrheal diseases, but it is not always effective, our findings may help identify new anti-infective approaches. We also identified a specific molecular recognition system that macrophages use to detect and respond to UPEC. This finding may help lead to the development of new ways of combating urinary tract infections.

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 2013, we have continued to discover specific molecular mechanisms that result in excessive macrophage inflammatory responses. We are now working on approaches to block the activity of these pathways, as this may provide new avenues for the development of anti-inflammatory drugs.

DR KATE SCHRODER INFLAMMATION AND INNATE IMMUNITY



The innate immune system is the body's first line of defence against microbial attack. The innate immune system recognises situations of cellular danger through receptors such as NOD-like receptors (NLRs), which sense microbial structures and activate inflammatory responses that underpin our ability to fight infectious disease. Many NLRs do so by forming molecular complexes called inflammasomes upon cellular infection with pathogenic bacteria, viruses and fungi. However, these innate immune responses can also be triggered in uninfected people by cell damage or metabolic stress, leading to diseases such cancer, gout and diabetes.

Our research focuses on understanding how immune cells launch healthy inflammation to fight infection and unhealthy inflammation to promote disease. By understanding exactly how the body fights infection, we can help identify new drug targets or vaccines to combat infectious disease, which causes 13 million deaths globally each year. By understanding how unhealthy inflammation is initiated, we may also be able to design new strategies for the treatment of common diseases such as cancer, gout and diabetes.

During the past 12 months, we have made significant progress toward understanding the molecular mechanisms regulating inflammasome activation, and the cell types critical for inflammasome-mediated host defence and disease.

RESEARCH PROGRAMS



PhD student Barbara Maier (Little Lab)

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 for 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.

Researchers 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 2013, the division supported research in the following areas:

- > disorders of sex development, infertility and testicular cancer
- > kidney development, damage, repair and regeneration
- development of blood and lymphatic vessels
- > genetics and cell biology of cardiac development
- > nuclear hormone receptors and metabolic disease
- melanocytes and skin cance
- > primary cilia development and human ciliopathies
- > cancer and cell signalling.

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

Major funding sources include the National Health and Medical Research Council, Australian Research Council, Cancer Council Queensland, Australian Cancer Research Foundation, Queensland Government, the US National Institutes of Health, Human Frontiers Science Program, Cariplo Foundation Italy, John Trivett Foundation, and industry partners.

Division Head

> Professor Peter Koopman

Laboratory Heads

- > Dr Mat Francois
- > Dr Ben Hogan
- > Professor Melissa Little
- > Professor George Muscat
- > Dr Kelly Smith
- > Associate Professor Rick Sturm
- > Professor Brandon Wainwright
- > Associate Professor Carol Wicking

PROFESSOR PETER KOOPMAN DISORDERS OF SEX DEVELOPMENT, INFERTILITY AND TESTICULAR CANCER

Our research focuses on genes that regulate sex development the molecular process that determines 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, which affect up to 1 in every 250 children born each year, so that these disorders can be diagnosed more accurately and managed more effectively.

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 current research is focused on understanding how these signals act. This work is helping us find the causes of infertility and testicular cancer, two of the most common reproductive disorders whose incidence continues to rise.

More broadly, the study of embryo development provides insight into mechanisms of disease, including cancer, and provides a molecular and cellular basis for new molecular diagnostics and targeted therapies.

PROFESSOR MELISSA LITTLE KIDNEY DEVELOPMENT, DAMAGE, REPAIR AND REGENERATION

Chronic kidney disease is a growing health problem, with one in three Australians now at risk of developing the disease. In 2010, 2257 new patients began treatment for end-stage kidney failure in Australia, and treatment for chronic kidney disease accounted for 15 per cent of all hospitalisations in the country. Currently, the only treatments available for end-stage renal disease are dialysis or organ transplantation, creating an urgent need for improved treatments.

In 2013, our team identified the six key genes that can be used to transform adult cells into kidney stem cells, a discovery that was published in the world's leading nephrology journal, the *Journal of the American Society of Nephrology*. Building on this finding, our team achieved another world first, growing a mini-kidney using human stem cells. This breakthrough made headlines across the world and was published in the prestigious scientific journal, *Nature Cell Biology*.

Through this research, we discovered it was possible to make

human stem cells turn into the components of the kidney, and that these key cell types would 'talk' to each other to self-organise into a mini-kidney when grown together in a dish. Moreover, the fact that stem cell populations can organise themselves into such complex structures within the laboratory bodes well for the future of tissue bioengineering. Here we hope to be able to make miniorgans to test new drugs for kidney disease, an advance that could save considerable time and money when it comes to developing better drugs.

In future, these findings could also help us bioengineer kidneys for individual patients. Our next step is to make mini-kidneys in culture from the cells of different patients with kidney disease so that we can try to determine what has caused their particular disease, and develop personalised treatments.

Going forward, we hope to determine if we can use the same stem cell transformation process we used to grow kidneys to make nephrons, which are the filtration units of the kidney and are essential for kidney health. We will also continue to collaborate with scientists and clinicians in the Netherlands, Italy and the UK on a research project to prevent kidney transplant rejection and to treat acute renal injury using mesenchymal stem cells.

DR BEN HOGAN MOLECULAR GENETICS OF VASCULAR DEVELOPMENT



Our vascular system is comprised of two vital and interconnected networks: a network of blood vessels responsible for distributing blood cells, oxygen, hormones and essentials 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 cancer metastasis.

Our research investigates how blood and lymphatic vessels form from pre-existing vessels. We aim to discover new genes and molecular pathways that regulate vascular growth during the development of the embryo and in disease. 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.

In 2013, we discovered new molecular mechanisms that regulate the formation of lymphatic vessels, identifying a crucial link between the genes CCBE1, VEGFC and VEGFR3, all of which are mutated in inherited lymphoedema syndromes. Together with IMB's Francois Lab, we discovered unexpected crossregulation between growth factor and transcription factor pathways controlling the formation of arteries and veins. We also identified several new genes controlling lymphatic vessel growth in the embryo. This work has significant implications for how we view pathological processes in disease, specifically in inherited disorders and metastasis.

Finally, we have completed a large, integrated, next-generation genetic screen to identify unique zebrafish mutants that fail to form lymphatic vessels. This will lead to a vastly deeper understanding of the molecules needed for lymphatic development and function in health and disease.

DR MAT FRANCOIS TRANSCRIPTIONAL REGULATION OF BLOOD AND LYMPHATIC VESSELS IN HEALTH AND DISEASE

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 pre-clinical mouse models of cancer or lymphoedema 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 pioneered 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 expertise in zebrafish biology, medicinal chemistry and live imaging.

During the past 12 months, we uncovered the embryonic function of vascular endothelial growth factor D (VEGF-D), which controls how blood vessels develop and spread by modulating the activity of the transcription factor Sox18 in both mouse and fish model systems. By understanding the cellular and molecular modes of action of VEGF-D, we can develop targeted therapeutics to control vascular expansion during cancer to block tumour growth and metastasis.

DR KELLY SMITH GENETICS AND CELL BIOLOGY OF CARDIAC DEVELOPMENT



The heart is essential for life support and any defects that alter its structure or function can be fatal. Our laboratory, which was established in April 2013, investigates how the heart forms by using forward genetics to identify new, previously unidentified genes that regulate cardiac development.

In the embryo, the heart begins as a simple straight tube. During development, it undergoes a series of complex folding events, growth and tissue specialisations to give rise to a multichambered, beating organ made up of many tissue types. Any defects that occur during this process result in structural anomalies known as congenital heart defects, which are the most common form of birth defects. Expanding our fundamental knowledge of heart development provides a framework for understanding cardiac disease, both inherited structural malformations and acquired heart disease. Understanding what cellular changes take place during heart development and defining the genetic regulators orchestrating this process are essential for devising strategies for cardiac repair.

To study heart development, our research primarily uses the zebrafish model. Zebrafish develop external to the mother (from the one-cell stage) and are optically transparent, permitting live imaging of the heart as the organ forms. We use the zebrafish model for this ease-of-use in functional gene identification, taking advantage of its amenability for high-throughput genetic screening as well as its tractability in live imaging. We are also translating our research into mammalian systems—such as mouse models and cell culture—validating the relevance and application of findings from the zebrafish model in mammals.

During 2013, we completed our first successful forward genetic screen for heart development mutants. With these novel mutants, we hope to identify new molecular and cellular regulators of cardiac development, significantly improving our understanding of how the heart forms. We also introduced a range of cutting-edge tools to help us conduct more targeted and efficient research, the findings from which will direct us in developing strategies for mending the diseased heart.



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 the 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 also 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.

In our breast cancer studies, we examined normal human breast tissue, estrogen receptor-positive and negative breast cancer cohorts and tissue adjacent to breast tumors. From this work, we identified NR targets for therapeutic exploitation, classification, and prognosis, and discovered epigenetic markers that could lead to metastasis-free survival for patients.

We also investigated the role of NRs in obesity and type 2 diabetes. In these studies, we produced transgenic mouse lines with musclespecific expression of an activated form of the nuclear receptor NOR1. We then demonstrated that NOR1 signalling controls skeletal muscle reprogramming, metabolic capacity, glucose tolerance, physical endurance, and resistance to diet-induced obesity and hepatic triglyceride accumulation. These findings were the first of their kind and were published as a cover article in the leading international journal, *Molecular Endocrinology*. Our future research will identify novel muscle-specific agonists targeting these NRs for therapeutic uses in obesity, type 2 diabetes and improving exercise capacity.

During the year, we demonstrated that modulators of histone methylation and epigenomic regulation, which turn the genes

in DNA 'on' and 'off', in skeletal muscle cells are involved in the regulation of glycogen metabolism. Specifically, we found the modulator known as PRMT4 controls genes involved in human glycogen storage diseases, which affect a person's ability to exercise, levels of fatigue, and sensitivity to insulin. We also identified and characterised the regulatory role of the c-ski oncogene in genetic programs that control susceptibility to diet-induced obesity, and insulin signalling in skeletal muscle.

In collaboration with IMB's Parton Lab, we demonstrated that caveolin-1 (CAV1)—the main structural protein of caveolae regulates liver lipid accumulation, and that this process involves regulation of bile acids and signalling by the nuclear receptor FXR. This provides new targets for the treatment of obesity and hepatic steatosis, also known as fatty liver disease. Furthermore, in collaboration with IMB's Stow Lab, we demonstrated that an NR called ROR-alpha controls the expression of cholesterol 25-hydroxylase in macrophages, an important gene that controls responses to infection and immunity.

Finally, insights gained from studies in lean, obese and diabetic murine models are helping our team to profile the expression of NRs, NR-associated co-factors, 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.

ASSOCIATE PROFESSOR RICK STURM MELANOCYTES AND SKIN CANCER



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.

A study of 600 volunteers from Queensland has documented pigmentation and common mole phenotypes to combine with genotypic information from this data set. Notably, we found a significant association between the dominant dermoscopic pattern and MC1R genotypes. We also reported on six patients in our cohort who carry the SUMOylation-deficient MITF E318K mutation that has recently been described as a medium-penetrance melanoma gene. The phenotype of these individuals showed a commonality of fair skin, high total nevi count, and all were multiple primary melanoma patients. There was also a high incidence of amelanotic melanomas found within the group, suggesting a genetic interaction between the MITF E318K allele and MC1R RHC homozygous genotype. These findings have direct clinical relevance to medical practitioners and how they diagnose melanoma in their patients.



ASSOCIATE PROFESSOR CAROL WICKING DEVELOPMENTAL GENES AND INHERITED DISEASE

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 hair-like cellular projection 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.

As part of a national and international network of clinicians and researchers, my laboratory has been involved in the discovery and characterisation of novel ciliopathy genes through high-throughput sequencing of patient cohorts. Our role is primarily to validate and extend the mutation discoveries through functional characterisation in animal- and cell-based models. To date, we have described two novel genes causing Jeune and short-rib polydactyly syndromes, ciliopathies characterised by severe skeletal defects. This work demonstrates the value in a multidisciplinary approach, allowing us to cover the full gamut of ciliopathy research from gene discovery to functional studies.

Our second approach to ciliopathy gene discovery involves analysis of mice generated through random forward genetic screening approaches. This has 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 cleft palate.

PROFESSOR BRANDON WAINWRIGHT CANCER AND CELL SIGNALLING



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 Basel 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 identified the core genetic components that lead to the development of medulloblastoma. This work will enable the therapeutic targeting of every medulloblastoma, not just a subset, leading to more powerful clinical trials and ultimately more effective treatment options.



JOINT APPOINTMENTS **AND AFFILIATES**

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.

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, San Francisco

Dr Nathan Cowieson Australian Synchrotron

Professor Norelle Daly James Cook University

Dr Melissa Davis The University of Melbourne

Professor John Funder Prince Henry's Institute

Professor Frank Gannon QIMR Berghofer Medical Research Institute

Professor Wanjin Hong Institute of Molecular and Cell Biology

Professor David Hume The Roslin Institute

Professor David Julius University of California, San Francisco

Professor Sangkot Marzuki AM Eijkman Institute for Molecular Biology

Professor John Mattick AO Garvan Institute

Dr Wim Meutermans Audeo Oncology

Dr Grant Montgomery QIMR Berghofer Medical Research Institute

Dr Josh Mylne University of Western Australia Professor Nicos Nicola Walter and Eliza Hall Institute of Medical Research

Mr Ken Roberts Former Managing Director of Wellcome Australasia Limited

Dr Greg Smith SciVentures Investments Pty Ltd

Professor Peter Turnbull QFAB Bioinformatics

Professor Peter Visscher Queensland Brain Institute

Dr Dagmar Wilhelm Monash University

Professor Marino Zerial Max Planck Institute of Molecular Cell Biology and Genetics

UQ affiliates

Dr Antje Blumenthal Diamantina Institute

Dr Mikael Boden School of Chemistry and Molecular Biosciences

Professor Matthew Brown Diamantina Institute

Dr Richard Clark School of Biomedical Sciences

Dr Marcel Dinger Diamantina Institute

Professor lan Frazer Translational Research Institute

Associate Professor Bryan Fry School of Biological Sciences

Professor Elizabeth Gillam School of Chemistry and Molecular Biosciences

Associate Professor Stuart Kellie School of Chemistry and Molecular Biosciences Professor Bostjan Kobe School of Chemistry and Molecular Biosciences

Dr Gary Leong Mater Children's Hospital (Qld)

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

RESEARCH SUPPORT **FACILITIES**





ACRF Cancer Biology Imaging Facility user, Dr Selwin Wu

ACRF Cancer Biology 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 is home to 23 high-performance microscopes and supporting image data analysis workstations, with facility staff on-site to provide users with expert technical support and training.

During the past 12 months, 206 unique users across the university used the facility for a total of 18,800 hours 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. Capabilities of the facility include laser scanning and spinning disc confocal microscopy, deconvolution, high-throughput multi-wall imaging, and 3D optical projection tomography (OPT).

Data generated from facility equipment in 2013 featured in more than 20 publications, and highlighted a range of discoveries, including a protocol that prompts stem cells to form all the required cell types to 'self-organise' into a mini-kidney in a dish, and the discovery of a protein in cells that could block the escape route of potentially cancerous cells and stop them spreading to other parts of the body.

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.

High-Throughput Genomics Facility

IMB's Queensland Centre for Medical Genomics (QCMG) houses a high-throughput DNA sequencing and microarray facility that is capable of delivering genomic data at unprecedented speeds and scales. With 30 scientists and bioinformaticians working

within the QCMG, the facility is used on a daily basis to conduct pioneering research and meet the objectives and milestones for the International Cancer Genome Consortium (ICGC) project. During 2013, the facility initiated a small number of cross-discipline research collaborations when it commenced

its sequencing service for IMB scientists.

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.

Mass Spectrometry Facility

IMB's Mass Spectrometry Facility 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.

In 2013, the facility provided technical advice, and research and training support for 125 unique users from across South-East Queensland working on a diverse range of projects. This support ranged from concept through experimental approach, design, methodology, data acquisition, data processing, and project reporting and publication.



Mass Spectrometry Facility user, Dr Jenny Zhang

Biomolecular NMR Facility Manager, Dr Peta Harvey

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.

Some of the discoveries made in 2013 using the facility included the identification and characterisation of potential therapeutic molecules from natural product extracts using de-novo peptide sequencing; and revealing the quantitative bioavailability characteristics of new molecules in the discovery and development of potential therapeutic molecules for a number of targeted diseases, including chronic pain, breast and ovarian cancer and chronic kidney disease. The implementation of new technology in the facility, such as the nano-HPLC-AB SCIEX Triple TOF 5600, has allowed users to study complex biological systems-for example, those found in cone snail venom-in greater depth and with greater sensitivity.

The facility acknowledges funding from ARC LIEF Project LE110100186.

Biomolecular NMR Facility

IMB's Biomolecular Nuclear Magnetic Resonance (NMR) Facility makes the powerful technique of NMR spectrometry accessible to our research and industry clients. The facility comprises a 600 MHz spectrometer with a cryoprobe and autosampler, and a 500 MHz spectrometer, equipped with a robotic sample changer. In addition to the institute's extensive NMR infrastructure, IMB researchers also have access to a 900 MHz spectrometer equipped with a cryoprobe and sample changer, making it the most powerful stateof-the-art NMR spectrometer in Australia. This instrument is located at UQ and is an instrument of the Queensland NMR Network.

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


Solar Biofuels Research Centre

of molecular size and oligomerisation state; investigation of dynamic properties; and metabonomic studies of various biofluids.

Key discoveries made in 2013 using the facility include structural characterisation of an oxytocic plant peptide that modulates the human oxytocin/vasopressin receptor, and of numerous venoms, including those from cone snails, snakes and scorpions; and the determination of self-association properties of cyclic peptides.

The facility is available on a user-pays system to researchers from a range of scientific disciplines across UQ. The facility also holds collaborations with researchers from other Australian universities as well as several international collaborations, most recently with scientists from Austria, China, and the US.

Solar Biofuels **Research** Centre

The Solar Biofuels Research Centre (SBRC) provides an advanced pilot-scale test facility and ancillary laboratories for the development of advanced microalgae systems for the production of food, fuel, biofuels, bioproducts and bioremediation. It is designed to provide a research hub to build synergy between industry and university partners skilled in biology, engineering and systems development.

The \$3.48 million SBRC project has the potential to benefit regional communities by developing economically viable methods of producing biofuels and other commodities including animal feeds. Capabilities of the SBRC include: strain purification; cryopreservation; nutrient and light optimisation; metabolic engineering; high value product development and screening; photobioreactor and raceway system design; and technoeconomic analysis.

The SBRC, located at Pinjarra Hills in Brisbane, was developed by IMB in partnership with the Queensland Government, KBR Inc., Neste Oil Corp., Cement Australia Pty Ltd, Siemens, and Bielefeld University and the Karlsruhe Institute of Technology in Germany.

QFAB Bioinformatics

QFAB Bioinformatics (QFAB) provides bioinformatics and biostatistics services for life science researchers to integrate, analyse and manage large-scale genomics, proteomics, field and clinical datasets.

In 2013, QFAB undertook 58 projects for clients from industry, universities, medical research institutes, and government departments.

Some of these projects included assisting with a retrospective genomic analysis and real-world evaluation of clinical features of oral malignant disorders and oral epithelial dysplasia; developing a cancer genomics data linkage software application; and creating a dynamic omics data visualisation and interaction toolbox.

QFAB's support services range from experimental design, data capture and mining, through to genomics, proteomics and metabolomics analyses, and data visualisation. They are also experts in crossdomain integration of multiple data types, including linkage to clinical data.

QFAB provides a fast and flexible service operating on a fee-for-service basis. QFAB's training division provides integrated workshops through to customised solutions in all areas of bioinformatics and experimental design.

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 enables investigations across the biological continuum from systems and chemi-biology perspectives.

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

UQ ROCX Crystallisation and X-ray Diffraction Facility

UQ ROCX Crystallisation & X-ray Diffraction 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 investigated with small quantities of protein. The diffraction facility has Queensland's brightest research X-ray source and the state's only robotic sample storage and retrieval system, which allows for multiple data sets to be collected without user intervention

In 2013, 61 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.

Collectively, users performed 100,000 crystallisation experiments, collected 56 diffraction data sets and published 15 scientific papers supported by UQ ROCX access in 2013.

Some of the discoveries reported in 2013 using the facility included identification and characterisation of a protein essential for pathogenicity in the infectious disease melioidosis, and a potential bioweapon; characterisation of the mechanism by which cells use PX-FERM proteins to move diverse transmembrane cargos around the body; the discovery and characterisation of potent enzyme inhibitors with antimalarial activity; and the discovery of how bacteria find the specific metals they need to function.

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

GRANTS, FELLOWSHIPS **AND AWARDS**



Grants

Competitive grant funding represented more than 58 per cent (\$36 million) of IMB's total income in 2013 (\$62 million), reflecting the high quality and scientific importance of our research.

The institute performed well in the major competitive grant rounds offered during the year by the Australian Research Council (ARC), National Health and Medical Research Council (NHMRC), and the Queensland Government. IMB achieved above national average success rates, recording a 47.4 per cent success rate against a national average success rate of 21.4 per cent for ARC Discovery Project grants, and a 45 per cent success rate against a national average success rate of 20.5 per cent for NHMRC Project grants.

During 2013, IMB received funding to lead a number of international research projects with some of the world's top scientists in their respective fields. Notably, work began on the institute's first NHMRC-European Union Collaborative Research Grant. Led by Professor Melissa Little, the collaborative project involves a multinational research team investigating cellular therapies for kidney disease. Professor Matt Cooper also received funding to lead an Australia-India Strategic Research Fund project to identify cellular immunotherapy targets and develop acid-stable analogues suitable for future development as new treatments for type 2 diabetes and other inflammatory disorders.

In 2013, funding commenced for the following grants:

- 1 Australia-India Strategic Research Fund project grant totalling \$282,365
- 1 NHMRC Development grant totalling \$513,630
- > 1 NHMRC EU FP7 Collaboration grant totalling \$754,448
- 1 NHMRC Program grant totalling \$7,228,415
- 17 NHMRC Project grants totalling \$9,714,037
- > 5 ARC Linkage grants totalling \$2,361,845
- 9 ARC Discovery Project grants totalling \$4,035,000.

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, IMB Fellows have the opportunity to conduct valuable research with the potential to advance global scientific progress and improve the health and wellbeing of people around the world.

Total competitive fellowships held in 2013:

- > 1 ARC Australian Laureate Fellowship
- > 1 ARC Discovery Outstanding Researcher Award (DORA)
- > 7 ARC Future Fellowships
- 5 ARC Discovery Early Career Researcher Awards (DECRA)
- > 2 NHMRC Australia Fellowships
- > 11 NHMRC Research Fellowships
- 1 NHMRC Career Development Fellowship
- > 4 NHMRC Early Career Fellowships
- > 1 Queensland Smart Futures Fellowship.
- Fellowships commencing in 2013:
- > 1 ARC DORA totalling \$545,958
- > 1 ARC Future Fellow totalling \$755,320
- > 1 ARC DECRA totalling \$375,000
- 5 NHMRC Research Fellows totalling \$3,544,078.

Competitive grant income



2013 sources of competitive funding:

- > ANZ Trustees
- > Australia-India Strategic Research Fund
- > Australian Academy of Science
 - > Australian Cancer Research Foundation
 - > Australian Research Council
 - > Bioplatforms Australia Limited
 - > Cancer Council Queensland
 - > Cariplo Foundation (Italy)
- > EMBO (Germany)
- Grain Research and Development Corporation
- > Great Barrier Reef Foundation
- > Human Frontier Science Program (France)
- > James S McDonnell Foundation (US)
- > National Breast Cancer Foundation
- National Health and Medical Research Council
- > National Institutes of Health (US)
- Queensland Emory Development Alliance (Qld/US)
- > Queensland Government
- > The Kids' Cancer Project
- > Wellcome Trust (UK)
- > Wound Management Innovation CRC.



Professor David Craik (Image credit: Australian Academy of Science)

Awards

Our researchers do great science every day. Awards play an important role in publicly recognising the significant contributions our people make to our global research efforts.

2013 IMB award highlights included:

- Professor David Craik was elected as a Fellow of the Australian Academy of Science, in recognition of his pioneering research into a new type of molecule that may lead to improved treatments for pain and other diseases.
- Professor Glenn King received the Beckman Coulter Discovery Science Award from the Australian Society of Biochemistry and Molecular Biology (ASBMB) for his leadership in the field of venoms-based drug discovery. He was also awarded the Sir Bob Robertson Award from the Australian Society for Biophysics.
- Professor Alpha Yap was named the Australia and New Zealand Society for Cell and Developmental Biology 2013 President's Medal winner in recognition of his seminal contributions to cell biology.
- Professor Matt Cooper won an NHMRC Achievement Award for having the topranked development grant out of the 102 applications nationwide in 2012. This funding will allow his laboratory to develop improved treatments for tuberculosis, including drug-resistant strains.
- Professor Rob Parton won an NHMRC Achievement Award for having the equal top-ranked project grant out of nearly 3000 applications nationwide in 2012. This funding will allow his laboratory to study a cellular pathway that appears to play a crucial role in cell migration around the body, including the spread of cancer cells.
- Dr Lachlan Coin received a \$90,000 UQ Foundation Research Excellence Award to better understand the genetic architecture of autoimmune disorders so improved therapeutics can be developed.
- Dr Kate Schroder received an \$80,000 UQ Foundation Research Excellence Award for research to pinpoint the pathways that allow our bodies to fight infectious diseases and develop drugs to boost our natural defences.

- Dr Kate Schroder and Dr Irina Vetter were named among Queensland's best and brightest young scientists, receiving Tall Poppy awards from the Australian Institute of Policy and Science. The awards recognise their outstanding research into infection and immunity (Schroder), and chronic pain (Vetter), and their efforts to inspire young Australians about science.
- > Dr Ryan Taft was named in *QWeekend's* Queensland's 50 Best and Brightest 2013 list for his discovery of a new disease, HBSL.



Professor Glenn King (Image credit: Lyndon Mechielsen; Source: The Australian)



Professor Alpha Yap



Professors Rob Parton (L) and Matt Cooper (R)



Drs Lachlan Coin (L) and Kate Schroder (R)



Dr Ryan Taft

LEARNING



PhD student Masuda Nabi (Alexandrov Lab)

INSTITUTE FOR MOLECULAR BIOSCIENCE ANNUAL REPORT 2013

RESEARCH TRAINING

IMB's postgraduate program gives students a strong start to their careers by surrounding them with world-class researchers, facilities, and support services.

As active members of our laboratory teams, IMB students are encouraged to expand their skill sets, seek answers to the big questions, and make the most of student life at IMB and UQ. Students are given the freedom they need to explore their scientific potential in a culture of research excellence. IMB's Postgraduate Office also provides students with a range of extra curricular activities and opportunities to accelerate career and personal development. Some of these opportunities-facilitated through the UQ Career Advantage PhD program-include training courses in bioethics, scientific writing, media and communications, and research support facilities. Students also participate in events organised by IMB's student association, SIMBA, which brings students together for social and professional networking and peer support.

In 2013, IMB supported 121 active research higher degree students (RHD)-including 26 new students-and continued to support an additional 22 students who had submitted their theses and were awaiting conferral. A record 34 PhD students graduated during 2013, and went on to secure positions at leading organisations around the world, including the Universities of Oxford and Cambridge in the UK, Lonza and the Children's Hospital of Pittsburgh in the US, and CSIRO and the Garvan Institute in Australia. During the year, 73 per cent (89 students) of IMB students were international students hailing from more than 35 countries, and 49 per cent (60 students) of students were female. We also supported all commencing PhD and MPhil students to secure full scholarships for their studies prior to commencing at IMB.

In February, we welcomed 11 new honours students, and saw our 6 continuing honours students graduate mid-year. Notably, 3 of our new honours students were awarded IMB Honours Scholarships valued at \$2500. Our honours students excelled in their studies, with more than 75 per cent achieving first class honours, which requires students to achieve a weighted average of 80 per cent or above for the duration of their degree.

During the year, we welcomed 13 undergraduate students, 9 coursework MPhil students, 13 summer students and 27 occupational trainees to complete research modules at IMB as part of their degree, with some of these students choosing to return to IMB to continue their studies in 2014. We also welcomed 7 students from Fudan University in China for a 6-week research experience at IMB, and hosted a US biology graduate who joined IMB on a prestigious Fulbright Postgraduate Scholarship, which supports American students to conduct research within an Australian postgraduate program for approximately 12 months.

Attracting talented and motivated students remained a priority for the institute in 2013. During the year, IMB's postgraduate team attended a number of local and international student recruitment events, including attending the China Scholarships Council Exhibition in Beijing and Shanghai; hosting prospective students at IMB's honours information session in April; joining in UQ's Faculty of Science's speed-dating event for high school students; and participating in a range of UQ engagement programs, including Careers that Shape the World, Experience Science, Young Scholars Program, Postgraduate Advice Night, Future Researchers Showcase, Market Day and Open Day.

Our students gave us many reasons to celebrate during the year. Third-year developmental biology PhD students Kathryn McClelland and Elanor Wainwright were selected from thousands of student and postdoctoral applicants to secure places in two of the most prestigious training courses in the world. Kathryn was 1 of only 23 participants chosen to attend the Woods Hole summer course in embryology in Massachusetts, and Elanor was 1 of only 14 participants chosen to attend the Cold Spring Harbor Laboratory's mouse development, stem cells and cancer course in New York. Moreover, Marga Gual Soler was selected from more than 10,000 applicants to undertake a 3-month traineeship with the United Nations in New York, and Selwin Wu was invited to give a talk at the Gordon Research Seminar on Cell Contact and Adhesion in Italy.

The high calibre of our students and their innovative research was further recognised during the year through their success in a number of competitive grant and award programs. IMB students Uru Malik, Bodil Carstens and Wilko Duprez were awarded travel grants to attend the American Peptide Symposium in Hawaii; Juliane Wolf was awarded a grant to attend the Universitas 21 Research Conference in Dublin; Atefeh Taherian and Jasmin Straube were awarded scholarships to attend the EMBL Australia PhD course in Melbourne; and Joelle Kartopawiro received a grant to attend the 14th Annual Australia and New Zealand Zebrafish Meeting in Queenstown, where her fellow IMB student Jessica De Angelis was awarded the best student talk at the conference. Furthermore, IMB PhD student Angie Jarrard was awarded the top student poster prize at the Australian Society for Microbiology annual conference, and undergraduate student Emily Furlong achieved the best results in her UQ second-year experimental chemistry course and biochemistry and molecular biology course.



IMB graduates at UQ's July graduation ceremony



IMB graduates at UQ's December graduation ceremony



Professor Jenny Stow (centre) meets with students from UQ's Advanced Study Program in Science



PhD student Elanor Wainwright attended Cold Spring Harbor Laboratory's course in New York



PhD student Marga Gual Soler undertook a three-month internship at the United Nations in New York



2013 SIMBA Executive Committee (L-R): Thomas Clairfeuille, Angie Jarrad, Kelvin Tuong, Amelia Soderholm, Kathryn McClelland, and Claudio Cortes

RESEARCH HIGHER DEGREE STUDENTS



Nikita Abraham Rubbiya Ali Juliana Ariffin Sungmin Baek Sassan Rahnama Haojing Shao Megha Bajaj Sheila Barbero Niraj Bende Guillaume Bernard Lou Brillault Tony Bui Bodil Carstens Kaiwen Chen Mu Cheng Yash Chhabra Ivy Chiang Shiao Chow Thomas Clairfeuille Nicholas Condon Anne Conibear Claudio Cortes Rodriguez Baptiste Coxam Ben Cristofori-Armstrong (honours) Daniel Croker Zhenling Cui Kaustav Das Gupta Jessica De Angelis Charlotte Dsouza

Minh Tam Duong Wilko Duprez Mriga Dutt Jordan Follett Rajesh Ghai Joel Goode Daniela Grassini Xiaocong Huang Makerita leremia (honours) Gisela Jakob Angie Jarrad Prerna Jha Pengxiang Ji Prashanth Jutty Rajan Pamela Kairath Oliva Pabasara Kalansuriya Joelle Kartopawiro Sanjaya Kc Zeinab Khalil Julie Klint Emily Knauth Marija Kojic Keerthana Krishnan Fabian Kurth Soohyun Kwon Christian Larney Carus Lau Hyun Lee Joanne Leerberg Xuan Liang

Chao Liu Piyush Madhamshettiwar Bruno Madio Tunjung Mahatmanto Barbara Maier Uru Malik Rosa Martinez Kathryn McClelland Ahmed Mehdi Justin Mitchell Masuda Nabi Caroline Nelson Pratik Neupane Daniel Nielsen Timothy O'Connor Tae Gyu Oh Rakesh Origanti Jeroen Overman Samuel Perry Wanida Phetsang Pritesh Prasad Rashmi Priya Xiaying Qi Kelly Quek Michelle Quezada Iniguez Divya Ramnath Swarmi Ravipati Timothy Reeks Asma Rehman

Clarissa Rios Rojas

Alan Robertson Silmara Rodrigues de Sousa Jessica Rowlev Darshani Rupasinghe Anne Sawyer Zoe Schofield Zhuo Shang Jasmin Straube Atefeh Taherian Fard Wei Teo Vikas Tillu Zewen Tuong Eivind Undheim Darya Vanichkina Elanor Wainwright Josh Wingerd Juliane Wolf David Wood Selwin Wu Wei Xu David Yap (honours student) Jennifer Yarnold Yun Kit Yeoh Alina Zamoshnikova Kerstin Zoidl

* Students listed granted permission to be named. Note: not all students are listed here.

2013 **PHD CONFERRALS**

NAME	SUPERVISOR	DEGREE	THESIS TITLE	GRADUATE POSITION
Stephen Ainger	Associate Professor Rick Sturm	PhD	UVR skin protection by dopachrome tautomerase	Research Officer, Sturm Lab, IMB
Nicholas Ariotti	Professor Rob Parton	PhD	A structural and functional characterisation of caveolae	Research Officer, Parton Lab, IMB
Nilesh Bokil	Associate Professor Matt Sweet	PhD	Identification and characterisation of anti-microbial pathways in human macrophages	Research Officer, Sweet Lab, IMB
Fabian Buske	Dr Tim Bailey	PhD	The role of triplex formation in gene regulation and its potential in biotechnological applications	Garvan Institute (Sydney)
Maurizio Chioccioli	Professor Ben Hankamer	PhD	Exploring new strategies for a more accurate estimation of microalgae growth rate and light harvesting complexes' antennae size	University of Cambridge (UK)
Minh Tam Duong	Dr Mat Francois	PhD	The role of SOX18 protein in vascular development in health and disease	Research Assistant, Francois Lab, IMB
Alysha Elliott	Dr Josh Mylne	PhD	A new class of daisy seed peptides	Research Officer, Cooper Lab, IMB
Selene Fernandez Valverde	Professor John Mattick	PhD	Characterisation and discovery of small RNAs in Metazoa	School of Biological Sciences, UQ
Dennis Gascoigne	Professor John Mattick	PhD	Identification, classification and annotation of protein-coding and non-coding RNAs in mammalian genomes	Director Engineering Services, Tenterfield Shire Council
Rajesh Ghai	Dr Brett Collins	PhD	Structure-function studies of the PX-FERM proteins in endosomal trafficking	Postdoctoral Fellow, University of New South Wales (Sydney)
Xiaocong Huang	Professor Rob Capon	PhD	Biodiscovery search for marine-derived inhibitors of P-gp, BCRP and MRP1 as a means to improve cancer chemotherapy	Brisbane
Marco Inserra	Professor Richard Lewis	PhD	Pharmacological characterisation of alpha-conopeptides with therapeutic potential	Research Officer, Lewis Lab, IMB
Jonas Jensen	Professor Glenn King	PhD	Dissecting the interaction between the sea anemone toxin APETx2 and its analgesic target, acid-sensing ion channel 3	LC-MS Field Service Engineer, Waters Chromatography (Denmark)
Zeinab Khalil	Professor Rob Capon	PhD	Innovations in microbial biodiscovery, targeting silent metabolism and new chemical diversity	Research Assistant, Capon Lab, IMB
Carol Kistler	Professor Rob Parton	PhD	Functional characterisation of Rab18	Department of Agriculture, Fisheries and Forestry, Australian Government
Julie Klint	Professor Glenn King	PhD	Characterisation of spider venom peptides that target voltage-gated sodium channels: pharmacological tools and potential therapeutic leads for the treatment of chronic pain	Research Officer, King Lab, IMB
Monika Koehnke	Professor Kirill Alexandrov	PhD	New insights into prenylation in disease	Lonza (US)
Marta Kubala	Professor Kirill Alexandrov	PhD	Elucidating regulatory mechanisms of protein prenyltransferases	University of California, San Francisco (US)
Junxian Lim	Professor David Fairlie	PhD	Links between inflammation and obesity	Research Officer, Fairlie Lab, IMB
Piyush Madhamshettiwar	Professor Mark Ragan	PhD	Gene regulatory networks in cancer systems biology	CSIRO (Canberra)
Ahmed Murtaza Mehdi	Associate Professor Mikael Boden	PhD	Computational models of nucleo-cytoplasmic trafficking by integrating heterogeneous data	Research Officer, Diamantina Institute, UQ
David Morgenstern	Professor Glenn King	PhD	The bio-logic of venom complexity: a chemical and evolutionary investigation into the role of venom complexity in two orders of venomous animals	Postdoctoral Fellow, Proteomics Resource Centre, NYU Langone Medical Centre (US)
Caroline Nelson	Professor Mike Waters	PhD	The molecular basis for the anti-obesity action of growth hormone	Research Officer, Waters Lab, IMB
Yu Leng Phua	Professor Melissa Little	PhD	The role of Crim1 in obstructive nephropathy and progressive renal fibrosis in the Crim1KST264/KST264 mice	Childrens Hospital of Pittsburgh (US)
Asma Rehman	Professor Jenny Martin	PhD	Characterisation of the Munc18c/SNARE complex assembly	India
Andrew Ringsmuth	Professor Ben Hankamer	PhD	Multiscale analysis and optimisation of photosynthetic solar energy systems	Research Assistant, Hankamer Lab, IMB
Natalie Saez	Professor Glenn King	PhD	Characterising the molecular basis of the interaction between the putative drug target ASIC1a and pi-TRTX-Pc1a	Postdoctoral Fellow, Aix-Marseille University (France)
Melanie Shakespear	Professor Matt Sweet	PhD	Regulation of TLR4 signalling in macrophages by histone deacetylases	Research Officer, Sweet Lab, IMB
Jennifer Smith	Professor Paul Alewood	PhD	Novel Australian scorpion toxins	Research Officer, King Lab, IMB
David Thomson	Professor Matt Cooper	PhD	Bionanotechnology approaches to amplification-free detection of nucleic acid	Policy Officer, Deparment of Industry, Australian Government (Canberra)
Louise Thorstholm	Professor Norelle Daly	PhD	MCoTI-II and chronic myeloid leukaemia cyclic peptides as therapeutic leads in the treatment	Novo Nordisk (Copenhagen)
Zakir Tnimov	Professor Kirill Alexandrov	PhD	Novel approaches for understanding prenylation and Rho GTPase membrane targeting	Research Officer, Alexandrov Lab, IMB
Patricia Walden	Professor Jenny Martin	PhD	Structure and function of DSB redox proteins	Research Officer, Martin Lab, IMB
			Molecular modelling and drug design of alpha-conotoxins with therapeutic	Postdoctoral Fellow, University of







SCIENTIFIC ENGAGEMENT

IMB's researchers play an active role within Australia's scientific and medical research community 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.

The following highlights represent a small sample of the many valuable contributions made by our research staff during the past 12 months.

Appointment highlights

- IMB researchers were appointed and re-appointed to the editorial boards of a number of leading international scientific journals, including Developmental Cell, Journal of Cell Biology, Current Biology, Molecular Biology of the Cell, Endocrinology, Traffic, Journal of Biological Chemistry, Journal of Leukocyte Biology, Genome Medicine, Developmental Biology, and PLOS One.
- Professor Jenny Martin was appointed to the National Health and Medical Research Council (NHMRC) Women in Health Science Working Committee.
- Professor Sean Grimmond was appointed to the board of the Australian Genome Research Facility; as the Australian representative on the International Cancer Genome Consortium's (ICGC) scientific steering committee; and as a co-leader of the ICGC's pancreatic cancer translation program.
- Professor Melissa Little continued her appointment as a member of the Strategic Review of Health and Medical Research McKeon Review expert panel, which delivered its 10-year strategic health and medical research plan for the nation to the Australian Government in April.
- Professor Mark Ragan was appointed to the UK Medical Research Council's College of Experts, as part of its Initiative in Medical Bioinformatics.
- The Australian and New Zealand Society for Cell and Developmental Biology (ANZSCDB) appointed a number of IMB researchers to its 2014 executive committee, including Associate Professor Carol Wicking as President; Associate Professor Rohan Teasdale as Treasurer; Dr Jo Bowles as Secretary; Dr Fiona Wylie as Newsletter Editor; and Dr Mat Francois and Dr Kelly Smith as its Queensland committee representatives.

- Dr Kelly Smith established the Australian Network for Cardiac and Vascular Developmental Biologists Inc. and was appointed secretary of the association.
- Professor Rob Parton, Professor David Craik and Associate Professor Rick Sturm were appointed to the NHMRC Assigners Academy, a prestigious body of eminent researchers that give expert advice to the NHMRC CEO.
- Professor Rob Parton and Dr Kate Schroder were appointed to NHMRC Grant Review panels, which provide confidential, independent and expert assessment of eligible NHMRC project grant applications. Professor Jennifer Stow was appointed to the NHMRC Peer Review Panel for Research Fellowships.

Presentations and event highlights

- > IMB hosted more than 40 internationally renowned guest speakers during the year as part of its Friday seminar series.
- Professor David Craik presented 22 plenary and keynote lectures in 10 countries, including India, China, USA, Thailand, Switzerland, Brazil, Japan, France, Ukraine and Australia. Notable among them was a major lecture at the 23rd American Peptide Symposium held in Hawaii, US, in June.
- Professor Sean Grimmond chaired and presented at the cancer genomics session of the American Association of Cancer Research annual meeting, held in Washington, DC, US, in April.
- Professor Paul Alewood chaired the 10th Australian Peptide Symposium hosted in Penang, Malaysia, in September. The event attracted 250 participants and also celebrated the 21st anniversary of the Australian Peptide Association.
- Professor George Muscat was an invited speaker at the International Diabetes Federation's World Diabetes Congress held in Melbourne in December, and the Asia-Pacific Diabetes and Obesity Study

Group Symposium held in Tokyo, Japan, in October.

- Professor Matt Cooper delivered the inaugural Howard Florey oration to 350 delegates attending the Australian Society for Antimicrobials annual scientific meeting held in Sydney in February. He was also an invited speaker at the 4th International NanoMedicine Conference held in Sydney in July.
- Dr Lachlan Coin gave an invited presentation at the Australian Society for Microbiology annual scientific meeting held in Adelaide in July.
- Associate Professor Tim Bailey presented a keynote speech at the International Society for Computational Biology's Translational Bioinformatics Conference held in Seoul, South Korea, in October.
- Many IMB lab heads chaired sessions and gave presentations at Combio2013— Australia's premier biology conference held in Perth in September. Notably, Professor Alpha Yap delivered the President's Medal plenary address.
- Dr Kelly Smith, assisted by Dr Ben Hogan and Dr Mat Francois, hosted the 2nd meeting of the Australian Network of Cardiac and Vascular Developmental Biologists, which was held on the Gold Coast in October.
- Dr Nick Hamilton, Lanna Wong and Professor Mark Ragan organised the 10th annual Winter School in Mathematical and Computational Biology, an event hosted annually by IMB. Held from 1-5 July, the event attracted 36 expert speakers and 281 participants from 48 Australian and 9 overseas institutions from Austria, Brazil, Iran, Japan, New Zealand, Saudi Arabia, UAE and the US.
- Professor Jenny Stow and Dr Kate Schroder co-chaired the Inflammation, Cytokines and Disease Symposium, which attracted more than 200 participants and was held at IMB in November.
- > IMB senior researchers delivered 181 lectures to UQ undergraduate students.

COMMUNITY ENGAGEMENT

Our research aspires to change the world. And as such, we have a responsibility to share our findings with the community—informing them of what our research is about, why it is important, and how the new knowledge we discover will affect their lives.

During 2013, we welcomed 2674 external visitors to the institute, including students, donors, scientific collaborators, industry partners, media, politicians and community supporters. Our visitors joined us for a range of events, including laboratory tours, public seminars, scientific conferences, and student information sessions.

Notably, we hosted tours and research briefings for senior state and federal politicians and staff, including the Hon lan Walker, Minister for Science, Information Technology, Innovation and the Arts; and the Hon Lawrence Springborg, Minister for Health. The then-Shadow Minister for Universities and Research, Senator Brett Mason, also toured IMB and met with young researchers in a visit organised by the Australian Early- and Mid-Career Researcher Forum of the Australian Academy of Science. We were also fortunate to host visits from our friends at Kidney Health Australia, the Springwood/Rochedale branch of National Seniors of Australia, and the Australian Cancer Research Foundation and their corporate partners, Deloittes and RBS Morgans.

In March, Dr Bethan Hughes and Dr Sarah Molton from the Wellcome Trust presented a seminar on translational funding opportunities at the UK-based foundation. And in September, we had a special visit from Stephen Damiani, Chairman and Co-founder of the Mission Massimo Foundation, where we presented Stephen with the inaugural IMB Champion award, in recognition for his tireless efforts in advocating for patients and families of children affected by a rare group of inherited diseases called leukodystrophies.

During the year, IMB staff actively took their research to the community by participating in events such as the Queensland Government's Science in Parliament session; sharing their latest research in briefings with clinicians and patient support groups; and participating in the Queensland committee for National Science Week, which plays a vital role in planning and supporting the almost 400 National Science Week events held in 2013 throughout the state. We also participated in UQ's Research Week activities in September, including the BrisScience/ UQ Research Week Public Lecture where Professor Jenny Martin presented a keynote talk on 'How are new medicines discovered?'

Our students and early-career researchers (ECRs) honed their science communication and engagement skills through their involvement in our Science Ambassador program. Interest in this program was high in 2013, with 10 new ambassadors joining the existing cohort of 18 ambassadors. As always, our ambassadors played a vital role in showcasing our research to the public at a range of events, and inspiring future students to choose a career in science.

ECR Dr Evan Stephens, Manager of IMB's Solar Biofuels Research Centre, was a national finalist in Fresh Science, a nationwide science communication competition. Dr Stephens was able to share his research, which is investigating how to create biofuels from algae, with media across the country, reigniting the community conversation about the role of biofuels in meeting future energy demands.

In May, we thanked our generous donors at UQ's annual Celebration of Giving for their valuable contribution to our breakthroughs, and we hosted a special reception to recognise Dr Rosamond Siemon and her grandson Andrew Stallman and his wife Jill Stallman, who have endowed a postgraduate scholarship in kidney research in Professor Melissa Little's laboratory, which was first established in 2006 and will continue in perpetuity.

We also had the privilege of helping Mrs Beverley Trivett, a past IMB donor, to launch The John Trivett Foundation's new campaign to raise \$1.5 million to recruit a senior research fellow in brain cancer at UQ for five years. This senior research fellow will be responsible for coordinating the excellent brain cancer research happening in Brisbane, and will be based at IMB and the Queensland Brain Institute.

Communication through mass media remained the most efficient way of sharing our research news with the community. Importantly, we grew our mainstream media presence, securing more than 2000 mentions of our research and advocacy efforts in print, broadcast and online media. Some of the major outlets to publish our research in detail included ABC TV's programs *Australian Story, Four Corners, Catalyst* and *News 24*; Channel 10's *Scope*; ABC local radio, ABC *Radio National*, and ABC *AM* and *PM* programs; the news broadcasts of channels 7, 9, 10 and ABC; and an impressive list of daily and weekly newspapers and online publications from across the country and the world.

We boosted our presence on social media, launching a Facebook page and regularly posting updates to Facebook and our Twitter account about our efforts to improve quality of life for those living with disease and solve some of the greatest challenges facing our society, including better fuels and improved pesticides for crops. Social media is the best way for people around the world to follow our progress, so please like our Facebook page (www.facebook.com/ InstituteforMolecularBioscience) and follow us on Twitter (@IMBatUQ) to keep up-to-date in 2014 and beyond.

Thanks to our 2013 IMB Science Ambassadors:

- > Nikita Abraham (Lewis Lab)
- > Rubbiya Akram Ali (Hankamer Lab)
- > Sheila Barbero (Fairlie Lab)
- > Nilesh Bokil (Sweet Lab)
- > Andrew Brooks (Waters Lab)
- > Tania Brooks (Waters Lab)
- > Natasha Chaudhary (Parton Lab)
- > Shiao Chow (Fairlie Lab)
- > Thomas Clairfeuille (Collins Lab)
- > Baptiste Coxam (Hogan Lab)
- > Mark Crowe (QFAB Bioinformatics)
- > Mathilde Desselle (QFAB Bioinformatics)
- > Anh Do (Fairlie Lab)
- > Wilko Duprez (Martin Lab)
- > Guillermo Gomez (Yap Lab)
- > Angie Jarrad (Cooper Lab)
- > Prashanth Jutty Rajan (Lewis Lab)
- > Julie Klint (King Lab)
- > Tunjung Mahatmanto (Craik Lab)
- > Uru Malik (Craik Lab)
- > Emma Markham (Grimmond Lab)
- > Kathryn McClelland (Koopman Lab)
- > Katia Nones (Grimmond Lab)
- Yu Leng Phua (Little Lab)
- Rashmi Priya (Yap Lab)
- > Anne Sawyer (Hankamer Lab)
- > Christina Schroeder (Craik Lab)
- > Darya Vanichkina (Taft Lab).

Keep in touch with IMB

Subcribe to our newsletter **Donate** to our research Follow us on Twitter

www.imb.uq.edu.au/subscribe www.imb.uq.edu.au/donate www.twitter.com/IMBatUQ



IMB donor Rosamond Siemon (centre) with kidney researcher Professor Melissa Little (right), and Rosamond Siemon Postgraduate Scholarship recipient, Barbara Maier



IMB Director Professor Brandon Wainwright (centre) with Brisbane neurosurgeon, Dr Sarah Olson (left), and The John Trivett Foundation Founder, Mrs Beverley Trivett (right)



IMB researchers actively shared their discoveries with the media during the year



IMBers hosted an Australia's Biggest Morning Tea, raising funds in support of Cancer Council Queensland



Professor Sean Grimmond (left) and IMB Champion, Stephen Damiani, chat about the nstitute's genomics research program



Science Ambassador Dr Nilesh Bokil spoke with delegates from the International Youth Leaders Forum



research with Health Minister Lawrence Springborg (centre), and Science Minister Ian Walker



Springwood/Rochedale branch of National Seniors of Australia toured IMB



Professor Brandon Wainwright welcomed friends of the Australian Cancer Research Foundation during a tour



IMBers welcomed Dr Bethan Hughes (left) and Dr Sarah Molton (second from left) from the Wellcome Trust (UK) during a visit to IMB



the institute's research discoveries



support of Movember



Science Ambassador Dr Katia Nones updates visitors on



RESEARCH COMMERCIALISATION

IMB researchers collaborate with three of the world's top five pharmaceutical companies, demonstrating the relevance and value of the institute's research to industry.

Working together with The University of Queensland's commercialisation company, UniQuest, IMB continued to advance its intellectual property (IP) and life sciences discoveries towards translation.

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 research.

During 2013, IMB expanded its commercial activities in partnership with leading national and international organisations. A new collaboration agreement was signed with a top 10 European pharmaceutical company to apply IMB's patented technology to engineer biologically active peptides with oral bioavailability. This would hopefully allow the future drug to be administered as a pill, which would be preferable for patients over current peptide-based drugs, which are usually administered via injection.

Additionally, the institute signed two new licensing agreements allowing companies to use its proprietary assay methodology for measuring human growth hormone. A number of other technologies in the life sciences and biotechnology fields are being discussed with potential partners as the institute seeks to expand its global industry collaborations.

The institute continued its successful track record in the Australian Research Council's (ARC) Linkage grants scheme which supports research and development projects between higher education researchers and industry. In 2013, IMB secured collaboration agreements with five international and domestic companies. including Janssen, Elanco, Phylogica, Alchemia (via its subsidiary Audeo Discovery Pty Ltd) and Innovate Ag. Janssen and Alchemia will leverage IMB's expertise and capabilities in ion channel pharmacology and pain biology. This work will build on their previous relationships with the institute, demonstrating the value IMB's translational research has contributed to both companies. Furthermore, Elanco and Innovate Ag will focus on agricultural projects, specifically on the treatment of livestock parasites and crop pests, respectively. Finally, Phylogica will work with IMB to develop a powerful discovery platform for peptide-based therapeutics.

Research diversity is one of IMB's great strengths, and during 2013 the institute collaborated with leading companies across

the industry sectors of health, agriculture, reagents and biofuels, just to name a few. Notably, in the area of infectious disease, we partnered with a biotech to in-licence a clinical candidate and strengthen our IP for the project. We also progressed our pipeline of novel drug candidates, specifically in the areas of infectious disease, pain and inflammation.

In 2013, IMB managed an IP portfolio of 25 patents including patents related to diagnostics, therapeutics and platform technologies. Four of IMB's patent applications were granted in 2013 and new provisional patents were filed, including those for technologies such as an improved method for transforming human embryonic stem cells to kidney cells, a biosensor for the improved detection of proteases, and a novel algae strain for the production of hydrogen gas.

During the past decade, IMB has produced several spin-out companies and continues to maintain close relationships with many of these, including Protagonist Therapeutics, which has discovery operations at IMB, maintaining the biotech's access to IMB expertise and capabilities. In 2013, Protagonist Therapeutics raised \$18 million from Series B private financing. The biotech is developing oral drugs for diseases whose current treatments must be injected, providing a safer, more effective, convenient and affordable choice for patients and the healthcare system.

IMB further strengthened its commercial networks, attending major industry events including BIO2013 in Chicago, US, and AusBiotech in Brisbane, showcasing IMB technologies and commercialisation opportunities to potential industry partners. During the year we also welcomed to the institute visitors from several multinational companies, including Novo Nordisk, Pfizer, Janssen, Elanco, AstraZeneca, Eli Lilly, Shionogi, and Bayer Crop Sciences.

The institute remained committed to training its postgraduate students and early career researchers in how to work with industry to take their discoveries out of the lab and into the community. One way we achieved this was through UniQuest's annual two-day commercialisation workshop. In 2013, 29 IMB researchers attended the workshop, where they received advice on identifying and protecting IP, through to the different funding options and routes available to commercialise IP and knowledge.



UniQuest will continue to work alongside IMB's research teams in the year ahead 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 and pesticides; and in biotechnology, including microalgae-based biofuels and production of high-value materials.

*Pictured above: IMB's commercialisation team (L-R): Dr Stephen Earl, Dr Robert McLachlan, and Dr Mark Ashton

Patent portfolio by research area





GLOBAL COLLABORATIONS

IMB is a globally recognised research institute with a strong network of collaborators and alumni around the world. During 2013, our scientists teamed up with colleagues from 213 organisations—including universities, hospitals, industry and not-for-profit organisations—to solve some of the most complex challenges facing our community.



Australia

Academic

- > Australian National University (Canberra)
- Baker IDI Heart & Diabetes Institute (Melbourne)
- > Centre for Cancer Biology (Adelaide)
- > Eskitis Institute, Griffith University (Brisbane)
- Garvan Institute of Medical Research (Sydney)
- > James Cook University (Townsville)
- > La Trobe University (Melbourne)
- > Liggins Institute (Auckland)
- > Monash University (Melbourne)
- > Peter MacCallum Cancer Centre (Melbourne)
- > RMIT University (Melbourne)
- > Telethon Kids Institute (Perth)
- > The University of Western Australia (Perth)
- > University of Auckland
- > University of Melbourne
- > UQ Australian Centre for Ecogenomics (Brisbane)
- > UQ Australian Infectious Diseases Centre (Brisbane)
- > UQ Australian Institute for Bioengineering and Nanotechnology (Brisbane)
- > UQ Centre for Integrative Legume Research (Brisbane)
- > UQ Centre for Microscopy and Microanalysis (Brisbane)
- > UQ Queensland Brain Institute (Brisbane)
- > UQ School of Agriculture and Food Science (Brisbane)
- > UQ School of Biological Sciences (Brisbane)
- > UQ School of Biomedical Sciences (Brisbane)
- > UQ School of Chemistry and Molecular Biosciences (Brisbane)
- > UQ School of Mathematics and Physics (Brisbane)
- > UQ School of Molecular and Microbial Sciences (Brisbane)
- > Walter and Eliza Hall Institute (Melbourne)

Clinical

- > Australian Red Cross (Brisbane)
- > Brien Holden Vision Institute (Sydney)
- Chronic Kidney Disease in Queensland (Brisbane), UQ
- > Fremantle Hospital
- > Genetic Health Queensland (Brisbane)
- Greenslopes Hospital (Brisbane)
- Ingham Institute for Applied Medical Research (Western Sydney)
- > John Hunter Hospital (Newcastle)
- > Liverpool Hospital (Sydney)
- > Mater Children's Hospital (Brisbane)
- > Mater Hospital (Brisbane)
- > Mater Medical Research Institute
- (Brisbane)
- Mater Pathology (Brisbane)
- > Menzies School of Health Research (Darwin)
- Murdoch Childrens Research Institute (Melbourne)
- > Pathology Queensland (Brisbane)
- > Prince Henry's Institute (Melbourne)
- > Princess Alexandra Hospital (Brisbane)
- Princess Margaret Hospital for Children (Perth)
- > QIMR Berghofer Medical Research Institute (Brisbane)
- > Royal Brisbane and Women's Hospital
- > Royal Children's Hospital (Melbourne)
- > Royal Melbourne Hospital
- > SA Pathology (Adelaide)
- > St George Hospital (Kogarah)
- > St Vincent's Institute (Fitzroy)
- The Children's Hospital at Westmead (Sydney)
- > The Prince Charles Hospital (Brisbane)
- > The University of Adelaide
- > Translational Research Institute (Brisbane)
- > University of Newcastle
- > University of New South Wales (Sydney)
- > University of Sydney
- > UQ Centre for Clinical Research (Brisbane)
- > UQ Diamantina Institute (Brisbane)
- Victor Chang Cardiac Research Institute (Sydney)

 Victorian Clinical Genetics Services (Melbourne)

collaborating organisations

> Westmead Hospital

Industry

- > Alchemia (Brisbane)
- > Antisense Therapeutics (Melbourne)
- > BioAustralis (Sydney)
- > Bioproton (Brisbane)
- > Cement Australia (Brisbane)
- > Eli Lilly Australia (Sydney)
- > Growth Agriculture (Wee Waa)
- > Hexima (Melbourne)
- > Innovate Ag (Wee Waa)
- > Janssen (Sydney)
- > Johnson & Johnson (Sydney)
- > KBR (Brisbane)
- > Microbial Screening Technologies (Sydney)
- > Phylogica (Perth)
- > Protagonist Pty Ltd (Brisbane)
- > SYNthesis med chem (Melbourne)

Not-for-profit

- Australian Red Cross Blood Service (Brisbane)
- Australian Synchrotron (Melbourne)
- > Great Barrier Reef Foundation (Brisbane)
- > Kidney Health Australia (Melbourne)
- > Mission Massimo Foundation (Melbourne)
- National Breast Cancer Foundation (Sydney)
- > The Kids' Cancer Project (Sydney)

GLOBAL COLLABORATIONS

organisations

Europe

Academic

- > Bielefeld University (Germany)
- > Cambridge University (UK)
- > Cancer Research Centre Nantes-Angers, Centre National de Recherche Scientifique (France)
- Cancer Research UK Cambridge Institute (UK)
- > Curie Institute (Paris, France)
- > University Paris Descartes (France)
- Friedrich-Alexander-University Erlangen-Nuremberg (Germany)
- > Erasmus MC, University Medical Center (Rotterdam, The Netherlands)
- > Hubrecht Institute for Developmental Biology and Stem Cell Research (Uppsalalaan, The Netherlands)
- > IFOM-IEO Campus (Milan, Italy)
- > Imperial College London (UK)
- > Institute of Child Health (London, UK)
- Fundación Investigación Hospital, Clínico-INCLIVA (Valencia, Spain)
- Karlsruhe Institute of Technology (Munich, Germany)
- Max Planck Institute for Infection Biology (Berlin, Germany)
- Max Planck Institute of Molecular Physiology (Dortmund, Germany)
- Max Planck Institute of Molecular Cell Biology and Genetics (Dresden, Germany)
- Medical University of Vienna (Austria)
 Technische Universität München
- (Germany)
- > The John Innes Centre (Norwich, UK)
- > University College London (UK)
- > University of Barcelona (Spain)
- > University of Basel (Switzerland)
- > University of Copenhagen (Denmark)
- > University of Edinburgh (UK)
- > University of Glasgow (UK)
- > University of Hamburg (Germany)
- > University of Heidelberg (Germany)
- > University of Iceland (Reykjavík)
- > University of Lausanne (Switzerland)
- University of Leuven KU Leuven (Belgium)
- > University of Montpellier (France)
- > University of Oslo (Norway)
- > University of Oxford (UK)
- > University of Paris (France)
- > University of Porto (Portugal)

- > University of Stockholm (Sweden)
- > Uppsala University (Sweden)
- > University of Würzburg (Germany)

Clinical

- > Cochin Institute (INSERM) (Paris, France)
- Great Ormond Street Hospital (London, UK)
- > Guy's Hospital (London, UK)
- > Leiden University Medical Centre (The Netherlands)
- Ludwig-Maximilian University (Munich, Germany)
- Mario Negri Institute for Pharmacological Research (Bergamo, Italy)
- > Medical University of Graz (Austria)
- St George's University Hospital (London, UK)
- > University of Brescia (Italy)
- > University of Leeds (UK)
- > VU University (Amsterdam, The Netherlands)

Industry

- > Adenium Biotech (Copenhagen, Denmark)
- > Boehringer Ingelheim (Ingelheim, Germany)
- > Neste Oil (Keilaranta, Finland)
- > Siemens (Munich, Germany)
- > University of Bristol (UK)
- > Zealand Pharma (Glostrup, Denmark)

North America

Academic

- > Baylor College of Medicine (Texas, US)
- Cardiovascular Research Institute at University of California, San Francisco (US)
- > Emory University (Georgia, US)
- George Washington University (Washington DC, US)
- > McGill University (Québec, Canada)
- > Oak Ridge National Laboratory (Tennessee), US Department of Energy
- > Rockefeller University (New York, US)
- > University of Alberta (Canada)
- > University of Arizona (US)
- > University of Calgary (Alberta, Canada)
- > University of California, San Francisco (US)
- > University of California, Santa Barbara (US)
- > University of California, Santa Cruz (US)
- > University of Chicago (Illinois, US)
- University of Cincinnati, College of Medicine (Ohio, US)
- > University of Houston (Texas, US)
- > University of Illinois at Urbana-Champaign (US)
- > University of Michigan (US)
- > University of North Florida (US)
- > University of Ohio (US)
- University of Southern California (California, US)
- > University of Texas Health Science Centre (US)
- > University of Texas Medical School at Houston (US)
- > University of Washington (US)
- Washington University in St Louis (Missouri, US)
- > Wistar Institute (Pennsylvania, US)
- > Yale University (Connecticut, US)

Clinical

- Children's National Medical Centre (Washington DC, US)
- > Cincinnati Children's Hospital (Ohio, US)
- Fred Hutchinson Cancer Research Center (Washington DC, US)
- Institute of Metabolic Disease, Baylor College of Medicine (Texas, US)
- Lucile Packard Children's Hospital at Stanford University (California, US)
- Mayo Clinic Children's Center (Minnesota, US)
- Montreal Children's Hospital McGill University Health Centre (Québec, Canada)
- Moser Centre for Leukodystrophies, Kennedy Krieger Institute (Maryland, US)
- Mount Siani Hospital (New York, US)
- > Primary Children's Hospital (Utah, US)
- > Seattle Children's Hospital (Washington, US)
- > St Jude Children's Research Hospital (Tennessee, US)
- > Stanford University (California, US)
- > The Hospital for Sick Children (Ontario, Canada)
- > University of Utah (Utah, US)
- University of Washington (Washington, US)

Industry

- > Elanco (Indianapolis, US)
- > Illumina (California, US)
- > Ironwood Pharmaceuticals (Massachusetts, US)
- > Isis Pharmaceuticals (California, US)
- Johnson & Johnson Pharmaceutical Research and Development (California, US)
- > Organovo (California, US)
- > Pfizer (Massachusetts, US)
- > Progenra (Pennsylvania, US)
- Protagonist Therapeutics Inc. (California, US)
- > Versatis Inc. (California, US)

South America

Academic

- > Universidad Católíca de Brasilia (Brazil)
- > Universidad de Chile (Santiago, Chile)
- > Universidad de la Frontera (Araucania, Chile)
- > Universidad Sao Paulo (Brazil)

collaborating organisations

SUPPORTING INFORMATION

UQ Advanced Study Program in Science student, Emily Furlong, received an IMB Undergraduate Research Scholarship to undertake training in Professor Matt Cooper's lab

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FINANCIAL STATEMENT



INCOME	2011	2012	2013
PEER-REVIEWED (COMPETITIVE) INCOME	\$'000	\$'000	\$'000
ARC grants	7,500	9,702	7,280
NHMRC grants	20,866	21,753	21,732
Queensland Government grants	1,663	3,946	2,224
Other peer reviewed grants - domestic	5,577	4,207	3,328
Other peer reviewed grants - international	2,794	2,462	1,624
OPERATING INCOME			
UQ awarded grants	4,769	4,580	3,742
UQ operating funding	6,539	6,812	6,803
Queensland Government operating grant	10,000	10,000	10,000
Sales and services revenue	1,278	957	1,337
OTHER INCOME			
Philanthropy	133	168	217
Commercialisation	2,884	3,525	2,740
Other income and recoveries	670	782	918
TOTAL INCOME	64,674	68,893	61,945
EXPENDITURE	2011	2012	2013
REMUNERATION EXPENDITURE	\$'000	\$'000	\$'000
Researchers	31,206	34,598	36,328
Infrastructure	2,752	3,016	2,816
Administrative	2,002	2,414	2,145
RESEARCH EXPENDITURE			
Research services	16,371	15,525	17,753
Commercialisation	1,200	600	356
Research higher degree support	1,384	1,387	1,570
UQ internal collaborations and agreements	810	1,413	912
OPERATING EXPENDITURE			
Capital equipment	5,530	5,104	3,230
Information technology	674	529	438
Administration and support	359	382	290
Infrastructure and development	1,010	733	749
TOTAL EXPENDITURE	63,298	65,701	66,587
NET SURPLUS/(DEFICIT)	1,375	3,192	(4,642)



CORRECTION TO 2012 ANNUAL REPORT FINANCIALS

Please note: IMB's 2012 net income (now 'net surplus/deficit') published on page 49 of IMB's 2012 Annual Report was incorrectly listed as a deficit of \$3,192,000. The correct 2012 net income figure is a surplus of \$3,192,000. This error has been corrected in the table included here.

OUR **PEOPLE**



IMB's IT team

Alexandrov Lab

PhD student Claudio Cortes and Dr Vicki Metzis

Research staff

Alewood Lab: Paul Alewood (Lab Head), Andreas Brust, Zoltan Dekan, Jean Jin

Alexandrov Lab: Kirill Alexandrov (Lab Head), Christina Bollenbach, Yann Gambin, Nichole Giles, Zhong Guo, Regine Hartmann, Wayne Johnston, Sergey Mureev, Marinna Nilsson, Fabien Plisson, Mark Polinkovsky, Rachel Quin, Veronika Schreiber, Emma Sierecki, Viktor Stein, Zakir Tnimov

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

Capon Lab: Rob Capon (Lab Head), Zeinab Khalil, Andrew Piggott, Angela Salim, Soumini Vijayasarathy, Sean Xiao

Coin Lab: Lachlan Coin (Lab Head), Sarah Song

Collins Lab: Brett Collins (Lab Head), Oleksiy Kovtun, Suzanne Norwood

Cooper Lab: Bernd Becker, Mark Blaskovich, Alberto Boucas Da Silva, Tanya Bradford, Mark Butler, Fenny Chong, Matthew Cooper (Lab Head), David Edwards, Alysha Elliott, Frank Fontaine, Alejandra Gallardo-Godoy, Reena Halai, Karl Hansford, Johnny Huang, Geraldine Kaeslin, Tomislav Karoli, Angela Kavanagh, Fredrik Lindahl, Sreeman Mamidyala, Ruby Pelingon, Jan Pinder, Soumya Ramu, Andrea Ranzoni, Avril Robertson, Chris Steel, Daniel Watterson, Zyta Ziora, Johannes Zuegg

Craik Lab: Angeline Chan, Olivier Cheneval, Barbara Colless, David Craik (Lab Head), Thomas Durek, Edward Gilding, Ingrid Hamernig, Peta Harvey, Crystal Huang, Mark Jackson, Quentin Kaas, Annie Kan, Thao Le, Han Lee, Emma Miles, Susan Northfield, Aaron Poth, Tina Schroeder, Philip Sunderland, Joakim Swedberg, Sonia Troeira Henriques, Phillip Walsh, Conan Wang, Anderson Wang Fairlie Lab: Adam Cotterell, Johnathan Faber, David Fairlie (Lab Head), Lyn Fairlie, Tim Hill, Huy Hoang, Abishek Iyer, Woan Mei Kok, James Lim, Ligong Liu, Rink-Jan Lohman, Andrew Lucke, Jeffrey Mak, Fabien Plisson, Robert Reid, Martin Stoermer, Jacky Suen, Annika Yau

Francois Lab: Cameron Curtis, Emmanuelle Frampton, Mathias Francois (Lab Head), Cathy Pichol-Thievend, Renae Skoczylas

Grimmond Lab: Matthew Anderson, Peter Bailey, Tim Bruxner, Angelika Christ, Lynn Fink, Maely Gauthier, Sean Grimmond (Lab Head), Deborah Gwynne, Ivon Harliwong, Shiv Hiriyur Nagaraj, Oliver Holmes, Senel Idrisoglu, Stephen Kazakoff, Conrad Leonard, Ramya Mandyam, Suzanne Manning, David Miller, Felicity Newell, Katia Nones, Ehsan Nourbakhsh, Craig Nourse, Ann-Marie Patch, John Pearson, Darrin Taylor, Nic Waddell, Nick Waddell, Shivangi Wani, Peter Wilson, Scott Wood, Christina Xu

Hamilton Lab: Oliver Cairncross, Matthew Dean, Nick Hamilton (Lab Head), Timothy Lamberton, James Lefevre

Hankamer Lab: Lou Brillault, Naomi Epstein, Ben Hankamer (Lab Head), Michael Landsberg, Melanie Oey, Ian Ross, Rosalba Rothnagel, Evan Stephens

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

King Lab: Raveendra Anangi, Rikki Andersen, Yanni Chin, Maggie Hardy, Volker Herzig, Maria Ikonomopoulou, Glenn King (Lab Head), Julie Klint, Linlin Ma, Joseph O'Neill, Sandy Pineda Gonzalez, Lachlan Rash, Sebastian Senff, Jennifer Smith, Brit Winnen

Koopman Lab: Josephine Bowles, Tara Davidson, Jessica Ineson, Peter Koopman (Lab Head), Kim Miles, Ee Ting Ng, Alex Quinn, Cassy Spiller, Liang Zhao Lewis Lab: Asa Andersson, Fernanda Caldas Cardoso, Sebastien Dutertre, Tamarind Hamwood, Marco Inserra, Richard Lewis (Lab Head), Thea Monks, Blessy Paul, Lotten Ragnarsson-McGrath, Silmara Rodrigues De Sousa, Irina Vetter

Little Lab: Han Chiu, Alexander Combes, Pei Er, Kylie Georgas, Ali Ju, Joan Li, Melissa Little (Lab Head), Norseha Mohamed Suhaimi, Bree Rumballe, Minoru Takasato, Jessica Vanslambrouch, Lorine Wilkinson

Martin Lab: Julia Archbold, Prabhakar Bachu, Karl Byriel, Maria Greenup, Shu-Hong Hu, Russell Jarrott, Gordon King, Prem Lakshmanane, Roisin McMahon, Asma Rehman, Patricia Walden, Andrew Whitten

Mattick Lab: Guy Barry, Michael Clark, John Mattick (Honorary Professor)

Muscat Lab: Natalie Eriksson, Rebecca Fitzsimmons, Patrick Lau, George Muscat (Lab Head), Michael Pearen, Mary Wang

O'Neill Lab (based in Cairns): Sarah Flenley, Scott O'Neill (Lab Head), Andrew Turley

Parton Lab: Nicholas Ariotti, Michele Bastiani, Doris Berchtold, Charles Ferguson, Tom Hall, Rachel Hancock, Mark Howes, Harriet Lo, Robert Luetterforst, Kerrie-Ann McMahon, Susan Nixon, Satomi Okano, Robert Parton (Lab Head), Maaike Pols, James Rae

Ragan Lab: Graham Cameron, Cheong Xin Chan, Melissa Davis, Elham Gharazi, Gavin Graham, Josha Inglis, Webber Liao, Stefan Maetschke, Chanyarat Paungfoo-Lonhienne, Mark Ragan (Lab Head), Eric Powell, Sriganesh Srihari, Alex Varlakov, Jessica Vogt, Lanna Wong

Schroder Lab: Ayanthi Richards, Kate Schroder (Lab Head), Flor Vasquez Sotomayor

Smith Lab: Sam Capon, Jun Chen, Kelly Smith (Lab Head)



Sweet Lab

Koopman Lab

and Professor Jenny Martin

Smythe Lab: Miranda Coleman, Gregory Bourne, Christina Kulis, Jaimee McMahon, Eva Mowe, Craig Murphy, Sonya Scott, Mark Smythe (Lab Head), Simone Vink, Jenny Zhang

Stow Lab: Darren Brown, Nicholas Condon, Tatiana Khromykh, Nathan King, Lin Luo, Amanda Stanley, Jennifer Stow (Lab Head), Juliana Venturato, Adam Wall, Fiona Wylie

Sturm Lab: Stephen Ainger, Kasturee Jagirdar, Katie Lee, Darren Smit, Rick Sturm (Lab Head)

Sweet Lab: Nilesh Bokil, Daniel Hohenhaus, Greg Kelly, Kolja Schaale, Melanie Shakespear, Matt Sweet (Lab Head)

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

Teasdale Lab: Hadiya Agada, Andrea Bugarcic, Michael Hanzal-Bayer, Markus Kerr, Genevieve Kinna, David Liebl, Rohan Teasdale (Lab Head), Zhe Yang

Wainwright Lab: Christelle Adolphe, Lena Constantin, Laura Genovesi, Alex Koon, Brandon Wainwright (Lab Head)

Waters Lab: Andrew Brooks, Tania Brooks, Narelle Manzie, Caroline Nelson, Kathryn Tunny, Michael Waters (Lab Head)

Wicking Lab: Ashley Cooper, Andrew Courtney, Vicki Metzis, Maria Rondon, Carol Wicking (Lab Head)

Yap Lab: Srikanth Budnar, Hayley Cox, Guillermo Gomez, Magdalene Michael, Maedeh Naghibosadat, Suzie Verma, Selwin Wu, Alpha Yap (Lab Head)

Support staff

Administration support: Sue Allen, Megan Craig*, Margarette Elsmore*, Katrina Garner-Moore (from 14/10/13), Susannah Hawtin*, Gail Howard, Tricia Howarth, Desla Shand*, Nick Jones

Finance: 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, Miki Miyagi, Darren Paul, James Springfield, Anne Tobin*

Workshop and maintenance: Gary Carloss, 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, Dawn Walsh (Manager)

Safety manager: Paul Lovelock

Human resources: Caraine Gomez, Liza Leibbrandt, Felicity Ray (Manager)

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

Advancement services: June Cullen*, Amanda Whelan (Deputy Director, Advancement)*

Communications: Bronwyn Adams (Manager), Gemma Ward

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

UniQuest: Mark Ashton (Manager), Rachel De las Heras*, Stephen Earl, Amanda Smith*, Rob McLachlan

QFAB Bioinformatics: Jeremy Barker (CEO), Pierre-Alain Chaumeil, Emma Cowie, Xin-Yi Chua, Mark Crowe, Mathilde Desselle, Dominique Gorse, Anne Kunert, Kim-Anh Le Cao, Roxane Legaie, Leo McHugh*, Jeremy Parsons, Margaret Puls*, Nicholas Rhodes, Stephen Rudd, Justin Scott, Angeline Stelling*, Sarah Williams*

* 2013 departing support staff

ORGANISATIONAL STRUCTURE





OCCUPATIONAL HEALTH AND SAFETY

IMB prides itself on its strong culture and successful track record of workplace safety, which is championed by its staff, students and visitors.

In 2013, IMB's occupational health and safety (OHS) program underwent significant changes to improve compliance and simplify auditing systems. On a trial basis, senior managers were provided with formal OHS performance reports for discussion with senior staff undergoing their annual performance appraisals. This was trialled at senior levels, and will be broadened in 2014 to include all lab heads and supervisors.

The institute's annual Workplace Health and Safety Coordinator Safety Audit process was also simplified for general workplaces and chemical storage and handling system audits, with all audits completed by the end of December. Chemical safety training online module completion rates were also introduced as a standing agenda item at IMB's safety committee meetings, along with fire safety and general safety completions.

Several IMB facilities underwent structural and procedural changes with OHS implications. Reviews of safe operating procedures were carried out for the lentivirus suite and for live cell work in the ACRF Cancer Biology Imaging Facility, with new guidelines established for the users of those facilities. The aquarium was decommissioned, decontaminated, and renovated for use as a guarantine aguarium facility. A new fume and dust extraction fan system was installed in IMB's mechanical workshop and, with the assistance of the OHS division, new soundproofing casings were purchased for some of the vacuum pumps in the building.

Several audits were carried out on-site at the Solar Biofuels Research Centre at Pinjarra Hills, including an audit by UQ OHS, and minor corrective actions were implemented. All of the institute's radiation laboratories and storage facilities, the quarantine aquarium facility and most PC2 laboratories were inspected and recertified for use.

While unsealed radiation use at the institute continues to decline slowly, the Radiation Safety and Protection Plan was reviewed by IMB and approved by Queensland Health. Copies of the plan were circulated to all current users.

In collaboration with other Queensland Bioscience Precinct (QBP) tenants-CSIRO; the Department of Agriculture, Fisheries and Forestry (DAFF); and the Queensland Alliance for Agriculture and Food Innovation (QAAFI)we updated the QBP Emergency Evacuation Plan to achieve greater consistency in planned emergency responses by the different organisations. During the year, IMB also participated in a desktop exercise of the UQ Critical Incident Manual with other sectors of the university, based on a simulated emergency in the QBP. From this emergency response exercise, valuable information was gathered and recommended actions for improvement of UQ systems were adopted in the plan.

Contact with external regulators remained positive, with IMB passing all DAFF and the Office of Gene Technology Regulator (OGTR) audits during the year. IMB also worked closely with DAFF biosecurity on several occasions to secure clearance for biological and chemical materials that arrived uninspected or without documentation.

OHS highlights included:

- > held 40 QBP safety committee meetings
- inducted 212 visitors, staff and students into IMB
- > inducted 38 external contractors into the Queensland Bioscience Precinct
- > recertified or trained 36 fire wardens
- achieved an average 99 per cent compliance with UQ general workplace safety online training
- achieved an average 97 per cent compliance with UQ fire safety online training
- achieved an average 76 per cent compliance with UQ chemical safety online training.



SCIENTIFIC PUBLICATIONS



During 2013, IMB researchers contributed to 354 scientific publications, including 50 high-impact publications with an impact factor greater than 10.

Scientific publications—which include peer-reviewed papers, book chapters and conference papers—help IMB researchers to share their discoveries with research colleagues around the world. They are also a key indicator of the institute's excellent research quality and output.

Total IMB scientific publications



High-impact peerreviewed papers (impact factor >10)

Alexandrov, Ludmil B., Lakhani, Sunil R., Pearson, John V., Waddell, Nicola, Grimmond, Sean M., Nik-Zainal, Serena, Wedge, David C., Aparicio, Samuel A. J. R., Behjati, Sam, Biankin, Andrew V., Bignell, Graham R., Bolli, Niccolo, Borg, Ake, Borresen-Dale, Anne-Lise, Boyault, Sandrine, Burkhardt, Birgit, Butler, Adam P., Caldas, Carlos, Davies, Helen R., Desmedt, Christine et al. (2013) Signatures of mutational processes in human cancer. *Nature*, 5007463: 415-421. **JF: 38.597**

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Gonzalez-Perez, Abel, Fink, J. Lynn, Kassahn, Karin S., Pearson, John V., Mustonen, Ville, Reva, Boris, Ritchie, Graham R. S., Creixell, Pau, Karchin, Rachel, Vazquez, Miguel, Bader, Gary D., Boutros, Paul C., Muthuswamy, Lakshmi, Ouellette, B. F. Francis, Reimand, Jüri, Linding, Rune, Shibata, Tatsuhiro, Valencia, Alfonso, Butler, Adam, Dronov, Serge et al. (2013) Computational approaches to identify functional genetic variants in cancer genomes. *Nature Methods*, 10 8: 723-729. **IF: 23.565**

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