LA TROBE UNIVERSITY

LA TROBE INSTITUTE FOR MOLECULAR SCIENCE

Annual Report 2012

LA TROBE INSTITUTE FOR MOLECULAR SCIENCE

latrobe.edu.au/lims

Contents

A snapshot of our achievements

Demonstration that mutations in the "fused in sarcoma" gene induces endoplasmic reticulum stress in the motor neuron disease Amyotrophic Lateral Sclerosis

Development of a yeast-based method for evaluating drug-mediated inhibition of apoptotic pathway regulators Bcl-2 and caspases

Determination of the three-dimensional structure of two key virulence factors in the uropathogenic bacteria Escherichia coli

Development of a monoclonal antibody against a novel biomarker that prevents and reverses cancer cachexia

Synthesis of novel macrocyclic and macrobicyclic ligands for radiopharmaceutical applications

Synthesis of iodine polycations as oxidising agents for high-oxidation state catalytically relevant transition metal complexes

Development of ultra-low cost paper microfluidic sensors by ink jet printing for electrochemiluminescence applications

Completion of a feasibility study for the use of functionalized lipid nanostructures: inverted cubic phase "cubosomes" for the detection of chemical warfare agents

Identification of a family of innate defence molecules with novel anti-cancer properties

Determination of the three-dimensional structure of an alternative respiratory complex I in yeast

Determination of the three-dimensional structure of an essential enzyme in the grapevine lysine biosynthesis pathway

Development of a novel system for “knocking out” genes in cultured human cells

Discovery of the first example of a crystallographically characterized indium(III) coordination polymer and an unusual example of a cationic aluminium cage

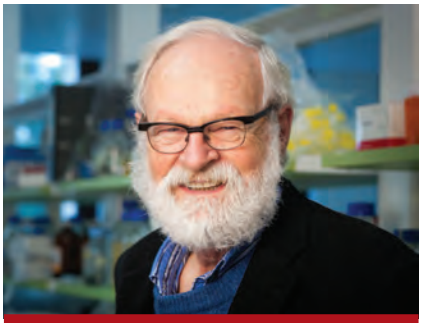
Development of an in vivo screening strategy to identify novel conserved factors important for stem cell self-renewal and differentiation

Demonstration that desert spring surrounding Lake Eyre in central Australia are home to a unique suite of animals that exist nowhere else

Development of an efficient method for removing various heavy metal species form contaminated soils.

La Trobe Institute for Molecular Science (LIMS) building

Director report



NICK HOOGENRAAD

Executive Director, LIMS
Head, School of Molecular Sciences

As I write this report, we are in the final stages of moving into the new LIMS 1 building, a beautiful six-storey building that commenced construction just over two years ago. We were intimately involved in the working parties which established the architectural brief for the interior of the building and now we are in the building we wanted to have – one which has been specifically designed to meet the needs of a modern scientific outfit, like LIMS. It is therefore worth restating the aims we had for the way LIMS would enable us to work more effectively as academics and molecular scientists.

- The LIMS 1 building was designed to house both undergraduate laboratory training facilities and research facilities. At universities, teaching should be co-located with research as teaching should be informed by research.
- The teaching labs are designed with a view to maximising the use of our first class teaching spaces. These spaces include laboratories and break-out rooms for group work and have the latest IT facilities to support the learning experience.
- The research floors are designed to maximise interactions between scientists. The labs are separated by minimal barriers so there can be ready overflow of researchers from one lab to another. The labs are adjacent to support labs and meeting and IT facilities to encourage sharing between occupants on each research floor.
- The LIMS buildings have a single, large common room to encourage interaction and collaborations between scientists from different disciplines. This concept of convergence – the bringing together of life scientists with physical scientists – is very much the agenda for LIMS.

In the next six months, we will complete the refurbishment of Physical Sciences 4 – our old home adjacent to the new LIMS 1 building – to provide us with an additional four floors of research and student training space, and a new home for our secondary student outreach programs.

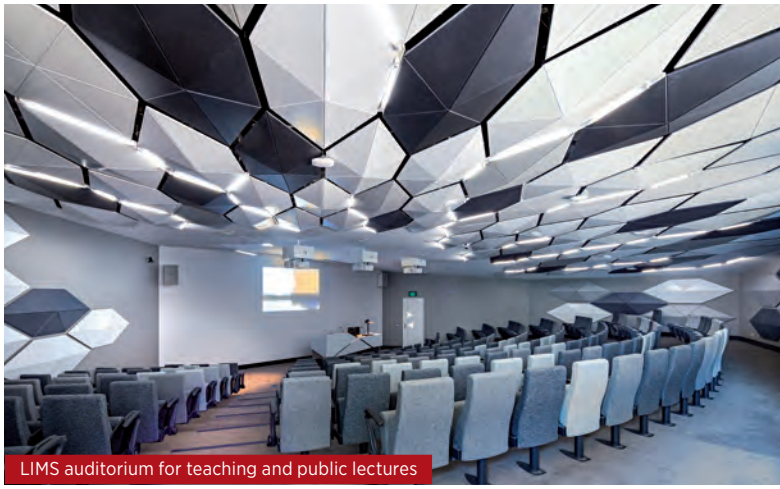
In 2012, we welcomed to the Biochemistry department Future Fellow Matthew Perugini from the Bio21 Institute, Melbourne University; Weisan Chen, who joined LIMS as a professor of immunology from the Ludwig Institute; Megan Maher from the Centenary Institute, University of Sydney, and Begõna Heras from the Institute for Molecular Bioscience, University of Queensland, as LIMS fellows and structural biologists.

The second Excellence in Research for Australia round provided an excellent outcome for disciplines within LIMS. Once again, the biology discipline was rated at the maximum score of 5 as did biochemistry and cell biology (this time sharing this top rating with Newcastle University). Our allied discipline of microbiology also received a rating of 5, to which the parasitologists in LIMS made a substantial contribution. We were also delighted with a rating of 5 for analytical chemistry, up from 3 in 2010.

As we recalibrate our activities to align with the new challenges placed before us by a new Vice-Chancellor and a substantially new senior management team, we look forward to another good year in 2013.

Exterior of the LIMS building

Research and support laboratories



LIMS auditorium for teaching and public lectures

Mission

Research laboratory

LIMS is an institute set within the academic fabric of the School of Molecular Sciences. Its broad mission is to educate students in an environment where world class research is being carried out.

The mission of LIMS is to:

- Train the next generation of scientists to carry out research in biochemistry and cell biology, molecular genetics, biotechnology, chemistry and nanotechnology.
- Carry out both first class basic research and translational research that will lead to the production of commercial products such as therapeutic and diagnostic reagents and biotechnology products such as those used in agricultural or veterinary production.
- Vertically integrate the educational process by placing undergraduate and postgraduate students in the same environment where world class research is performed.
- Stimulate the interest of students in science via an extensive outreach program for secondary schools.
- Combining different disciplines (biochemistry, chemistry, genetics and pharmacy) to achieve aims that would not be possible in the traditional academic setting. Thus LIMS brings together diverse scientists for education and training, setting the mould for the next generation of scientists who can pool their talents to work on projects that would not otherwise be possible.

Income and expenditure

	2012 $'000	Last Year $'000
Commonwealth Grants – DEEWR	17,718	16,636
Student Contributions	3,972	3,911
Research Revenue	13,689	12,396
Student Fees	4,909	4,486
Commercial Revenue	31	91
Other Grants and Donations	81	63
Other Revenue	276	543
Internal Revenue	219	190
Total Revenue	**40,894**	**38,315**
Employee Benefits and On Costs	17,424	16,190
Infrastructure Related	1,113	1,300
Depreciation	1,333	1,005
Professional Fees	47	45
Student Related	846	931
General Operating	3,108	2,885
Staff Related	495	510
Financing Costs	1	
Other Expenses	741	207
Profit / Loss on disposal of Assets	2	202
Central Cost Allocations	17,360	15,306
Internal Expense Transfers	-625	464
Non-Salary Expenditure	24,421	22,856
Total Expenses	41,845	39,047
Operating Result	**-951**	**-732**
Internal Transfer Reserves and Abnormals	75	-64
Net (Surplus) / Deficit	**-876**	**-796**

Governance

LIMS ADVISORY BOARD

Professor Frances Shannon (Chair)
Professor Marilyn Anderson
Professor Tim Brown
Professor Nick Hoogenraad
Dr Bruce Kefford
Professor Brian McGaw
Professor Andrew Peele
Dr Tony Radford
Professor Michael Ryan
Dr Nick Samaras

LIMS EXECUTIVE COMMITTEE

Professor Nick Hoogenraad (Chair)
Dr Michael Angove
Dr Anne Evans
Dr Warwick Grant
Dr Mark Hulett
Dr Ian Potter
Professor Michael Ryan
Dr Damian Spencer

LIMS RESEARCH COMMITTEE

Dr Mark Hulett (Chair)
Dr Chris Bradley
Dr Adam Mechler
Dr Conor Hogan
Dr Christine Hawkins
Dr Warwick Grant
Dr Kaye Truscott

LIMS FUND MANAGEMENT COMMITTEE

Emeritus Professor Robin Anders (Chair)
Professor Tim Brown
Professor Nick Hoogenraad
Professor Brian McGaw
Dr Nick Samaras

Teaching report

DAMIAN SPENCER

Director, Academic

DESIGN FOR LEARNING

Almost four years ago, La Trobe University embarked on an ambitious endeavour to renew and redesign the undergraduate curricula. The *Design for Learning* process has enhanced student engagement and learning outcomes while developing rigorous, comprehensive standards for academic performance. The School of Molecular Sciences has contributed significantly to this program. In 2012, all undergraduate subjects (except Honours) have undergone review, redesign and implementation. This has involved extensive consultation between subject coordinators, curriculum fellows and departmental and faculty leaders. The process was iterative and step-wise, so 2012 saw subject review and redesign at third and fourth year, rolling out of redesigned subjects at second year, and the reporting of fully embedded graduate capabilities in first year cornerstone subjects. Various third year subjects were also identified as capstone subjects. Here, students incorporate the knowledge and skills they have acquired during their studies and apply conceptual, analytical and problem solving strategies to tasks informed by the graduate workplace. Development and design of these subjects commenced at the end of 2012 and will continue in 2013.

PROFESSIONAL DEVELOPMENT

Dr Greg Somers, Dr Linda Ward, Dr Jeff Yeoman, Dr Michelle Spencer and Dr Jason Dutton completed La Trobe University's workshop on Effective Teaching for Higher Learning in 2012. Thirty-two Molecular Sciences staff have completed the workshop since its inception in 2009. In addition, Ms Zoia Hristova and Dr Fiona Carroll are currently completing their Graduate Certificate in Higher Education (Curriculum, Teaching and Learning) with the aim to graduate in 2013.

Dr Fiona Carroll chaired the CUBEnet Graduate Destinations Working Group and attended the CUBE and VIBE Network assessment workshops. Dr Damian Spencer attended the Science Discipline Scholars workshop on implementing the National Science Threshold Learning Outcomes (TLOSs).

ACHIEVEMENTS

The LIMS Chemistry team's project entitled "Progressive building of skills and capabilities in the chemistry undergraduate laboratory" was accepted as a Science and Mathematics Network of Australian University Educator's action-learning project. The team, including Dr Stefan Huth, Dr Ian Potter (Chemistry), Emma Yench and Dr Elizabeth Johnson (FSTE), have commenced their 4-year redevelopment of the senior Chemistry laboratory program and presented preliminary results at two conferences. Dr Damian Spencer was awarded the 2012 La Trobe University Dean's Award for Excellence in Teaching and the 2012 Vice Chancellor's Award for Teaching Excellence.

LIMS meeting room

TEACHING PUBLICATIONS AND CONFERENCE HIGHLIGHTS

Barradell S, Down S, **Spencer D**, Peseta T (2012) Negotiating new research identities through the Graduate Certificate in Higher Education, *HERDSA News*, 34: 13-14.

Huth S, Yench E, **Potter I**, Johnson E (2012), Change process for a laboratory program, *Australian Conference on Science and Mathematics Education*, University of Sydney (poster).

Dutton JL (2012) Interesting chemistry demonstrations: a guide for teachers, *Science Teachers Association of Victoria Lab Tech Conference*, Quantum Victoria (plenary lecture).

Macaulay J, **Carroll F**, Jones S, Speed C, Mohideen M (2012) Transforming undergraduate biomedical science: assessing student learning (CUBEnet workgroup), *Proceedings of the CUBEnet/VIBEnet/QS forum* (poster).

Macaulay J, **Carroll F**, Colthorpe, K, Gregory S-J, Hinton T, Luka L, Muir M, Saint D, Sharma M, Stuppans I, (2012) CUBEnet Science education—applied research working group, *Proceedings of the CUBEnet/VIBEnet/QS forum* (poster).

Hart A, **Chan C-K**, **Carpinelli M** (2012) Peer assessment of graduate capabilities in a capstone undergraduate genetics subject, *5th Annual Curriculum, Teaching and Learning Colloquium*, La Trobe University (talk).

Huth S, Yench E, **Potter I**, Johnson E (2012) Change process for a laboratory program, *5th Annual Curriculum, Teaching and Learning Colloquium*, La Trobe University (talk).

Carroll F (2012) Developing national discipline networks to advance teaching and learning, *5th Annual Curriculum Teaching and Learning Colloquium*, La Trobe University (poster).

The new LIMS facility will enhance the student experience and provide opportunities for exciting and effective learning. New laboratory spaces, small-group and computing areas are conducive to learning, including an AV system in the laboratories, a 50-dual boot iMac computer/modelling lab, small, student-directed learning areas and the provision for the integration of technology into teaching. Classes will share facilities with our researchers, creating an environment where there is mixing of experts and students. Molecular Sciences staff will participate in effective, innovative teaching and develop new learning frameworks in line with the La Trobe Future Ready plan.

Outreach report

FRANCESCA CALATI

Outreach Programs Manager

LIMS Executive Director, Professor Nick Hoogenraad, initiated a pilot Science Outreach program with Ivanhoe Grammar School in 2007, against a backdrop of gloomy educational forecasts. The evidence pointed to a declining interest in science, technology, engineering and mathematics subjects among secondary school students. With a lifelong passion for science education and a parallel educational philosophy, Professor Hoogenraad decided something had to be done.

In his own words:

"... within the same environment, we should have not just researchers and post-graduate students, but also the best undergraduate students, that way they can start to get a feeling for what it is like to work in a research lab in a research environment."

"We have an obligation to help with the education of kids before they come to University. In universities we are only too ready to complain about the quality of students we get in and the curriculum they're taught, but we rarely see it as our responsibility to make a contribution."

"We needed to do something about it."

The 2007 La Trobe-Ivanhoe Grammar School pilot introduced 150 Year 9 students to the "campus-as-classroom" concept, and a series of self-directed learning projects in which they engaged with school-age peers, undergraduates, postgraduates and academic researchers to investigate science-based solutions to global social problems. This small but ambitious project became the prototype for the School of Molecular Sciences' Science Outreach Program that introduced a new range of vertically integrated Middle Years science programs to other local schools. In 2008 the Ivanhoe Year 9 program expanded laterally: by the end of 2009 when Pascoe Vale Girls College joined the program there were 520 Middle Years students from three local schools participating.

With $30,000 in Higher Education Participation and Partnerships Program (HEPPP) funding in 2010, SMS Outreach then developed the Ivanhoe Grammar School "campus-as-classroom" experience for six other schools in Melbourne's northern region. The schools selected were participants in the Schools Access La Trobe (SALT) partnership scheme, which enables students to apply for admission to university degree courses based on school recommendations.

SMS staff fully support the outreach activities, giving generously of their time and expertise, particularly in giving lectures to high school students. Professor Nick Hoogenraad has led by example: since the beginning of the program he has delivered his lecture on pandemics and magic bullets many times.

Further HEPPP funds enabled the development and presentation of practically-based VCE programs in biology and chemistry aligned with the Victorian Curriculum Assessment Authority (VCAA) curriculum. The HEPPP funding also ensured regional students would have access to the same VCE-related science workshops as their Melbourne peers, giving them the opportunity to improve their Australian Tertiary Admission Rank (ATAR) scores without being compromised by socio-economic or geographic disadvantage. Focused principally on SALT schools, the VCE workshops also proved popular with fee-paying schools such as Methodist Ladies College, Kingswood College, Ivanhoe Grammar, Penleigh and Essendon Grammar School and Ruyton Girls' School.

Federal Government funding facilitated workshops in chemistry and the emerging sciences, particularly nanotechnology. Funded by the Department of Industry Innovation Science Research and Tertiary Education (DIISRTE), the PD workshops offered two-way opportunities to evaluate science teachers' current and future development needs.

Outreach students

"... within the same environment, we should have not just researchers and post-graduate students, but also the best undergraduate students, that way they can start to get a feeling for what it is like to work in a research lab in a research environment."

Professor Nick Hoogenraad
Executive Director, LIMS

An integrated student-teacher project initiated in 2008 also introduced pre-service teachers from the University's Faculty of Education to the Year 9 Ivanhoe Grammar and St Helena programs. Jointly developed with FOE science education lecturer Ian Bentley, this project offered young teachers practical experience in innovative science education, and for some, future job placements.

By the end of its second year, the School of Molecular Sciences had a fledgling but vibrant Outreach Program with 1460 students and 560 teachers from 60 secondary schools participating in an expanding range of outreach activities. In 2010 we had an intake of 1600 VCE and Year 9 students and 500 teachers from 70 local and regional schools, and the Year 9 Out-of-Class Program had 300 students participating from five local schools - Ivanhoe Grammar School, Pascoe Vale Secondary College, Epping Secondary College and Parade College. By the end of 2011 a previously fragmented patchwork of Outreach activities had been successfully coordinated into one coherent program under an SMS – LIMS banner; with a HEPPP grant of $143,000 enabling continued program delivery in 2012.

In 2012, the Middle Years program saw more than 1000 students through its doors. LIMS Outreach presented four VCE Chemistry workshops, two VCE Biology workshops, and eight Middle Years 'Science Experience' programs on the University's Melbourne campus, with more than 1500 VCE students from 56 schools participating in the VCE workshops, and 140 Years 9 and 10 students from six schools attending the Middle Years programs, not including the 200 students participating in the now iconic "campus-as-classroom" program.

LIMS and the School of Molecular Sciences have successfully piloted the University's fledgling Science Outreach program to a path-setting and immediately sustainable future, with $195,000 in total secured funding into 2013.

Biochemistry report

PROFESSOR MIKE RYAN

Head, Biochemistry

The Department of Biochemistry reaffirmed its commitment to excellence in research and teaching in 2012.

STAFF

During the year, we welcomed a number of group leaders to the Department. Professor Weisan Chen is an NHMRC Senior Research Fellow and focuses on T cell biology and vaccine development. He has published more than 65 research articles with an average citation of 40 and H index of 29. Professor Chen currently serves as a chief investigator on the NHMRC influenza program led by Nobel Laureate Professor Peter Doherty. Dr Megan Maher (formerly of the Centenary Institute, Sydney) joined the Department as a LIMS Research Fellow. Her work focuses on the structural biology of metals in biological systems, with particular emphasis on protein crystallography. Dr Begõna Heras moved from the University of Queensland to La Trobe as a LIMS Fellow. Dr Heras' research focuses on the structure and function of bacterial virulence factors.

ACHIEVEMENTS

Many departmental members also received accolades for their work. Professor Marilyn Anderson was awarded the title Charles La Trobe Professor in recognition of her 'exceptional record of achievement.' Marilyn is an internationally renowned plant scientist and was elected as a Fellow to the Australian Academy of Sciences last year. Professor Nick Hoogenraad was reappointed to the Biological and Biotechnological Sciences Research Evaluation Committees (RECs) for Excellence in Research for Australia (ERA). Dr David Stroud was awarded a Young Investigator Award at the 37th Lorne Conference on Protein Structure and Function. Ralf Ottofuelling (Dougan/Truscott lab), Tanja Kitevska (Hawkins lab) and Jen Payne (Anderson lab) were all awarded student poster prizes at the meeting. In 2012, 20 students completed the honours course, with Kristen Priebatsch receiving the top mark. Many of these students will be returning in 2013 to undertake postgraduate study. The Masters Coursework programs that are run through the Department continued to be successful and enrolments increased substantially. A number of recent graduates are commencing their PhD in Biochemistry and this reflects well on the success of the program. Many of our PhD students submitted their theses during the year and had their degree conferred. They included Dr Catherine Palmer, Dr Richard Beaumont, Dr Nufail Khan, Dr Ken Choong and Dr Ayenachew Bezawork-Geleta.

In August, Biochemistry held its second Open Day attended by staff and students from the wider university community. This event, which included displays and poster presentations, was a great prelude to the University's Open Day.

GRANTS

NHMRC project grants were awarded to Dr Suzi Cutts (A new strategy to prevent anthracycline-induced cardiotoxicity while improving anti-cancer activity) and Professor Mike Ryan and Dr Diana Stojanovski (Molecular mechanisms controlling mitochondrial dynamics). Dr Suresh Mathivanan was awarded an ARC Discovery grant (The importance of exosomal membrane composition in intercellular signaling) and Dr Julie Atkin received a grant from the Motor Neuron Disease Research Institute of Australia to research the cellular mechanisms of toxicity in amyotrophic lateral sclerosis (ALS). Dr Mark Hulett, Dr Hamsa Puthalakath and Professor Nick Hoogenraad were awarded an ARC LIEF grant for the purchase of an animal imaging system.

Chemistry report

DR IAN POTTER

Head, Chemistry

This was a year of consolidation for the Department of Chemistry with the establishment of research groups associated with recent academic staff appointments, and the introduction of changes to the chemistry curriculum translating into increased undergraduate student enrolments.

STAFF

Dr Belinda Abbott returned from maternity leave to begin a 60% appointment for the next 2 years.

ACHIEVEMENTS

Dr Anne Richards presented invited keynote lectures at Xiamen University, China, the University of Melbourne and the University of Sydney. Dr Michelle Spencer gave an invited seminar at the University of Melbourne and an oral presentation at the Conference on Optoelectronic and Microelectronic Materials and Devices (COMMAD). Dr Jason Dutton gave invited lectures at the University ofMelbourne and the Science Teachers Association of Victoria Lab Tech Conference.

Dr Brian Smith (Chair), Dr Michelle Spencer and Dr David Wilson organised the Melbourne Meeting of Molecular Modellers (M^4) symposium at VLSCI, Melbourne.

Dr Elizabeth Ankers and Dr David Leaver had their PhD degrees awarded during 2012. The honours cohort consisted of 10 students this year with Tina Tezgerevska achieving the top mark.

GRANTS

Dr Brian Smith received an ARC Discovery grant to develop open-source computer software to predict the pharmacokinetic properties of small molecules. Brian was also a joint investigator of a NHMRC Project grant (Functional analysis of the Toxoplasma myosin driving tissue dissemination and host cell invasion) with colleagues from the Walter and Eliza Hall Institute. Dr Jason Dutton received an ARC DECRA (Base stabilised dicarbon as a new building block for supramolecular organometallic chemistry), a La Trobe Early Career Researcher Award and a La Trobe eResearch grant with Dr David Wilson. Dr Michelle Spencer was awarded a National Computational Infrastructure (NCI) Merit Allocation Scheme grant and a Pawsey funded iVEC Grant for supercomputing time. Dr Stefan Huth and Dr Ian Potter, with Faculty of Science, Technology and Engineering colleagues Dr Elizabeth Johnson and Emma Yench, received support from the Science and Mathematics Network of Australian University Educators (SaMnet) for an action-learning project (Progressive building of skills and capabilities in the chemistry undergraduate laboratory). The preliminary results from this project were presented at the Australian Conference for Science and Mathematics Education (ACSME) and the La Trobe University Teaching and Learning Colloquium.

Genetics report

WARWICK GRANT

Head, Genetics

The academic staff of the Department of Genetics remained constant during 2012, with Dr Warwick Grant as head of department, with Dr Chee Kai Chan, Dr Adam Hart, Dr John Mitchell, Dr Nick Murphy, Dr Jan Strugnell, Dr Greg Somers and Ms Jodie Young as continuing academic staff.

STAFF

Dr Stephen Doyle joined the Department as an Early Career Development Fellow, with the research component of his appointment in collaboration with Dr Grant, and teaching roles in second and third year Genetics subjects. Dr Jan Strugnell was promoted to a level C position.

ACHIEVEMENTS

Dr Jan Strugnell served on the steering committee of the Cephalopod Sequencing Consortium, and was a Scientific Committee member of the Molluscs Conference 2012, organised by the Malacological Society of Australasia. She was an invited plenary speaker at the Cephalopod International Advisory Council, Brazil, and presented an invited talk at the "Science at the Shine Dome: Antarctic Science: from Mawson's expedition to today" event. Dr Warwick Grant was appointed to the inaugural editorial board of a new BMC journal, *Infectious Diseases of Poverty*, and continued as a member of the World Health Organisation/Tropical Disease Research reference group on Helminth infections. Dr Grant was also involved in the publication of a special issue of the journal *PLoS Neglected Tropical Diseases*, and of a WHO Technical Report Series monograph based on the work of the WHO/TDR reference group on Helminth infections.

Dr John Mitchell was the lead scientist on the first report of next generation re-sequencing of intact mitochondrial and Y-chromosome DNA from Aboriginal peoples as a component of the National Geographic Genographics program.

Dr Adam Hart and Dr Greg Somers served on the organising committee of the Genetics Society of Australasia (GSA) conference held in Melbourne in July 2012. Dr Hart, Dr Somers and Dr Grant chaired sessions at the conference and Professor Emma Whitelaw delivered a plenary address.

Research from the department contributed to ERA 5 in Molecular and Cell Biology and in Veterinary Sciences, an ERA 4 in Ecology and an ERA 3 in Genetics.

GRANTS

Dr Warwick Grant was awarded a grant from the World Health Organisation/ Tropical Disease Research and "in kind" grant support from the Victorian Life Science Computational Initiative.

Dr Stephen Doyle won a world-wide competition run by Illumina corporation to identify ground-breaking applications of next-generation sequencing. His proposal used next-generation sequencing to discover drug resistance (and other clinically relevant) genes in pathogens causing neglected diseases of poverty. The prize was a MiSeq next generation sequencer plus reagents for one year. Dr Jan Strugnell was awarded a grant from the Ian Potter Foundation, and La Trobe University eResearch and Early Career grants. Dr Chee Kai Chan was a partner in a commercialisation grant on "Fitgenes" as a part of the Women's Health Initiative and Nutrigenomics.

Pharmacy and Applied Science report

MIKE ANGOVE

Head, Pharmacy and Applied Science

The School of Pharmacy and Applied Science reaffirmed its commitment to its well respected teaching program in 2012.

STAFF

There were no staffing changes in 2012. Emeritus Professor Kenn Raymond, having returned to Bendigo from Hong Kong, was involved in some sessional teaching during the year.

ACHIEVEMENTS

Fourteen students completed the honours course with Ainslie Hammer (pharmacy) receiving the top mark. Two students will be returning in 2013 for postgraduate study. Dr Saleh Imaid, Dr David Hayes and Dr Chris Maslunka received their PhDs. Hannah Soon and Melissa Austin were finalists in the Pharmacy Student of the Year award and Cobie Mulqueen won the David Nolte award, which is an annual prize awarded for the best presentation for a clinical pharmacy case study. The entries in 2012 were quite outstanding and were the highest overall quality we have had for this award. Joy Spark presented at the International Conference for Pharmacy Practice in Thailand, and Rick Morrison and Cheree Fitzgibbon presented in France at an International Meeting in Medicinal Chemistry. Zoe Dyson presented at an International Waste-Water conference in Denmark, and won a best presentation award – a highly prestigious achievement at such a major conference.

The first batch of La Trobe graduates completed and graduated from Asia Metropolitan University in Malaysia and have all obtained hospital pharmacy positions since their recent graduation.

The School of Pharmacy and Applied Science hosted a range of professional seminars and events for the pharmacy profession. These included the David Nolte Award evening, meetings for the Pharmaceutical Society, and the 11th Bendigo Association of Pharmacy Students (BAPS) Pharmacy Ball. The ball was organised by our students and raised $6000 for a local charity to assist in the care of intellectually disabled children. BAPS also submitted a bid for the 2014 Pharmacy Student Congress meeting, and won the right to host this prestigious event.

GRANTS

Dr Daniel Tillett is an investigator on a successful ARC linkage application (Bacteriophages for foam control in wastewater processing).

Staff

EXECUTIVE DIRECTOR

Professor Nick Hoogenraad

DISTINGUISHED PROFESSORS

Professor Jenny Graves

PROFESSORS

Professor Marilyn Anderson
Professor Weisan Chen
Professor Liam O'Connor
Professor Michael Ryan
Professor Richard Simpson

ASSOCIATE PROFESSORS

Dr Michael Foley
Dr Warwick Grant
Dr Andrew Hughes
Dr Nena Kustrin
Dr Robert Mitchell
Dr Joseph Tucci

PRINCIPAL FELLOWS

Dr Brian Smith

FUTURES FELLOWS

Dr Suzanne Cutts
Dr Christine Hawkins
Dr Matthew Perugini
Dr Hamsa Puthalakath
Dr Anne Richards
Dr Colin Smith
Dr Kaye Truscott

SENIOR RESEARCH FELLOWS

Dr Andrew Coley
Dr Con Dogovski
Dr David Dougan
Dr Nathan Hall
Dr Ji Hong
Dr Marc Kvansakul
Dr Megan Maher
Dr Jacqueline Orian
Dr Gert Talbo

SENIOR LECTURERS

Dr Jasim Al-Rawi
Dr Michael Angove
Dr Julie Atkin
Dr Peter Cartwright
Dr Conor Hogan
Dr Mark Hulett
Dr Adam Mechler
Dr Ian Potter
Dr Evan Robertson
Dr Jan Strugnell
Dr Daniel Tillett
Dr David Wilson

LECTURERS

Dr Belinda Abbott
Dr Peter Barnard
Dr Christopher Bradley
Dr Fiona Carroll
Dr Chee Kai Chan
Dr Jason Dutton
Dr Michelle Gibson
Dr Adam Hart
Mr Steve Jones
Dr Chris Kettle
Dr David Morton
Dr Nick Murphy
Dr Julian Pakay
Dr Greg Somers
Mrs Joy Spark
Dr Damian Spencer
Dr Michelle Spencer
Dr Richard Summers
Dr Ian Swift
Dr Linda Ward
Dr Sabine Wilkens

RESEARCH FELLOWS

Dr Christopher Adda
Dr Filippa Brugliera
Dr Joanne Casey
Dr Wendy Cook
Dr Ira Cooke
Dr Kerry Dunse
Dr Pierre Faou
Dr Yolanda Gasper
Dr David Greening
Dr Kate Griffiths
Mrs Rosemary Guarino
Dr Karen Harris
Dr Begona Heras
Dr Amelia Johnston
Dr Vijay Kaul
Dr David Laine
Dr Fung Lay
Dr Rommel Mathias
Dr Suresh Mathivanan
Dr Simon Poon
Dr Diana Stojanovski
Dr Nicole Van Der Weerden
Dr Ross Weston

ASSOCIATE LECTURERS

Dr Carmel Abrahams
Mrs Christina Dennis
Dr Stephen Doyle
Ms Zoia Hristova
Dr Stefan Huth
Miss Anna Lister
Mrs Deepti Varghese
Dr Kylie White
Ms Pene Wood
Dr Jeff Yeoman
Ms Jodie Young

STAFF

RESEARCH OFFICERS

Ms Barbara Barbeta
Mr Richard Beaumont
Mr Ayenachew Bezawork-Geleta
Dr Mark Bleackley
Dr Sofia Caria
Dr Denison Chang
Dr Srgjan Civciristov
Dr Peter Dracatos
Dr Kirstin Elgass
Dr Kerstin Emmrich
Miss Shelley Evans
Mrs Manal Farg
Dr Jennifer Fox
Dr Trudi Higginson
Ms Laura Jenkinson
Ms Vita Levina
Mr Kevin Lim
Mr Owen McCorkelle
Mr James McKenna
Mrs Ekaterina Mouradova
Ms Zena Nath
Dr Catherine Palmer
Ms Delara Pantaki
Mrs Kathy Parisi
Mrs Kruti Patel
Dr Francine Perrine-Walker
Dr Steve Petrovski
Dr Ivan Poon
Dr Andrew Pow
Miss Gemma Ryan
Dr Kai Ying Soo
Ms Iolanda Stacey
Dr Jackie Stevens
Dr David Stroud
Ms Katerina Viduka
Dr Adam Walker
Mrs Julie White
Mr Damien Zanker

RESEARCH ASSISTANTS

Mr Ismael Aguirre Maclennan
Ms Dinesha Cooray
Mr Phuc Dang
Mr Dorian Friendship
Miss Christa George
Ms Laura James
Mr Krishnath Jayatilleke
Ms Eunice Lee
Mr Ahmad Rahimi
Ms Jennifer Rieger
Mr Tushar Sahay
Miss Srishti
Miss Shaily Vasa
Mr Prem Veneer

EMERITUS PROFESSORS

Professor Robin Anders
Professor Bob Brownlee
Professor Bob Cattrall
Professor John Hill
Professor Jim Morrison
Professor Don Phillips
Professor Kenn Raymond
Professor Robert Seviour

EMERITUS SCHOLARS

Dr Terry Cardwell
Dr Maureen McKay
Dr Michael Westerman
Dr Neville White

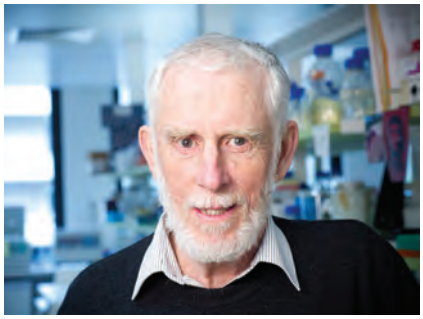
ADJUNCT PROFESSORS

Dr Peter Colman
Dr Seb Marcuccio
Dr Raymond Norton
Dr Nick Samaras
Dr John Silke
Professor David Vaux

SUPPORT STAFF

Ms Dot Andison
Dr Elizabeth Ankers
Ms Margarita Bakalova
Mr Graham Bratspies
Mr Matthew Carabott
Ms Alison Cukier
Mr Bradley East
Dr Anne Evans
Ms Kirsten Grant
Mr John Hamilton
Mrs Joan Hoogenraad
Mr Michael Imsic
Ms Monica Ivanyi
Dr Gianna Kalc
Mr Allan Lee
Dr Peter Lock
Mr Darren Martinus
Mrs Jenny Mitchell
Ms Sue Mullins
Mr David Osborne
Mrs Fabienne Perani
Dr Giselle Roberts
Mr Andrew Robinson
Ms Sue Schrieber
Mr Ian Shaw
Ms Anjina Singh
Ms Elizabeth Smith
Ms Grace Stanley
Mrs Joy Stubbings
Ms Jee Too Tan
Mr Ian Thomas
Ms Fay Traianou
Ms Barbara Udale
Mrs Lesley Williams
Mr Kun Xiao

Biochemistry



PROFILE

Robin Anders

Emeritus Professor
Sexual blood-stage malaria vaccine antigens

With collaborators at the Monash Institute of Pharmaceutical Sciences and the Burnet Institute, we seek to gain an understanding of the structural and antigenic characteristics of merozoite surface antigens as potential components of a malaria vaccine.

Research focus

- structural determinants of antibody binding to the malaria antigens AMA1 and MSP2
- vaccine design to overcome antigenic polymorphisms
- significance and mechanism of amyloid formation by merozoite surface protein 2.

Achievements

Antigenic characterization of MSP2

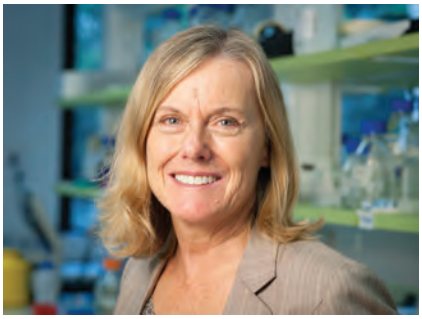
The *Plasmodium falciparum* merozoite surface protein is an intrinsically unstructured protein and this characteristic may complicate the development of MSP2 as a malaria vaccine component. A panel of monoclonal antibodies shows that the parasite is more ordered than recombinant MSP2, resulting in the preferential display of variable region antibody epitopes on the merozoite surface.

Adda C, Macraild C, Reiling L, Wycherley K, Boyle M, Kienzle V, Masendycz P, **Foley M**, Beeson J, Norton R, **Anders R** (2012) Antigenic characterization of an intrinsically unstructured protein, *Plasmodium falciparum* merozoite surface protein 2, *Infection and Immunity*, 80: 4177 – 4185.

Lipid interactions of MSP2

NMR studies show that the highly conserved N-terminal region of MSP2 interacts with lipid micelles. In DPC micelles this region of MSP2 adopts an α-helical structure that modulates the recognition of this region of the antigen by anti-MSP2 antibodies.

Macraild C, Pedersen M, **Anders R**, Norton R (2012) Lipid interactions of the malaria antigen merozoite surface protein 2, *BBA - Biomembranes*, 1818: 2572 – 2578.



PROFILE

Marilyn Anderson

Charles La Trobe Professor
Plant innate immunity proteins

We study defence molecules produced by plants for protection against insect pests and pathogens. The research spans basic work on the structure and function of these molecules to the practical application of creating crop plants which are protected from insect predation and disease. This practical application is being developed within the company Hexima Ltd, which is located in LIMS. Research is funded by the ARC and Hexima Ltd.

Research focus

- antifungal molecules, particularly plant defensins
- production of transgenic crop plants with resistance to fungal disease
- insecticidal molecules, mechanisms of action and application in plant protection.

Achievements

Fungal disease program

Hexima Ltd produced the 10,000th transgenic corn plant expressing antifungal proteins and produced several gene constructs that enhance resistance to fungal diseases when expressed in transgenic plants.

Mechanism of biosynthesis of cyclic peptides in plants

Cyclic peptides have great potential as pharmaceuticals because they are extraordinarily stable in biological systems and can be used as scaffolds for grafting and delivery of bioactive peptides. We have discovered that cyclotides accumulate in the plant vacuole and that the cyclisation reactions occur in that compartment. We have also identified the amino acids in the linear precursor proteins that are essential for production of the cyclic peptides.

Conlan B, Gillon A, Barbeta B, Anderson M (2012) Subcellular targeting and biosynthesis of cyclotides in plant cells, *American Journal of Botany*, 98: 2018 – 2026.

Insecticidal proteins from plants

We have had a long-term interest in plant proteinase inhibitors and their potential application in the control of insect pests. This work has become more relevant as insects are developing resistance to the insecticidal Bt – toxins which are used extensively for insect control on a global scale.

Stevens J, **Dunse K**, **Fox J**, **Evans S**, **Anderson M** (2012) Biotechnological approaches for the control of insect pests in crop plants, *Pesticides – Advances in Chemical and Botanical Pesticides*, 269 – 308.

PROFILE

Julie Atkin

Senior Lecturer
Mechanisms of neurodegeneration in Amyotrophic Lateral Sclerosis (ALS)

We study the cellular and molecular mechanisms leading to motor neuron death in ALS, with a focus on cellular stress pathways and intracellular trafficking processes. Research is supported by grants from the NHMRC, Motor Neuron Disease Research Institute of Australia, and the Bethlehem Griffiths Research Foundation.

Research focus

- cellular mechanisms of toxicity induced by proteins recently linked to ALS disruption of intracellular trafficking and dysfunction of axonal transport in ALS
- mechanisms of neuroprotection by protein disulphide isomerase (PDI) in ALS.

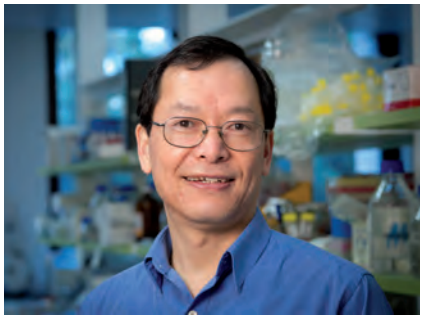
Achievements

Stress signalling from the endoplasmic reticulum

Recent evidence indicates that endoplasmic reticulum (ER) stress plays a central role in ALS pathogenesis. ER stress activates the unfolded protein response (UPR) which is one of the earliest events in motor neurons in rodent models of ALS. Genetic manipulation of ER stress in these models alters disease onset and progression, implicating the UPR in disease. Perturbation of the ER could occur in ALS cases associated with TDP-43, FUS and VCP, implicating ER stress as a potential upstream mechanism involved in both familial and sporadic forms of ALS.

Mutant FUS induces endoplasmic reticulum stress in ALS

Mutations in the gene encoding *fused in sarcoma* (FUS) are linked to ALS, but the mechanisms by which these mutants trigger neurodegeneration remain unknown. FUS is normally located in the nucleus but in ALS, FUS redistributes to the cytoplasm and forms inclusions. Our research demonstrates that mutant FUS induces ER stress in motor neuron cell lines, but only in cells in which FUS distributes to the cytoplasm. Mutant FUS also co-localised with PDI, an important ER chaperone, in NSC-34 cells and in human ALS motor neurons.



PROFILE

Weisan Chen

Professor
Cellular immunity to Influenza A virus (IAV) and tumours

We research the T cell response to IAV and tumour antigens in both mice and humans. Research is supported by the NHMRC.

Research focus

- T cell and dendritic cell interaction and the initiation of cellular immunity
- antigen processing and presentation T cell epitope discovery and vaccine design.

Achievements

Dendritic cells efficiently present soluble tumour antigen

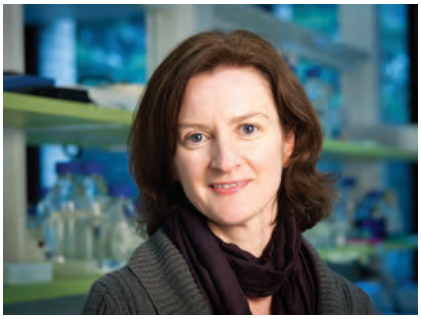
Dendritic cells are normally more capable of taking up particulate or cell associated antigens, rather than soluble antigens, and presenting the processed antigenic peptides to T cells, a process termed cross-presentation (of antigen). We discovered that the cross-presentation of an epitope from tumour antigen NY-ESO-1 is most efficient from soluble antigen forms.

Zhao R, Mifsud N, Xaio K, Chan K-F, Oveissi S, Jackson H, Dimopoulos N, Guillaume P, Knights A, Lowen T, Robson N, Russell S, Scotet E, Davies I, Maraskovsky E, Cebon J, Luescher I, **Chen W** (2012) A novel HLA-B18 restricted CD8$^+$ T cell epitope is efficiently cross-presented by dendritic cells from soluble tumor antigen, *PLoS One*, 7: e44707, doi:10.1371/journal.pone.0044707.

Cancer vaccine induces antigen-specific regulatory T cells (Tregs)

Tregs are important immune regulators to maintain immune homeostasis and prevent autoimmunity. However, they were shown to be increased in cancer patients. We discovered that under certain conditions, a cancer vaccine may induce antigen-specific Treg with the potential to be detrimental to anti-cancer immunity.

Ebert L, MacRaild S, Zanker D, Davis I, Cebon J, **Chen W** (2012) A cancer vaccine induces expansion of NY-ESO-1-specific regulatory T cells in late stage melanoma patients, *PLoS One*, 7(10): e48424. doi:10.1371/journal.pone.0048424.



PROFILE

Suzanne Cutts

ARC Future Fellow
Cellular responses to DNA interacting cancer drugs

We develop new therapeutic strategies for cancer treatment by understanding the mechanism of action of currently used anticancer drugs.

Research focus

- therapeutic strategies for prevention of anthracycline-induced cardiotoxicity
- development of tumour-targeted nanoparticles to activate anthracycline drugs
- elucidation of the mechanism of action of new clinically used anthracenedione drugs.

Achievements

Preventing anthracycline-induced cardiotoxicity

Cardiotoxicity is the most serious adverse event associated with the use of anthracyclines and has been attributed to the death of cardiac cells by the generation of reactive oxygen species.

This cardiotoxicity risk and the requirement for surveillance or intervention increase the cost of health care and compromise quality of life.

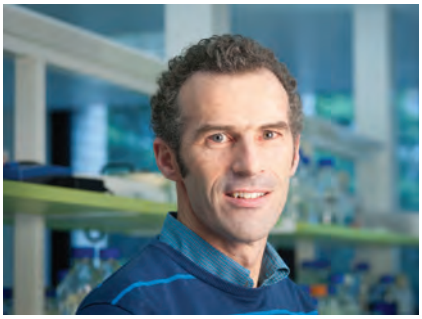
Since anthracyclines will continue to be widely used in the clinic, cardiotoxicity preventative strategies are urgently needed. We have shown that the formaldehyde prodrug AN-7 augments anthracycline anticancer potential while simultaneously reducing cardiotoxicity. Our research seeks to identify the mechanism by which the activated anthracyclines protect cardiac cells from undergoing cell death.

Tarasenko N, **Cutts S**, **Phillips D**, Inbal A, Nudelman A, Kessler-Icekson G, Rephaeli A (2012) Disparate impact of butyroyloxymethyl diethylphosphate (AN-7), a histone deacetylase inhibitor, and doxorubicin in mice bearing a mammary tumor, *PLoS One,* 7: e31393, doi:10.1371/journal.pone.0031393.

DNA damage responses

Drugs that bind covalently to DNA are processed by cell response mechanisms that determine whether the damage will be repaired or trigger a signal for cells to undergo apoptosis. We have shown that doxorubicin-DNA adducts induce cell death regardless of p53 status. Loss of the protein kinase ATR due to a DNA damage response was associated with abrogation of a drug-induced G2/M block and induction of mitotic catastrophe, while loss of ATM was associated with drug-induced apoptosis. These proteins may therefore be potential drug targets to achieve synergistic cytotoxic responses to doxorubicin-DNA adduct forming therapies.

Forrest R, **Swift L**, Rephaeli A, Nudelman A, Kimura K, **Phillips D**, **Cutts S** (2012) Activation of DNA damage response pathways as a consequence of anthracycline-DNA adduct formation, *Biochemical Pharmacology*, 83: 1602–1612.



PROFILE

David Dougan

ARC Australian Research Fellow
AAA+ machines in protein homeostasis

We investigate how protein homeostasis (proteostasis) is maintained in the cell. In particular, we focus on the role of ATP-dependent machines belonging to the AAA+ superfamily, and how they contribute to proteostasis in bacteria and the evolutionarily related eukaryotic organelle, the mitochondrion.

Research focus

- molecular dissection of the physiological role of ATP-dependent machines
- sensing and signalling of key stress response pathways
- deciphering the physiological role of the N-end rule pathway in bacteria.

Achievements

Regulated proteolysis and proteostasis

For many years intracellular protein degradation was thought of as a non-selective mechanism to recycle amino acids and remove trash from the cell.

The contemporary view is that protein degradation is a highly selective process that contributes to the removal of damaged proteins and regulates the cells responses to various stresses. In eukaryotes, the mitochondrial protease CLPXP has been implicated in the signalling of a mitochondrial-specific unfolded protein response, however little is known about this protease in mammals. To better understand the role of this proteolytic machine in mammalian mitochondria, we created a variant of human CLPX, which was able to "trap" interacting proteins. Using this mutant we were able to identify two novel proteins. In collaboration with researchers in USA and Germany, this study also identified a small compound that can activate the peptidase (CLPP) in the absence of its cognate unfoldase component (CLPX). This compound may prove to be a useful new tool to study the physiological role of this machine in mammalian cells.

Lowth B, Kirstein-Miles J, **Saiyed T**, Brotz-Oesterhelt H, Morimoto R, **Truscott K**, **Dougan D** (2012) Substrate recognition and processing by a Walker B mutant of the human mitochondrial AAA+ protein CLPX, *Journal of Structural Biology*, 179: 193–201.

Dougan D, **Micevski D**, **Truscott K** (2012) The N-end rule pathway: from recognition by N-recognins, to destruction by AAA+ proteases, *Molecular Cell Research*, 1823: 83–91.

PROFILE

Mick Foley

Associate Professor
Biotechnological approaches to disease

We study the molecular mechanisms that allow the malaria parasite to invade the human red blood cell. We use peptides, antibodies and a novel class of shark antibodies to examine the protein-protein interactions of malaria and other diseases.

Research focus

- understanding the role of malaria proteins AMA1 and MSP2 in invasion
- developing the AMA1 protein as a vaccine against malaria
- exploring the use of shark antibodies in diagnosis and therapy of infectious diseases.

Achievements

Apical membrane antigen 1 as a potential drug target

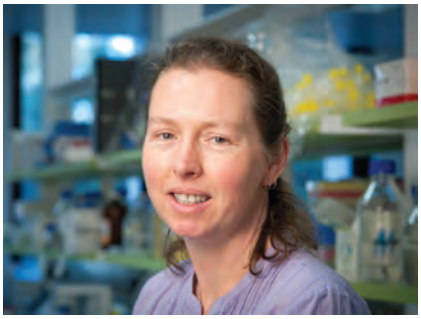
The *Plasmodium falciparum* protein AMA1, plays an important role in facilitating the invasion of parasites into human red blood cells which can lead to malaria.

Our research confirms that a variety of protein reagents such as peptides, single domain protein and monoclonal antibodies that target a hydrophobic trough on AMA1 are all able to block red blood cell invasion and inhibit the growth of malaria parasites. In collaboration with researchers at Monash University, we have discovered that this hydrophobic trough has deep cavities that may be amenable to small drug molecules that could be used to block parasite invasion.

Adda C, Macraild C, Reiling L, Wycherley K, Boyle M, Kienzle V, Masendycz P, **Foley M**, Beeson J, Norton R, **Anders R** (2012) Antigenic characterization of an intrinsically unstructured protein, *Plasmodium falciparum* merozoite surface protein 2, *Infection and Immunity*, 80: 4177 – 4185.

Shark antibody technology

AdAlta Pty Ltd is a spin-off company from the Cooperative Research Centre for Diagnostics. AdAlta is pioneering a new technology that uses modified shark antibodies for therapeutic interventions or diagnostic markers in disease. The process involves taking genes from sharks and modifying them in a laboratory by inserting random sequences – essentially mimicking the way the human immune system works – to develop antibodies capable of a repertoire of defensive responses. These novel libraries can then be screened in the lab against a target to identify a diagnostic or therapeutic lead candidate. In January 2012, AdAlta signed an agreement with international pharmaceutical company, Roche, to evaluate and identify shark antibody binders.



PROFILE

Christine Hawkins

ARC Future Fellow and Senior Lecturer
Apoptosis research

We study the molecular regulation of cell death. An NHMRC grant supports an investigation into how viruses enforce survival of infected cells to enable viral propagation and a Cancer Council-funded project supports an exploration for agents that may induce apoptosis specifically and directly in cancer cells.

Research focus

- identification and characterisation of viral anti-apoptotic proteins
- comparing the mutagenicity of direct apoptosis inducers and chemotherapy drugs
- developing a method for screening compounds for anti-cancer potential.

Achievements

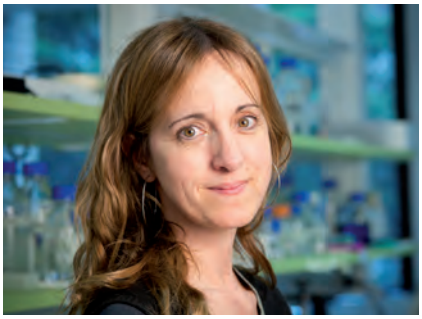
Identifying and characterising drugs targeting apoptotic pathways

Development of drugs targeting Bcl-2 relatives and caspases for treating diseases including cancer and inflammatory disorders typically involves measuring interactions with purified target molecules or cancer cell killing *in vitro*.

We established a yeast-based method for evaluating drug-mediated inhibition of Bcl-2 family members or caspases. We showed that the Bcl-2-targeting drugs ABT-737 or ABT-263 were selective in its specificity to a range of different Bcl-2 homologues. The caspase inhibitor Q-VD-OPh suppressed caspase-mediated yeast death. Yeast expressing human apoptotic regulators enable simple, automatable assessment of the activity and specificity of candidate drugs targeting Bcl-2 relatives or caspases.

Differential mutagenicity of direct apoptosis-inducing anti-cancer drugs

Chemotherapy and radiotherapy commonly damage DNA and secondarily provoke cancer cell death. Unfortunately, this can lead to mutagenesis of non-malignant surviving cells which can provoke second malignancies. Drugs that directly stimulate apoptosis may be useful anti-cancer agents, and because the cell death they stimulate does not require DNA damage, surviving normal cells may remain genetically unscathed. We have tested the genotoxicity of two classes of direct apoptosis inducers. We observed that, surprisingly, death receptor agonists like TRAIL were mutagenic. More promisingly, BH3-mimetic drugs were not. We are currently defining the mechanisms underlying this differential mutagenicity.



PROFILE

Begoña Heras

LIMS Fellow

Bacterial virulence factors: structure and function

We investigate the molecular mechanisms underlying Gram-negative bacterial infections to develop antibacterial drugs with novel modes of action not susceptible to existing resistance mechanisms.

Research focus

- role of disulfide catalyst in the biogenesis of virulence factors
- development of disulfide catalysts inhibitors as potential antimicrobials
- structural and functional studies of bacterial virulence factors.

Achievements

Disulfide catalysts in the biogenesis of virulence factors

In collaboration with researchers at Monash University and the University of Queensland, we investigated key processes in the biogenesis of virulence factors.

Most bacteria contain specialised pathways to catalyse the oxidative folding of virulence determinants. We uncovered primary enzymes necessary for bacteria to establish an infection, which represent potential targets for drug design and therapeutic intervention. We are currently targeting such enzymes for the development of putative antimicrobials.

Walden P, **Heras B**, Chen K, Halili M, Rimmer K, Sharma P, Scanlon M, Martin J (2012) The 1.2 Å resolution crystal structure of TcpG, the *Vibrio cholerae* DsbA disulfide-forming protein required for pilus and cholera toxin production, *Acta Crystallographica Section D*, 68:1290 – 1302.

Structural and functional studies of bacterial virulence factors

Combining structural biology and molecular microbiology, we investigate an array of virulence factors from uropathogenic *E. coli*, a major cause of hospital and community acquired infections worldwide. We have determined the three-dimensional structure of two key virulence factors to gain a better understanding of the biology of these Gram-negative pathogens. This research will provide valuable structure-function information to aid the development of new and more effective antibacterial therapeutics.

King N, Sakinc T, Ben Zakour N, Totsika M, **Heras B**, Simerska P, Shepherd M, Gatermann S, Beatson S, Schembri M (2012) Characterisation of a cell wall-anchored protein of *Staphylococcus saprophyticus* associated with linoleic acid resistance, *BMC Microbiology*, 12:8, doi:10.1186/1471 – 2180 – 12 – 8.

PROFILE

Nick Hoogenraad

Charles La Trobe Professor, Executive Director of LIMS and Head of Molecular Sciences
Mitochondrial infolded protein response and development of therapeutic antibodies against cachexia

We investigate the mitochondrial organelle's response to the accumulation of unfolded proteins and the role of molecular chaperons and proteins in this process. We also research cancer cachexia and the development of monoclonal antibodies to prevent this condition.

Research focus

- role of molecular chaperones in protein targeting to mitochondria
- mechanism of response of cells to the accumulation of unfolded proteins in mitochondria
- development of therapeutic monoclonal antibodies to prevent and treat cancer cachexia.

Achievements

Mechanism of cellular response to mitochondrial unfolded protein response

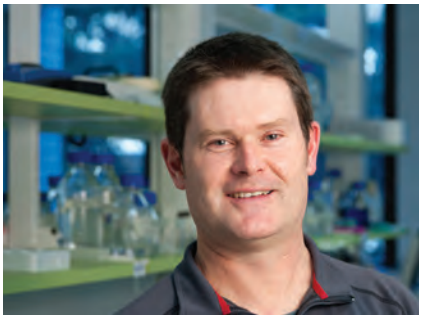
The accumulation of unfolded proteins in the mitochondrial matrix results in a cellular response that removes the unfolded protein and restores mitochondrial function and cell survival. This occurs through a mechanism of transcriptional activation of gene-encoding proteins which are targeted to mitochondria to rectify the situation, and also to the inhibition of protein translation, lessening the load of unfolded proteins in the organelle. Recently, a key regulator of this process was found to be the dsRNA activated protein kinase (PKR), which both activates translation though the phosphorylation of the initiation factor eIF2a and through to activation of the kinase MEK, leading to the activation of a suite of protein quality control genes.

Rath E, Berger E, Messlik A, Nunes T, Liu B, Kim S, **Hoogenraad N**, Sans M, Sartor R, Haller D (2012) Induction of dsRNA activated protein kinase links mitochondrial unfolded protein response to the pathogenesis of intestinal inflammation, *Gut*, 61:1269 – 78.

Development of therapeutic antibodies against cachexia

Our lab investigates the process that leads to cancer cachexia in mouse models of cancer. This has led to the discovery of a receptor (known to be activated in many cancers), as being responsible for a complex set of events that ultimately leads to severe muscle wasting and a general loss of body mass and function, known as cachexia. Monoclonal antibodies generated against this receptor were able to prevent the onset of cachexia and reverse cachexia once established. This work has led to the filing of a patent and potential Phase 1 clinical trials in humans.

Johnston A, **Silke J**, **Hoogenraad NJ** (2012) Patent: FN14 binding proteins and uses thereof.



PROFILE

Mark Hulett

Senior Lecturer
Regulators of cancer and inflammation

We study the molecular processes that promote the growth and spread of cancer and inflammatory disease. Research is supported by grants from the NHMRC and ARC, as well as the Melbourne biotechnology company, Hexima Ltd.

Research focus

- role of the heparin-sulphate degrading enzyme in tumour angiogenesis, metastasis, and inflammatory disease
- function of the serum protein, histidine-rich glycoprotein (HRG), in tumour progression and inflammation
- innate defence molecules as novel anti-cancer treatments.

Achievements

Heparanase is a novel regulator of metabolism and obesity

Heparanase is traditionally associated with leukocyte migration and tumour progression. We have generated heparanase deficient mice ($HPSE^{-/-}$) using gene targeting. Unexpectedly, the $HPSE^{-/-}$ mice were found to gain weight compared to wild-type mice as a result of increased fat deposition.

Gene expression analysis has identified dysregulation in a number of metabolism genes suggesting an important role for heparanase in metabolism and obesity.

Role of histidine-rich glycoprotein (HRG) in cell clearance

HRG is an abundant mammalian serum protein. We have identified HRG as a novel serum pattern recognition molecule that, in addition to aiding the clearance of necrotic cells, also acts as an innate immune molecule to help remove bacterial pathogens. We have shown that HRG functions as an adaptor molecule to recognise and promote the uptake and destruction of bacteria by phagocytes.

Innate defence molecules as novel anti-cancer agents

Innate defence molecules represent an attractive source of novel therapeutics for the treatment of cancer. We have identified a family of innate defence molecules that are potent killers of cancer cells, defined their mechanism of action and demonstrated their efficacy in preclinical models of tumour growth.

Lay F, **Mills G**, **Poon I**, Cowieson N, Kirby N, **Baxter A**, **Van Der Weerden N**, **Dogovski C**, **Perugini M**, **Anderson M**, **Kvansakul M**, **Hulett M** (2012) Dimerization of plant defensin NaD1 enhances its antifungal activity, *Journal of Biological Chemistry*, 287: 19961 – 19972.

PROFILE

Marc Kvansakul

NHMRC CDA Fellow and Senior Lecturer
Structural biology of cell death and host-pathogen interactions

We research the molecular basis of the regulation of cell death during viral infection and the use of small proteins in the defence against microbial threats.

Research focus

- subversion of host cell death during viral infections
- role of viral cell death inhibitors in the development of virus-associated cancers
- structural basis of small plant innate defence molecules' anti-cancer activity.

Achievements

BHRF1, a key inhibitor of cell death in Epstein-Barr virus (EBV)

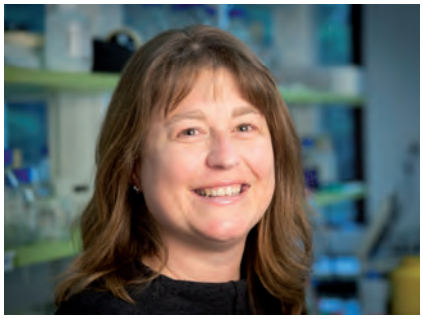
The ability of pathogenic viruses to disable the cell death machinery of invaded host cells is of critical importance for viral infectivity, persistence and replication. Viral infections, such as those by EBV, have been shown to be intimately linked to malignancies including Burkitt lymphoma. A key group of virulence factors allows gamma herpes viruses to overcome the apoptotic machinery of host cells and persist in the host as viral Bcl-2 proteins. We have designed a small molecule inhibitor to target BHRF1 as a highly specific chemotherapeutic agent, and using X-ray crystallography revealed the mode of binding to BHRF1.

Caria S, **Chugh S**, Nhu D, Lessene G, **Kvansakul M** (2012) Crystallization and preliminary X-ray characterization of Epstein-Barr virus BHRF1 in complex with a benzoylurea peptidomimetic, *Acta Crystallographica. Section F: Structural Biology and Crystallization Communications Online*, 68: 1521 – 1524.

Structural basis of small plant innate defence molecules' anti-cancer activity

Innate defence molecules represent an attractive source of novel therapeutics for the treatment of cancer and inflammatory disease. Certain plant molecules have been shown by our collaborators (Mark Hulett, LIMS) to be potent killers of human tumour cells. We are now defining their mechanism of action using biophysical methods to study their ability to kill cells.

Lay F, **Mills G**, **Poon I**, Cowieson N, Kirby N, **Baxter A**, **Van Der Weerden N**, **Dogovski C**, **Perugini M**, **Anderson M**, **Kvansakul M**, **Hulett M** (2012) Dimerization of plant defensin NaD1 enhances its antifungal activity, *Journal of Biological Chemistry*, 287: 19961 – 19972.



PROFILE

Megan Maher

LIMS Senior Research Fellow
Metallobiology

We research the roles of transition metals in biology, with particular emphasis on the three-dimensional structures of integral membrane metal transport proteins.

Research focus

- molecular details of inter-protein electron transfer
- structures of bacterial integral membrane metal transport proteins and their potential as targets for novel antibiotic design
- cellular mechanisms for transition metal homeostasis.

Achievements

Membrane protein structure evolution

Bioenergy is efficiently produced in the mitochondria by the respiratory system consisting of complexes I-V.

In various organisms, complex I can be replaced by the alternative NADH-quinone oxidoreductase (named Ndi1 in yeast). We solved the three-dimensional structure of Ndi1 and showed it to be a dimeric monotopic membrane protein, with a 70-residue membrane anchor domain. The structure showed two channels through the protein, which intersect at the active site (defined by the FAD cofactor). One channel leads from the matrix and accommodates the water-soluble substrate NADH and the other leads from the membrane and hosts the lipid-soluble quinone substrate. The overlapping positions of these binding sites represent a remarkable adaptation of the protein structure to accommodate molecules with such different structures and chemistries.

Iwata M, Lee Y, Yamashita T, Yagi T, Iwata S, Cameron A, **Maher M** (2012) The structure of the yeast NADH dehydrogenase (Ndi1) reveals overlapping binding sites for water- and lipid-soluble substrates, *Proceedings of the National Academy of Sciences*, 109: 15247-15252.

New classification of cation-dependent G-proteins

G-proteins are some of the most important and abundant enzymes. Recent experiments on a variety of GTPases have demonstrated that their activities are stimulated by potassium ions. The results from this analysis effectively re-define the conditions under which many of these G-proteins should be studied *in vitro*.

Ash M, **Maher M**, Mitchell G, Jormakka M (2012) The cation-dependent G-proteins: in a class of their own, *FEBS Letters*, 586: 2218 – 2224.

PROFILE

Suresh Mathivanan

NHMRC Peter Doherty and LIMS Fellow
Exosomes, secretome and systems biology

We study exosomes (40 – 100 nm diameter vesicles secreted by various cell types) and soluble secreted proteins in the context of intercellular signalling and cancer. Research is supported by the NHMRC.

Research focus

- role of oncogenic events in altering proteins that are secreted
- exosomes in intercellular signalling
- systems biology approaches to analyse multi-omic datasets.

Achievements

ExoCarta – a compendium of exosomal molecular components

ExoCarta is a compendium of previous exosomal protein, RNA and lipid studies. It is a manually curated repository hosted by La Trobe University and is freely available for the scientific community (exocarta.org). Currently, ExoCarta (version 3.1) contains information on 11 261 protein entries, 2375 mRNA entries and 764 miRNA entries that were obtained from 134 exosomal studies.

Mathivanan S, Fahner C, Reid G, **Simpson R** (2012) ExoCarta 2012: database of exosomal proteins, RNA and lipids, *Nucleic Acids Research*, 40: 1241–1244.

Extracellular micro vesicles (eMVs)

eMVs are a class of membrane-bound organelles secreted by various cell types including exosomes, ectosomes and apoptotic blebs. The field of eMVs currently faces obstacles with relevance to the purification protocols and the terminologies used in naming these vesicles. A review of these issues and prompts biomedical researchers to name the vesicles with consensus and use stringent purification protocols.

Simpson R, **Mathivanan S** (2012) Extracellular micro vesicles: the need for internationally recognised nomenclature and stringent purification criteria, *Journal of Proteomics and Bioinformatics*, 5: ii.

PROFILE

Jacqueline Orian

Senior Research Fellow
Multiple sclerosis research

We investigate mechanisms underlying neurodegeneration in multiple sclerosis (MS) to contribute to improved drug design for this condition. Research is supported by the National Multiple Sclerosis Society, Multiple Sclerosis Research Australia and Novartis Australia.

Research focus

- contribution of astrocytes to neuronal/axonal injury
- mechanisms of grey matter damage in neuro-inflammation, in the experimental autoimmune encephalomyelitis (EAE) model of MS.

Achievements

The contribution of astrocytes to neuronal/axonal injury

Glial fibrillary acidic protein (GFAP) is an intermediate filament protein consisting of a family of splicing isoforms.

We demonstrated highly conserved structure and features across species for GFAPα, but low conservation of structure and 3' end features for GFAPδ/ε and GFAPκ, both relative to each other and relative to GFAPα. The overall picture is one of distinct and tightly regulated functions for the 3' end isoforms, consistent with complex astrocyte biology.

Boyd S, Nair B, Ng S, Keith J, **Orian J** (2012) Computational characterization of 3' splice variants in the GFAP isoform family, *PLoS One*, 7: e33565, doi:10.1371/journal.pone.0033565.

Mechanisms of grey matter damage in the EAE model of MS

Similarly to MS, the emphasis of EAE investigations has been on white matter disease, while the contribution of grey matter damage to overall pathology has been overlooked. To further investigate mechanisms driving entry of inflammatory cells in grey and white matter, we have developed the techniques of *in situ* hybridisation and laser capture micro-dissection for evaluation of changing cellular interactions in each compartment. Quantification of markers of neuro-inflammation reveals distinct but overlapping pathological processes in the two compartments.

PROFILE

Matthew Perugini

ARC Future Fellow and Associate Professor
Lysine biosynthesis enzymes as novel antibiotic targets

We study the structure, function, regulation and inhibition of oligomeric enzymes functioning in the lysine biosynthesis pathway of bacteria and plants. Research is funded the NHMRC, ARC and US DTRA grants.

Research focus

- molecular evolution of enzyme quaternary structure allosteric regulation
- structure-based inhibitor design using high performance computing
- study of biomolecular interactions using advanced platform technologies (AUC, CD spectroscopy and ITC).

Achievements

Structure, function, and dynamics of grapevine DHDPS

In collaboration with the IBM Collaborator for Life Sciences – Melbourne, the structure, function and dynamics were determined for the essential enzyme, dihydrodipicolinate synthase (DHDPS), from *Vitis vinifera* (the common grapevine).

Our study employed contemporary synchrotron techniques of macromolecular crystallography and small angle X-ray scattering in combination with CD spectroscopy and analytical ultracentrifugation. We demonstrated that *V. vinifera* DHDPS adopts a back-to-back dimer-of-dimers opposite to the head-to-head architecture observed for bacterial DHDPS. High performance molecular dynamics simulations using the VLSCI IBM Blue Gene / Q supercomputer were also conducted to show that tetramerisation of *V. vinifera* DHDPS stabilises enzyme dynamics to afford efficient catalysis.

Atkinson S, **Dogovski C**, Downton M, Pearce F, Reboul C, Buckle A, Gerrard J, Dobson R, Wagner J, **Perugini M** (2012) Crystal, solution and *in silico* structural studies of dihydrodipicolinate synthase from the common grapevine, *PLoS One*, 7: e38318, doi:10.1371/journal.pone.0038318.

Bacterial lysine biosynthesis

Our research group were invited to contribute a book chapter on the structure, function, regulation and inhibition of enzymes of the lysine biosynthesis pathway in bacteria, including several we had characterised, such as DHDPS, DHDPR, DAPE and DAPDC.

Dogovski C, Atkinson S, Dommaraju S, Downton M, Hor L, Moore S, Paxman J, Peverelli M, Qiu T, Reumann M, Siddiqui T, Taylor N, Wagner J, Wubben J, **Perugini M** (2012) Enzymology of bacterial lysine biosynthesis, *Biochemistry*, 225 – 262.

PROFILE

Hamsa Puthalakath

ARC Future Fellow and Associate Professor
Regulation of apoptosis in health and disease

We study apoptosis regulation by Bcl-2 family protein (specifically Bim) in a variety of physiological contexts using in *vitro* techniques and using *in vivo* mouse models.

Research focus

- regulation of cardiomyopathy and heart failure
- regulation of apoptosis in the adaptive immune system including thymic and peripheral T cells, B cells and immune modulation during chronic stress and obesity
- regulation of apoptosis in tumorigenesis.

Achievements

Cre transgene results in global attenuation of the cAMP/PKA pathway

Use of the *cre* transgene in *in vivo* mouse models to delete a specific "floxed" allele is a well-accepted method for studying the effects of spatially or temporarily regulated genes. We discovered that *cre* expression either in cultured cell lines or in transgenic mice, results in global changes in protein kinase A (PKA) target phosphorylation which alters the gene expression profile and changes in cytokine secretion such as IL-6. These effects are dependent on its recombinase activity and can be attributed to the upregulation of specific inhibitors of PKA (PKI). These results may explain the cytotoxicity often associated with *cre* expression in many transgenic animals and explain many of the phenotypes observed in the context of Cre-mediated gene deletion.

Gangoda L, **Doerflinger M**, **Lee Y**, **Rahimi A**, Etemadi N, Chau D, **Milla L**, **O'Connor L**, **Puthalakath H** (2012) Cre transgene results in global attenuation of the cAMP/PKA pathway, *Cell Death and Disease*, 3: e365, doi: 10.1038/cddis.2012.110.

PROFILE

Mike Ryan

Professor and Head of Department
Mitochondrial biogenesis and disease

We research the nature of the mitochondrial network within the cell and the dynamics of protein complexes within the mitochondrial inner and outer membranes. Research is supported by the NHMRC, ARC and ARC Centre of Excellence for Coherent X-ray Science.

Research focus

- mitochondrial dynamics in health and disease
- assembly of mitochondrial complex I and defects in disease
- regulation of pro-apoptotic factors on the mitochondrial outer membrane.

Achievements

Importance of disulfides in small TIM chaperones

The small TIM family of chaperones sort hydrophobic precursors proteins in the intermembrane space.

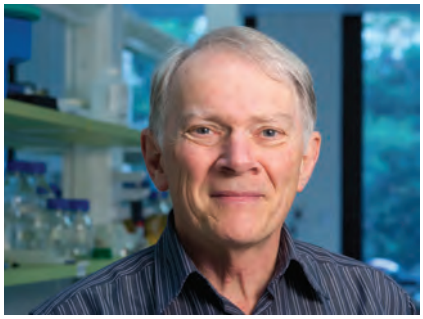
In our previous structural analysis (Webb et al., Mol Cell 2006; Baker et al., MBC 2009), we found that every small TIM contains two disulfide bonds. The most N-terminal cysteine residue of this motif has also been shown to be involved in protein biogenesis. Recently we found that no individual cysteine residue is required for the function of Tim9 or Tim10 but some defective assembly induces proteolytic clearance from mitochondria through a specific degradation machinery. We delineated a clearance mechanism for the mutant proteins and their unassembled wild-type partner protein within mitochondria.

Baker M, Mooga V, Guiard B, Langer T, **Ryan M**, **Stojanovski D** (2012) Impaired folding of the mitochondrial small TIM chaperones induces clearance by the i-AAA protease, *Journal of Molecular Biology*, 424: 227 – 239.

Understanding mitochondrial disease

With collaborators, we have investigated defects in cells from patients diagnosed with mitochondrial disorders. We have also used other models to determine the importance of specific genes in mitochondrial function. Recently we have successfully utilised TAL-effector nucleases (TALENs) to undertake gene knockouts in cultured human cells and showed the detrimental consequences to cell function. Our work provides new insights into the function of proteins that are involved in lethal mitochondrial disorders.

Ke B, Pepe S, Grubb D, Komen J, Laskowski A, Rodda F, Hardman B, Pitt J, **Ryan M**, **Lazarou M**, Koleff J, Cheung M, Smolich J, Thorburn D (2012) Tissue-specific splicing of an Ndufs6 gene-trap insertion generates a mitochondrial complex I deficiency-specific cardiomyopathy, *Proceedings of the National Academy of Sciences*, 109: 6165 – 6170.



PROFILE

Richard Simpson

Professor
Colorectal cancer – molecular basis to targeted therapeutics

We investigate new ways to detect colorectal cancer (CRC) by identifying cancer protein/RNA signatures and developing nanoparticle delivery systems (exosomes) for their *in vivo* and clinical application.

Research focus

- exosomes in colon cell maturation (crypt biology), cancer metastasis and drug delivery
- exosome membrane topography, target recognition and signalling complexes
- extracellular modulators of epithelial-mesenchymal transition (EMT) process.

Achievements

EMT

EMT, a process essential for morphogenesis during embryonic development, has been implicated in tumour metastasis. Using oncogenic H-Ras/TGF-β-mediated EMT in the MDCK model system, we have identified extracellular modulators of the EMT process, and shown that MDCK cells switch from cadherin-mediated to integrin-mediated adhesion following Ras/TGF-β-induced EMT. We are now characterising the functional role of exosomes in EMT and pursuing a number of identified extracellular effectors as potential markers of CRC metastasis.

Exosome characterisation

Exosomes, a distinct class of membranous nanovesicles (40–100 nm diameter) secreted from most cell types, play a critical role in cell-cell communication. We developed an immunocapture method for isolating exosomes from the CRC cell line LIM1215 which led to the definition, for the first time, of a CRC-specific exosomal signature. We have extended these studies to the LIM1863 cell line and discovered two discreet populations of exosomes (apical and basolateral) that differ at the level of protein, RNS (miRs and mRNA) and lipid content. Future studies will elucidate the functional role of exosomes in colonic crypt morphogenesis, dissecting their membrane topography to identify and characterise membrane complexes associated with cell-target recognition and exocrine/juxtacrine cell signalling.

Tauro B, **Greening D**, **Mathias R**, **Ji H**, **Mathivanan S**, Scott A, **Simpson R** (2012) Comparison of ultracentrifugation, density gradient separation, and immunoaffinity capture methods for isolating human colon cancer cell line LIM1863-derived exosomes, *Methods*, 56: 293–304.

PROFILE

Diana Stojanovski

ARC Post-doctoral Fellow
Protein trafficking

We research the mechanisms that govern trafficking of mitochondrial precursors to and within mitochondria and the role of cytosolic factors in this process.

Research focus

- precursor trafficking through the cytosol
- understanding mitochondrial transport machineries
- mitochondrial import and assembly in mammalian cells and links to disease.

Achievements

Understanding mitochondrial trafficking machineries

It has been estimated that as much as 20% of the entire cellular proteome is associated with functional mitochondria, thus homeostatic maintenance of this protein complement is essential for cellular function. The intermembrane space (IMS) accommodates many proteinaceous factors that play critical roles in mitochondrial and cellular metabolism, including the transfer of small metabolites, iron-sulfur clusters and the regulation of apoptosis and energy conversion. The machinery exploited for the import of IMS proteins, known as the MIA machinery, exploits the power of protein oxidation as a means to trap proteins within the IMS. The process of protein translocation into the mitochondrial IMS is tightly coupled to the process of protein oxidation. The mechanisms that come into play when there are glitches in the import and oxidation of IMS proteins have remained a mystery. We recently discovered a cellular rescue system that operates in the removal of improperly oxidised and misfolded IMS proteins in an effort to maintain protein homeostasis within this compartment.

Baker M, **Mooga V**, Guiard B, Langer T, **Ryan M**, **Stojanovski D** (2012) Impaired folding of the mitochondrial small TIM chaperones induces clearance by the i-AAA protease, *Journal of Molecular Biology*, 424: 227 – 239.

Stojanovski D, Bohnert M, Pfanner N, Van Der Laan M (2012) Mechanisms of protein sorting in mitochondria, *Cold Spring Harbor Perspectives in Biology*, 4: a011320, doi:10.1101/cshperspect.a011320.

PROFILE

Kaye Truscott

ARC Future Fellow
Mitochondrial protein homeostasis

We study mitochondrial protein biogenesis and the protective mechanisms that maintain protein integrity in this organelle. Research is supported by the ARC.

Research focus

- regulated degradation of mitochondrial proteins in health and disease
- signalling components of the mitochondrial unfolded protein response
- mitochondrial protein import, processing and assembly.

Achievements

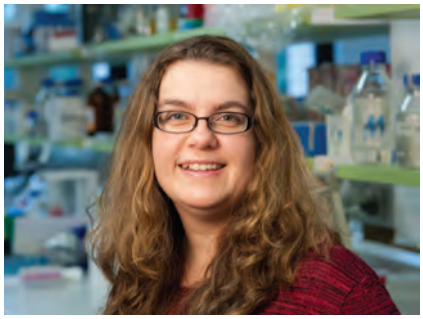
Elucidation of distinct protein assemblies contributing to mitochondrial protein folding and degradation

We examine the molecular pathways that contribute to the biogenesis and maintenance of a functional population of proteins in mitochondria. This includes the mechanism of action of the import machinery, molecular chaperones, oxidoreductases and proteases. Our research investigated the structural elements required for CLPX-mediated protein degradation by the mitochondrial CLPXP protease. This mitochondrial protease is activated to destroy proteins, in an uncontrolled manner, by antibiotic acyldepsipeptides. Another study confirmed that the yeast mitochondrial intermembrane space oxidative protein folding pathway progresses via a ternary complex between the substrate and Mia40 and Erv1. This indicates a direct functional cooperation of the two oxidoreductases and the target protein and extends our understanding of this recently discovered mitochondrial protein folding pathway.

Lowth B, Kirstein-Miles J, **Saiyed T**, Brotz-Oesterhelt H, Morimoto R, **Truscott K**, **Dougan D** (2012) Substrate recognition and processing by a Walker B mutant of the human mitochondrial AAA+ protein CLPX, *Journal of Structural Biology*, 179: 193 – 201.

Bottinger L, Gornicka A, Czerwik T, Bragoszewski P, Loniewska-lwowska A, Schulze-Specking A, **Truscott K**, Guiard B, Milenkovic D, Chacinska A (2012) In vivo evidence for cooperation of Mia40 and Erv1 in the oxidation of mitochondrial proteins, *Molecular Biology of the Cell*, 23: 3957 – 3969.

Chemistry



PROFILE

Belinda Abbott

Lecturer
Design and synthesis of medicinal compounds

We examine novel molecules needed to understand, prevent and treat conditions such as motor neurone disease, cancer and malaria.

Research focus

- design and synthesis of small molecule enzyme inhibitors
- development of synthetic oligonucleotides for antisense therapy
- synthesis of natural products of medicinal interest.

Achievements

Synthesis of phosphatidylinositol-3-kinase (PI3K) inhibitors

PI3K isoforms are involved in numerous cell signalling pathways associated with a range of diseases including cancer. We have developed a new tetrazole-based compound which has excellent potency against PI3K when delivered as a prodrug against the MCF7 cancer cell line.

Inhibitors of phosphoinositide-dependent kinase 1 (PDK1)

Using molecular modeling, we identified a series of potential PDK1 inhibitors and have synthesized three distinct classes of compounds. PDK1 is a master regulator of the AGC kinases which regulate cell metabolism, growth, proliferation and survival. With over 50% of human cancers possessing over-stimulation of the PDK1 pathway, inhibition of this enzyme is a promising anti-cancer target. The synthesised compounds are currently undergoing biological evaluation.

Antisense therapy using peptide nucleic acid

Peptide nucleic acid (PNA) is synthetic analogue of the biopolymers deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) which carry and encode genetic information. Our research focuses on improving the cellular uptake of PNA sequences which have shown efficacy in a transgenic mouse model for amyotrophic lateral sclerosis, a form of motor neurone disease. We have developed a convenient and efficient method for the synthesis of Fmoc/Boc protected PNA monomers.

Browne E, Langford S, **Abbott B** (2012) Peptide nucleic acid monomers: a convenient and efficient synthetic approach to Fmoc/Boc monomers, *Australian Journal of Chemistry*, 65: 539 – 544.

PROFILE

Peter Barnard

Lecturer
Synthesis and development of novel optical (fluorescent) and radiopharmaceutical agents for biological imaging applications

We research metal coordination complexes of N-heterocyclic carbenes and macrobicyclic ligands for use as diagnostic imaging agents (radiopharmaceuticals) and fluorescent probes for imaging and sensor applications.

Research focus

- synthesis of novel chelating ligands, including N-heterocyclic carbenes (NHCs) and macrocyclic/macrobicyclic ligands
- ligand radio-labelling studies with metallic radioisotopes (99mTc, 64Cu, 68Ga and 89Zr)
- conjugation of novel luminescent/radio-labelled coordination compounds to biomolecules (lipids and peptides).

Achievements

N-heterocyclic carbene ligands

N-heterocyclic carbenes (NHCs) are among the most important and widely studied ligand types in contemporary organometallic chemistry.

We discovered a series of Au-NHC complexes that have anti-tumour properties and are active via an anti-mitochondrial mechanism. We studied the potential medicinal applications of these ligands and developed a rapid method for labelling chelating NHCs with the radioisotope ^{99m}Tc for radiopharmaceutical imaging applications. We have also prepared a range of novel luminescent Au, Ru and Ir coordination complexes of chelating NHC ligands. These compounds show a range of emission wavelengths and we are investigating potential of these molecules in electro-chemiluminescent sensor applications.

Wedlock L, Aitken J, Berners-Price S, **Barnard PJ** (2012) Bromide ion binding by a dinuclear gold(I) N-heterocyclic carbene complex: a spectrofluorescence and X-ray absorption spectroscopic study, *Dalton Transactions*, doi: 10.1039/c2dt31817b.

Synthesis of novel macrocyclic and macrobicyclic ligands

Metal-tagged radiopharmaceuticals usually consist of a bioactive molecule, such as a peptide or monoclonal antibody (mAb), labelled with a metallic-radioisotope. For such imaging agents to function successfully the metal chelate complex must be inert to ligand exchange reactions. We have developed a series of novel macrocyclic and macrobicyclic (sarcophagine) ligands that form highly stabilised complexes with the positron emitting isotope of copper, ^{64}Cu. Ligand challenge experiments (histidine and cysteine) for one macrobicyclic ligand labelled with ^{64}Cu demonstrate that transmetallation does not occur with these common metal binding amino acids. These radiopharmaceutical projects are collaborative with researchers from the Australian Nuclear Science and Technology Organisation (ANSTO) and are supported by funding from the Australian Institute of Nuclear Science and Engineering (AINSE).

PROFILE

Jason Dutton

Lecturer

Synthesis of highly reactive, cationic compounds and functional organometallic polymers

We investigate new structure, bonding and reactivity for main group and transition metal elements. We examine the synthesis of highly charged, high-oxidation state species and organometallic polymers.

Research focus

- synthesis of ligand stabilized dicarbon as a building block for supramolecular organometallic frameworks
- development of iodine polycations as oxidizing agents for the synthesis of high-oxidation state, catalytically relevant transition metal complexes.

Achievements

Ligand stabilized diatomics

In conjunction with Dr David Wilson, our group has predicted that ligand stabilized dicarbon has properties rendering it a desirable synthetic target. A concise synthesis of an N-heterocyclic carbene (NHC) complex of dicarbon has now successfully been carried out.

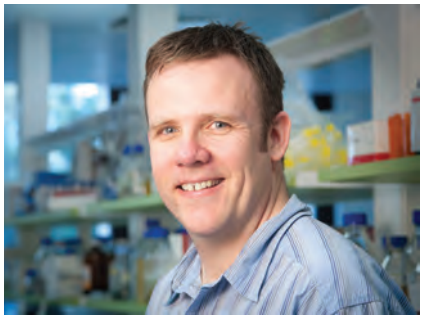
We are currently pursuing X-ray structural confirmation of the complex and preliminary survey of its ability to bind transition metals, with an eventual goal of generating organometallic polymers. A related theoretical study of ligand stabilized p-block diatomics has revealed that the bonding of phosphine and NHC ligands to p-block centres is different to the interaction between the respective ligands and transition metals. In transition metal chemistry phosphines are considered superior pi-acids, but our work has shown that in p-block chemistry NHCs are stronger pi-acids than phosphines.

Dutton J, **Wilson D** (2012) Lewis base stabilized dicarbon: Predictions from theory, *Angewandte Chemie (International Edition)*, 51: 1477 – 1480.

Wilson D, **Couchman S**, **Dutton J** (2012) Are N-heterocyclic carbenes "better" ligands than phosphines in main group chemistry? A theoretical case study of ligand-stabilized E 2 molecules, L-E-E-L (L = NHC, phosphine, E = C, Si, Ge, Sn, Pb, N, P, As, Sb, Bi), *Inorganic Chemistry*, 51: 7657 – 7668.

Synthesis of iodine polycations

Iodine dications based on a $[PhI(L)_2]^{2+}$ (L = neutral ligand) framework have been successfully synthesized and X-ray crystal structures have been obtained, representing the first crystallographically characterized iodine polycations. We will now use these compounds to oxidize transition metals (e.g. Pd, Au) and generate catalytically relevant high-oxidation state complexes.



PROFILE

Conor Hogan

Senior Lecturer
New sensing strategies based on electro-active and luminescent materials

We use electro active and luminescent materials to develop low detection limits, enhanced selectivity and miniaturized instruments which can be used outside of the laboratory setting. Research is supported by the ARC.

Research focus

- low cost diagnostics for the developing world
- electro-chemiluminescence: new optically and electrochemically active materials for sensing applications
- electrochemical control of emission wavelength for multiplexed detection.

Achievements

A new approach to sensing

Ultra-low cost paper microfluidic sensors produced by ink jet printing were used for electro-chemiluminescence based detection for the first time. We demonstrated that the electrochemically initiated emission could be captured using a mobile phone camera and used as the basis for quantitation.

Tuning luminescent emission color via electrode potential

We discovered that selective electro-chemiluminescence (ECL) of several ruthenium and iridium complexes in solution could be controlled simultaneously by electrode potential. These luminescent redox systems create a range of new possibilities for multianalyte ECL detection, assessment of interdependent electrochemical / spectroscopic properties, and colour tuning in light-emitting devices.

Doeven E, Zammit E, Barbante G, **Hogan C**, Barnett N, Francis P (2012) Selective excitation of concomitant electrochemiluminophores: tuning emission color by electrode potential, *Angewandte Chemie (International Edition)*, 51: 4354 – 4357.

Doeven E, Zammit E, Barbante G, Barnett N, Francis P, **Hogan C** (2012) A potential-controlled switch on / off mechanism for selective excitation in mixed electrochemiluminescent systems, *Chemical Science*, doi:10.1039 / C2SC21707D.

PROFILE

Adam Mechler

Senior Lecturer
Chemistry of self-assembly: from molecules to macrostructures

We investigate the physicochemical properties of surfaces, interfaces and self-assembled macrostructures including lipid membranes and protein fibres. We also study the design of three-dimensional surface nanostructures.

Research focus

- the molecular mechanism and environmental controls of phospholipid self-assembly into liposomes and supported biomimetic membranes
- the action mechanism of membrane-disrupting antimicrobial peptides
- design and characterization of functional nanomaterials.

Achievements

Development of inverted cubic phase lipid biosensors

With collaborators from the University of Melbourne, CSIRO and Monash University we completed a feasibility study using functionalized lipid nanostructures.

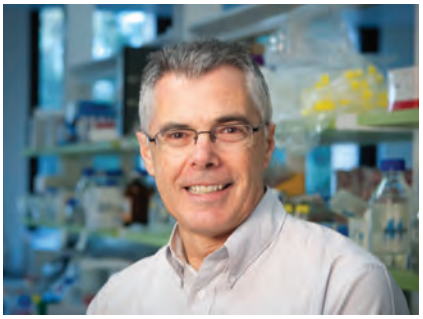
Cubosomes have a greatly enhanced active surface area compared to flat supported membranes due to the porous inverted bicontinuous cubic structure. This feature was used to enhance the sensitivity of detection per surface area when immobilizing the cubosomes on a quartz crystal microbalance sensor chip and measuring the mass change upon the binding of the analyte.

Fraser S, Mulet X, Martin L, Praporski S, **Mechler A**, Hartley P, Polyzos A, Separovic F (2012) Surface immobilization of bio-functionalized cubosomes: sensing of proteins by quartz crystal microbalance, *Langmuir*, 28: 620 – 626.

Spectroscopic imaging on the nanometer scale

The origin of the enhancement of Raman scattering in Tip Enhanced Raman Spectroscopy (TERS) was investigated experimentally by varying the probe design. With collaborators at Monash University and the University of Edinburgh, Scotland, we established that the material of the tip is not a crucial factor in achieving TERS. Indeed, TERS signals might be generated by using a tip and a surface that are not plasmonic materials. This is a potentially paradigm shifting result in the field of sub-wavelength spectroscopic imaging.

Asghari-Khiavi M, Wood B, Hojati-Talemi P, Downes A, McNaughton D, **Mechler I** (2012) Exploring the origin of tip-enhanced Raman scattering, preparation of efficient TERS probes with high yield, *Journal of Raman Spectroscopy*, 43: 173 – 180.



PROFILE

Ian Potter

Senior Lecturer and Head of Department
Biochemical responses: stimulus and detection

We develop methods to induce and quantify favourable biochemical responses in plants. We also develop extraction and sensing platforms incorporating molecular recognition sites for Endocrine Disruptor Chemicals (EDCs) and Pharmaceutical Personal Care Products (PPCPs) for environmental and biological applications.

Research focus

- "artificial leaf" incorporating activation sites for carbon dioxide
- clean coal technology
- metabolomics of naturally occurring biomarkers.

Achievements

Gasification of brown coal using clean coal technology

In collaboration with Clean Coal Technology Pty Ltd, we investigate chemical means to increase the thermal efficiency and reduce pollutants, including flue gases and particulates during the combustion of brown coal for power production.

Domazetis G, **James B**, Liesegang J, **Raoarun M**, Kuiper M, **Potter I**, **Oehme D** (2012) Experimental studies and molecular modelling of catalytic steam gasification of brown coal containing iron species, *Fuel*, 93: 404 – 414.

Biochemical responses in plants

In collaboration with the Department of Primary Industries (DPI) Victoria, we are developing methods to identify and detect chemical biomarkers to indicate early levels of stress in vines. We have successfully identified chemical biomarkers resulting from grape phylloxera infestation. This work is supported by grants from the Grape and Wine Research and Development Corporation. In another project with DPI staff, we are investigating indole glucosinolates that are induced in Brassica plants upon infection by plant bacterial pathogens. This work will identify bioactive compounds to be used in screening and breeding programs aimed at producing Brassica varieties with high human bioefficacy and plant disease resistance.

Benheim D, **Rochfort S**, **Robertson E**, **Potter I**, Powell K (2012) Grape phylloxera (*Daktulosphaira vitifoliae*): a review of potential detection and alternative management options, *Annals of Applied Biology*, 161: 91 – 115.

PROFILE

Anne Richards

ARC Future Fellow, Senior Lecturer
The design and synthesis of molecular cages, clusters and polymers as functional materials

Using a variety of synthetic strategies, organic, inorganic and organometallic, we prepare novel chelating ligands that are used as support molecules for the synthesis of molecular cages, clusters and polymers. These structural properties of these complexes are probed by X-ray crystallography and other pertinent techniques.

Research focus

- development of a novel ligand library of functionalized phosphonic acids
- synthesis of metal clusters
- design and synthesis of bifunctional materials.

Achievements

Molecular cages and coordination polymers

We discovered the first example of a crystallographically characterized indium(III) coordination polymer and an unusual example of a cationic aluminum cage. Both these materials have potential catalytic applications and studies in this area are currently underway.

Beavers C, **Richards A** (2012) Synthesis and structures of a pentanuclear Al(III) phosphonate cage, an In(III) phosphonate polymer, and coordination compounds of the corresponding phosphonate ester with GaI_3 and $InCl_3$, *Dalton Transactions*, 41:11305 – 09.

Synthesis of metal clusters

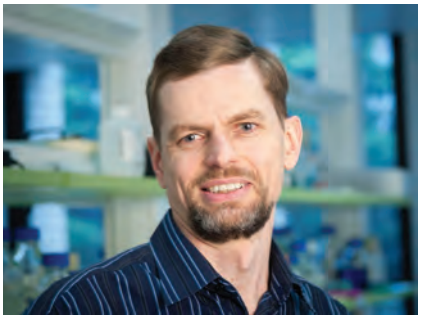
The synthesis of main group cages and clusters is an emerging research field. These novel materials, with their unique architectures are highly active reactants for gas sorption and can be used as model compounds for the interface between molecular and solid state chemistry to establish structure-property relationships and as molecular building blocks.

Aprile A, **Wilson D**, **Richards A** (2012) The synthesis and characterization of mono and dinuclear group 13 complexes derived from a Schiff base, *Dalton Transactions*, 41: 8550 – 8555.

Design and synthesis of bifunctional materials

Bifunctional materials are materials that combine two or more physical or chemical properties, for example, redox activity along with gas sorption. Using a high yielding synthetic strategy using a metallo-ligand we have been able to isolate a series of heterometallic cages. These cages show redox activity and in some cases good luminescent properties.

Richards A, **Aprile A**, **Hogan C** (2012) A 1D Schiff base zinc polymer as a versatile metallo-ligand for the synthesis of polynuclear zinc cages, *Dalton Transactions*, 41: 8361 – 8367.



PROFILE

Evan Robertson

Senior Lecturer
Optical spectroscopy for understanding atmospheric, interstellar and biomolecular chemistry

We use the power of optical spectroscopy to explore the properties of molecules relevant to pharmaceutics, the atmosphere, and even interstellar chemistry. Research is supported by the ARC, the Australian Synchrotron and National Computing Infrastructure.

Research focus

- laser spectroscopy and conformational shape of biomolecules
- characterisation of atmospheric aerosols
- synchrotron IR spectroscopy of atmospheric and interstellar molecules and aerosol clusters.

Achievements

Far infrared frontiers of water ice nanoparticles

Molecular ice particles play an important role in interstellar and atmospheric chemical processing where they can act as a reaction medium.

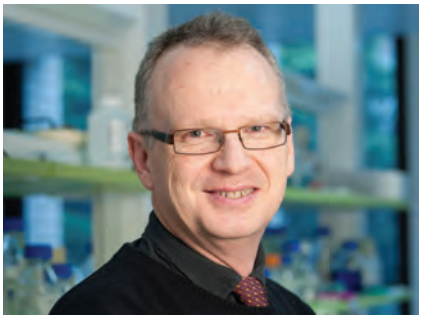
Interactions with infrared radiation are significant firstly in radiative energy transfer (with its implication for our climate), and secondly because infrared spectroscopy is uniquely suited to remotely probing the properties of these ices, including their temperature and particle characteristics. We have generated water ice aerosol particles in the nanoscale size regime (1.5 – 100 nm) by rapid collisional cooling and measured their spectra in the far-IR region for the first time, using synchrotron radiation. These spectra provide a means to assess optical constants required for radiative forcing calculations in many contexts.

Medcraft C, Thompson C, **Robertson E**, Appadoo D, McNaughton D (2012) The far-infrared rotational spectrum of ethylene oxide, *The Astrophysical Journal*, 753: 18, doi:10.1088/0004 – 637X/753/1/18.

Shedding light on the shape of neurotransmitters

Gas phase, laser-based techniques have been used to measure conformer selective infrared spectra of neurotransmitter molecules with an amine group attached to flexible side chain. Folded conformers that allow an intramolecular NH...π type hydrogen bond are favoured when the ethylamine side chain is free to rotate, as in p-aminophenethylamine. With the more constrained cyclopropyl group of tranylcypromine (known as antidepressant 'parnate'), the amine group is kept away from the ring and the molecule is found to maintain a flatter profile.

Lobo I, **Wilson D**, Bieske E, **Robertson E** (2012) A sting in the tail of flexible molecules: Spectroscopic and energetic challenges in the case of p-aminophenethylamine, *Physical Chemistry Chemical Physics*, 14: 9219 – 9229.



PROFILE

Brian Smith

LIMS Principal Research Fellow and Associate Professor
Molecular modeling of biochemical systems

We use computational methods to study biochemical processes, the structures of proteins, and the interactions of proteins with other molecules. Techniques include quantum mechanics, molecular dynamics, comparative modeling, protein X-ray crystallography and cheminformatics.

Research focus

- drug discovery and development
- structural studies of small molecule modulators of apoptosis
- structure and function of proteins from malaria.

Achievements

Sodium channel b1 subunits bind potassium channels in a site-specific manner

Sodium channel b1 subunits are able to modulate the activity of a diverse set of potassium channels.

We show that the interaction of b1 with the voltage sensing domain of the potassium channels results in changes in the activation kinetics and voltage-dependence of activation, whereas interaction with the channel's pore domain results in changes to inactivation and deactivation. A molecular model shows b1 lying in a crevice between the voltage-sensing and pore domains.

Nguyen H, Miyazaki H, Hoshi N, **Smith B**, Nukina N, Goldin A, Chandy K (2012) Modulation of voltage-gated K^+ channels by the sodium channel β1 subunit, *Proceedings of the National Academy of Sciences*, 109: 18577 – 18582.

Structure of the merozoite surface protein MSPDBL2 from Plasmodium falciparum

Invasion of red blood cells by the malaria parasite *Plasmodium falciparum* proceeds by the binding of specific parasite ligands to host cell receptors. We have solved the X-ray crystal structure of DBL2, a merozoite Duffy-like binding domain receptor, and show that a cleft on the surface of the protein, which is spared by polymorphic variation, is the likely binding site of the partner ligand on the red blood cell.

Hodder A, Czabotar P, Uboldi A, Clarke O, Lin C, Healer J, **Smith B**, Cowman A (2012) Insights into duffy binding-like domains through the crystal structure and function of the merozoite surface protein MSPDBL2 from *Plasmodium falciparum*, *Journal of Biological Chemistry*, 287:32922 – 32939.

PROFILE

Michelle Spencer

Lecturer
Materials and nanomaterials for electronic devices, sensors and batteries

We study a variety of materials and nanomaterials (including metals, oxides and semiconductors) which have applications in electronic devices, sensors and batteries. We seek to understand the structure, properties and dynamical processes of these materials using a computational approach.

Research focus

- novel metal oxide nanostructures for gas sensing
- nanoscale silicon for advanced electronic devices and batteries
- *ab initio* simulations of zinc oxide nanostructures.

Achievements

Novel silicon nanosheets

Silicon is one of the most important elements in our current society, forming the basis of most semiconducting electronic devices. In collaboration with researchers at the AIST Japan, Toyota Central R&D Labs Japan, RMIT University and CSIRO, we investigate ultrathin silicon-nanosheets whose unique properties show promise for electronic devices and battery applications. We discovered that the structure of these nanosheets and their ability to conduct electricity are dependent on their thickness. Such findings highlight the novelty of these materials and their significance for applications in electronic devices.

Spencer M, Morishita T, Snook I (2012) Reconstruction and electronic properties of silicon nanosheets as a function of thickness, *Nanoscale*, 4: 2906 – 2913.

Metal oxides for gas sensing

Air pollution can cause major environmental and health problems. Development of sensors to detect pollutant gases is therefore a highly critical area of research. With collaborators at RMIT University and Kyushu University Japan, we have determined the sensing mechanism of a variety of molecules with oxide based nanosensors. We found that the surface morphology, including the presence of surface defects, has a significant effect on the gas-sensor surface reaction.

Spencer M (2012) Density functional theory modeling of ZnO for gas sensor applications, *Chemical Sensors: Simulation and Modeling: Volume 1: Microstructural Characterization and Modeling,* 163 – 216.

PROFILE

David Wilson

Senior Lecturer
Computational quantum chemistry

We study computational quantum chemistry. We use computer calculations to model molecular structures and properties as well as energetics and mechanisms of reactions, with a particular focus on the interaction of molecules with light and electric / magnetic fields.

Research focus

- understanding molecular properties as they relate to the electronic structure of molecule and atoms
- interaction of molecules with electric and magnetic fields
- application of computational quantum chemical methods to chemical problems.

Achievements

Designing new molecules

"Doing" chemistry in a computer has many practical advantages – many more "reactions" can be probed and no waste is generated. We have predicted the first ligand-stabilised C2 molecule, which has been the target of synthetic efforts for several decades without success. We have predicted other stable yet unknown L-EE-L molecules (L = ligand, E = Group 14 / 15 element), for which a number have subsequently been synthesised. Efforts are underway to make the C2 species. These molecules have potential catalytic applications.

Dutton J, **Wilson D** (2012) Lewis base stabilized dicarbon: Predictions from theory, *Angewandte Chemie (International Edition)*, 51: 1477 – 1480.

Biomolecular modelling

We study biomolecular modelling for the purpose of drug design. One example system is HIV-1 protease. We have recently investigated the accuracy of modelling methods in accurately treating binding in HIV protease. Our work provides insight into the efficiency of biomolecular modelling and its limitations, which will aid in the design of new drugs.

Oehme D, **Brownlee R**, **Wilson D** (2012) Effect of atomic charge, solvation, entropy, and ligand protonation state on MM-PB(GB) SA binding energies of HIV protease, *Journal of Computational Chemistry*, 33: 2566 – 2580.

Genetics

PROFILE

Warwick Grant

Associate Professor and Head of Department
Evolutionary genetics of nematode parasites

We research the evolution of drug resistance in nematode parasites with a view to mining these data for novel, nematode specific, targets for drug or vaccine development.

Research focus

- drug resistance genetics in *Onchocerca volvulus* and *Teladorsagia circumcincta*
- application of large-scale next generation sequencing methods to parasite population and evolutionary genetics
- development of a model system in which to investigate the genetic basis of parasitism in nematodes.

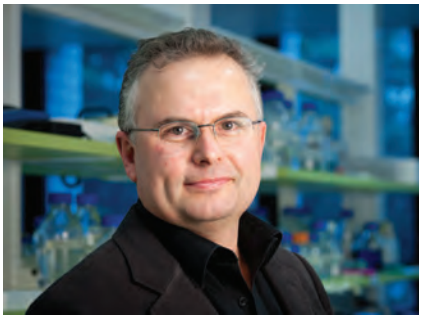
Achievements

Helminth parasite research

Helminth (nematode and flatworm) parasites are major contributors to diseases of poverty, as well as major agricultural pests, yet little is known of their basic biology and few compounds are available for their control. Work in the Grant lab is directed at understanding the evolution of drug resistance in nematode parasites, and includes analyses of the genetic structure of parasite populations and searches for regions of the genome that are under recent selection. Research involves the use of next generation sequencing technologies in addition to more conventional genotyping approaches.

Drug resistance and tropical disease

In collaboration with colleagues at McGill University in Canada, I have played a role in the establishment of a research consortium that is supported by the World Health Organisation special program on Tropical Disease Research (WHO/TDR) and the African Program for Onchocerciasis Control (APOC), and involves collaborations with research labs and ministries of health in Burkina Faso, Ghana and Cameroon. The project seeks to define genetic markers for surveillance of drug resistance selection in the causative organism of River Blindness, with a capacity building component that will see graduate students from endemic countries undertake research degrees in the Genetics Department.



PROFILE

Adam Hart

Lecturer
Molecular regulation of stem cells and cancer

We study the transcription factors that control pluripotency and lineage commitment in embryonic, germline, haematopoietic and cancer stem cells. Research is supported by the NHMRC, Australian Stem Cell Centre, Victorian Life Science Computation Initiative and the National Collaborative Research Infrastructure Strategy.

Research focus

- pluripotent stem cells from the testis
- marsupial stem cells
- molecular regulation of blood development and leukaemia.

Achievements

Marsupial stem cell growth factor identified

The Tasmanian Devil *Sarcophilus harrisii* is a highly endangered Australian dasyurid marsupial. We have utilized the recently completed Tasmanian Devil genome sequence to generate and test the bioactivity of recombinant Tasmanian devil growth factors capable of sustaining pluripotent stem cells in cell culture. We seek to produce pluripotent stem cells from the Tasmanian devil, both for species preservation and with the goal of engineering resistance to the devil facial tumor disease. This work resulted in a provisional patent application to the United States Patent and Trademark Office "Stem cell growth factor and its use in a stem cell bioassay."

Hart A (2012) Patent: Stem cell growth factor and its use in a stem cell bioassay.

The genetic basis of congenital birth defects

In collaboration with researchers at Monash University, Prince Henrys Medical Research Institute, Murdoch Childrens Research Institute and the Australian Phenomics facility, we developed a new high throughput genome sequencing approach to rapidly identify novel developmental disease genes in the mouse. We carried out a large-scale screen, discovering novel genetic lesions causing developmental defects in erythropoiesis and organogenesis of the kidney, lung, skeleton, gut and skin.

PROFILE

John Mitchell

Associate Professor
Human evolutionary genetics and forensic science

Our research explores human origins and migrations over the last 100,000 years focusing on southeast Asia and Australasia. To do this, we use DNA sequence variation to generate maternal and paternal lineages.

Research Focus

- mitochondrial and Y chromosome phylogenies and the genetic geography of Oceanic populations, especially Maori and Australian Aboriginal people
- forensic implications of trace DNA.

Achievements

Forensic aspects of DNA

The issue of transfer DNA is increasingly being raised in court cases with the advancement of DNA analytical techniques. Minute quantities of DNA (trace DNA) can easily be dislodged from a crime exhibit and be deposited on different item(s) in packaging or elsewhere on the exhibit. This area was underappreciated in forensic science, but since our paper more attention is being paid to issues of trace DNA by forensic labs.

Goray M, Van Oorschot R, **Mitchell R** (2012) DNA transfer within forensic exhibit packaging: potential for DNA loss and relocation, *Forensic Science International: Genetics*, 6: 158 – 166.

Human settlement of Oceania

The human settlement of Australia is both poorly understood and controversial. One reason for this is that we often lack appropriate DNA markers for the populations in this region as well as samples. We investigated a large forensic database of Aboriginal people's Y chromosome markers to determine the extent of admixture in the male lineage. The extent of admixture was high but variable across the regions of South Australia.

Taylor D, Nagle N, Ballantyne K, Van Oorschot R, Wilcox S, Henry J, Turakulov R, **Mitchell R** (2012) An investigation of admixture in an Australian Aboriginal Y-chromosome STR database, *Forensic Science International: Genetics*, 6: 532 – 538.

PROFILE

Nick Murphy

Lecturer
Molecular ecology

We use molecular methods to address issues in ecology, conservation biology and evolution, in particular, the impact of fragmented and isolated terrestrial and freshwater habitats on poorly dispersing fauna.

Research focus

- the evolution of desert spring invertebrates
- the impact of fire on terrestrial arthropods
- range limits in freshwater species.

Achievements

Microendemics

The desert springs surrounding Lake Eyre in central Australia are home to a unique suite of animals. Our research shows that species inhabiting this environment demonstrate incredibly small geographic ranges. We identified at least 13 new crustacean species, many of which exist in a small number of already degraded springs, with the rarest existing in single springs. The limited distributions of these taxa ensure they will be highly vulnerable to future habitat degradation and water extraction.

Ancient endemics

Genetic studies of three different groups of amphipods, isopods and snails in the desert springs surrounding Lake Eyre all show remarkably similar evolutionary histories. Most of the diversity within these groups has its origins prior to the formation of both deserts and the spring systems, suggesting that the fauna have no close relatives outside of the springs. The desert spring ecosystem represents a now otherwise extinct ecosystem; remnants of a time when inland Australia was much wetter.

Guzik M, Adams M, **Murphy N**, Cooper S, Austin AD (2012) Desert springs: deep phylogeographic structure in an ancient endemic crustacean (Phreatomerus latipes), *PLoS ONE*, 7: e37642, doi:10.1371/journal.pone.0037642.

PROFILE

Greg Somers

Lecturer
Molecular regulation of stem cell development

Our research seeks to identify and understand the molecular mechanisms regulating stem cell characteristics, including self-renewal and differentiation.

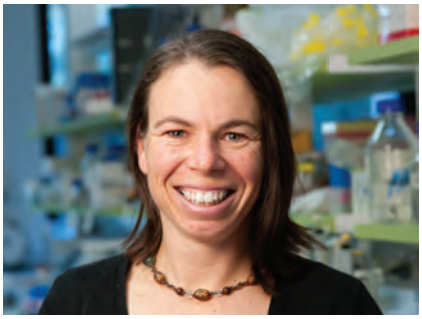
Research focus

- genetic screens involving *in vivo* stem cell populations
- understanding the molecular machinery involved in niche-stem cell interactions
- identifying novel tumour-suppressor factors, responsible for generating cancer stem cells.

Achievements

Identifying novel regulators of Drosophila germline stem cell development

We have developed an *in vivo* screening strategy, using the male germline of *Drosophila melanogaster,* to identify novel conserved factors important for stem cell self-renewal and differentiation. We identified alleles that behave as putative tumor-suppressors, as well as alleles essential for stem cell maintenance. One of the factors identified is the *Drosophila* orthologue (Rbf) of the Retinoblastoma protein (pRb). Disruption of Rbf results in supernumerary stem cells at the expense of more differentiated cell-types, a phenotype similarly seen with mammalian pRb proteins. However, the biological mechanisms of mammalian pRb proteins remain poorly understood. We have shown *Drosophila* Rbf functions non-cell-autonomously to regulate GSC differentiation. We have also shown *Drosophila* Rbf normally functions to restrict the self-renewing signals of the Bone Morphogenetic Pathway (BMP). Our work provides new insights into the mechanisms regulating stem cell development as well as shedding light on the evolution of multicellularity and tissue differentiation, one of the fundamental questions of animal biology.



PROFILE

Jan Strugnell

Senior Lecturer
Molecular biodiversity

We apply next generation sequencing tools to help solve bottlenecks in fisheries and aquaculture industries (e.g. lobster, abalone). We also investigate population and species level evolution in molluscs and Antarctic and deep-sea species in the context of past climatic change.

Research focus

- stress transcriptomics of commercially important abalone
- evolution in Antarctica and the deep sea
- cephalopod (octopus, squid) evolution.

Achievements

Genetic signatures of historic climatic events in an Antarctic octopus

Repeated cycles of glaciation have had major impacts on the distribution of genetic diversity of the Antarctic marine fauna. We used microsatellites and partial sequences of the mitochondrial CO1 gene to examine genetic structure in the direct-developing, endemic Southern Ocean octopod *Pareledone turqueti* sampled from a broad range of areas that circumvent Antarctica. We find that the overriding pattern of spatial genetic structure can be explained by hydrographic and bathymetric features. The Antarctic Peninsula region displays a complex population structure, consistent with its varied topographic and oceanographic influences. Genetic similarities between the Ross and Weddell Seas, however, are interpreted as a persistent historic genetic signature of connectivity during the hypothesized Pleistocene West Antarctic Ice Sheet collapses.

Strugnell J, Watts P, Smith P, Allcock A (2012) Persistent genetic signatures of historic climatic events in an Antarctic octopus, *Molecular Ecology*, 21: 2775 – 2787.

Southern ocean diversity

Southern ocean biodiversity reflects past climate, oceanographic, and tectonic changes. Molecular data from contemporary populations carry signatures of these processes. We review new molecular studies on southern ocean benthic fauna. Many of these studies focus on species with extensive geographic or bathymetric distributions, and resolve taxonomic questions. Reviewing all available data, we show that, in addition to reflecting life-history characteristics, the molecular signals found in these studies provide an insight into how species survived the last glacial maximum. We identify molecular signatures that are characteristic of surviving glacial cycles in small refuges on the continental shelf and distinguish them from molecular signatures that are indicative of surviving glacial cycles in the deep sea.

Allcock A, **Strugnell J** (2012) Southern ocean diversity: paradigms from molecular ecology, *Trends in Ecology & Evolution*, 27: 520 – 528.

Pharmacy

PROFILE

Mike Angove

Senior Lecturer and Head of Department
Colloid and environmental chemistry

We research surface phenomena responsible for the transport of toxic organic and inorganic chemical species through the environment. Various spectroscopic and modeling techniques are employed to elucidate chemical processes so that environmental transport can be predicted.

Research focus

- modeling and prediction of chemical transport in soil and sediment systems
- removal of toxic species from contaminated soils
- spectroscopic determination of chemical binding at surfaces.

Achievements

EPA Victoria HazWaste fund project

We completed a project funded by EPA Victoria to investigate possible strategies of removal of heavy metals from contaminated soils. This project found an efficient method of removing various heavy metal species form contaminated soil so that the soil could be categorized as 'for re-use.'

Sorption of uranium onto soil surfaces

The uptake of U(VI) onto a series of mixed oxide clays was investigated. The mixed oxide systems produced lower sorption than for systems containing individual clay. Competition between dissolved Fe(III) and U(VI) for sorption sites may also contribute to the observed decrease in U(VI) sorption. The study demonstrates the complexity of sorption in mixed systems, where the oxide phases do not necessarily behave in an additive manner, and has implications for U(VI) mobility in natural and impacted environments where Fe(III) (oxyhydr) oxides are usually assumed to increase the retention of U(VI). The bulk of this work was conducted at ANSTO who hosted an honours student who completed most of the experimental work.

Comarmond M, Payne T, Collins R, **Palmer G**, Lumpkin G, **Angove M** (2012) Inhibition of uranium(VI) sorption on titanium dioxide by surface iron(III) species in ferric oxide / titanium dioxide systems, *Environmental Science and Technology*, 46(20):11128 – 11134.

PROFILE

Daniel Tillett

Senior Lecturer
Bacteriophages for control of problematic environmental and clinical bacteria

We characterise novel bacteriophages for biocontrol of problematic bacteria in both the environment and clinic. Research is supported by grants from the ARC and industry.

Research focus

- isolation and characterisation of novel bacteriophages
- use of bacteriophages to control problematic bacteria in the wastewater industry
- use of bacteriophages to control medically important microbes on the skin.

Achievements

Identification of the smallest Siphoviridae *bacteriophage*

Bacteriophages are considered to be the most abundant biological entities on the planet. The *Siphoviridae* are the most commonly encountered tailed phages and contain double-stranded DNA with an average genome size of ~50 kb. We isolated the phage RRH1, which is polyvalent and which lyses five Rhodococcus species, from four different activated sludge plants. It has a capsid diameter of only 43 nm. Whole-genome sequencing of RRH1 revealed a novel circularly permuted DNA sequence (14,270 bp) carrying 20 putative open reading frames. RRH1 has the smallest genome yet of any described functional *Siphoviridae* phage. Lytic phage can be recovered from transforming naked DNA into its host bacterium, thus making it a potentially useful model for studying gene function in phages.

Petrovski S, **Dyson Z**, **Seviour R**, **Tillett D** (2012) Small but sufficient: the *Rhodococcus* Phage RRH1 has the smallest known *Siphoviridae* genome at 14.2 kilobases. *Journal of Virology*, 86: 358 – 363.

Prevention stabilized foam formation in activated sludge plants

Most activated sludge treatment plants suffer from the presence of foams on the surfaces of their aeration reactors. These are often stabilized by hydrophobic mycolic acid-synthesizing actinobacterial species. We have isolated and characterised a range of bacteriophages that in laboratory scale experiments, prevents stabilization of foams by the hydrophobic mycolic acid-synthesizing bacterial.

Petrovski S, **Tillett D**, **Seviour R** (2012) Genome sequences and characterization of the related *gordonia* phages GTE5 and GRU1 and their use as potential biocontrol agents, *Applied and Environmental Microbiology*, 78: 42 – 47.

Seminar program

MARCH

1 March

Dr Naomi Bishop
La Trobe University
Autism – all in the (gene) family

6 March

Dr John Tsanaktsidis
CSIRO Materials Science and Engineering
Chloroform as a hydrogen atom source in Barton Reductive Decarboxylations

7 March

Professor Michelle Barry
University of Alberta, Canada
Staying alive: poxvirus control of cell death

13 March

Professor Mark Rizzacasa
Bio21 Institute, University of Melbourne
Total synthesis: applications in structure, biosynthesis and biology

15 March

Professor Martin Pera
University of Melbourne
Defining pluripotency

21 March

Professor John Bateman
Murdoch Childrens Research Institute
Endoplasmic reticulum stress: a new player in the pathophysiology of skeletal dysplasias

26 March

Dr Paul Verma
Monash Institute of Medical Research
Harnessing pluripotency for biotech and biomedical applications

APRIL

4 April

Professor Weisan Chen
La Trobe University
Finding the dominant $CD8^+$ T cell responses to viral and tumour antigens

17 April

Dr Uta Wille
Bio21 Institute, University of Melbourne
Reactions of peroxyl radicals with alkynes: a new pathway to carbenes?

18 April

Professor Jenny Martin
Institute for Molecular Bioscience, University of Queensland
Bragging rights – the legacy of Lawrence Bragg

24 April

Dr Chris Burns
Walter and Eliza Hall Institute of Medical Research
The discovery of new anti-cancer agents

MAY

2 May

Dr Sheena McGowan
Monash University
The *Plasmodium falciparum* aspartyl aminopeptidase – controlling enzyme activity through self-association

8 May

Dr Spencer Williams
Bio21 Institute, University of Melbourne
Sweet medicine: molecular studies of the roles of carbohydrates in disease and wellbeing

10 May

Dr Nathan Hall
VLSCI/La Trobe University
Next-Gen Sequencing Bioinformatics – now and into the future

16 May

Professor Kate Loveland
Monash University
Regulated signalling and nuclear transport in spermatogenesis

24 May

Dr Michael Murray
University of Melbourne
Genetic regulation of epithelial / mesenchymal plasticity in *Drosophila*

30 May

Professor Joe Trapani
Peter MacCallum Cancer Centre
Structure and function of lymphocyte perforin and its role in disease

SEMINAR PROGRAM

JUNE

13 June

Dr Joakim Rodin
DPI Victoria
Phenotyping – bottleneck or blessing?

26 June

Dr Sam Wormald
WEHI Systems Biology and Personalised Medicine
Systematic mapping of genetic circuits governing stem cell self-renewal

27 June

Professor Ray Norton
Monash University
Drugs targeting malaria and bacteria: fragment - and structure-based approaches

JULY

11 July

Professor David Thorburn
Murdoch Childrens Research Institute
Mitochondrial OXPHOS disease: new genes found by massively parallel sequencing and new mouse models

25 July

Dr Ross Dickins
Walter and Eliza Hall Institute of Medical Research
Haematopoietic transcription factors in acute leukaemia genesis and therapy

AUGUST

8 August

Professor Rob Parton
Institute for Molecular Bioscience, University of Queensland
New insights into the formation and function of caveolae

9 August

Dr Sebastian Dworkin
Alfred Hospital and Monash University
The role of the grainy head-like (grhl) genes in vertebrate development – insights from zebrafish

14 August

Professor Jacqui Matthews
University of Sydney
Regulating transcriptional regulators

14 August

Professor Rob Lamb
University of Melbourne
Super-non stick surfaces – the face of a "little" roughness

21 August

Professor Tony Wedd
Bio21 Institute, University of Melbourne
How does biology cope with copper? It is toxic but essential

22 August

Professor Adrienne Clarke
Chancellor, La Trobe University
Biochemistry Open Day seminar

23 August

Dr Belinda Appleton
University of Melbourne
Bent-wing bats: colonisation and evolution

28 August

Professor Andrew Holmes
Bio21 Institute, University of Melbourne
Pericyclic processes in the synthesis of biologically active piperidine and indolizidine alkaloids

SEPTEMBER

5 September

Dr Marie-Liesse Asselin-Labat
Walter and Eliza Hall Institute of Medical Research
Regulation of adult stem cells: from breast to lung

19 September

Professor Jiri Neuzil
Griffith University
Mitochondrially targeted anti-cancer agents (mitocans): A new paradigm in efficient cancer treatment

20 September

Mr Michael Oellermann
Alfred Wegener Institute for Polar and Marine Research, Germany
Limited by blue blood? Genetic, structural and functional traits driving haemocyanin evolution and thermal adaptation in octopods

SEMINAR PROGRAM

OCTOBER

3 October

Professor Scott O'Neill
Monash University
Using Wolbachia infections to control dengue transmission

4 October

Dr Emma Carroll
University of Auckland
Cultural memory shapes population structure and demographic closure of New Zealand and Australian southern right whale calving grounds

9 October

Dr Oliver Warschkow
University of Sydney
A computational chemist's perspective on molecular nanotechnology and atomic scale device fabrication

16 October

Dr Alison Funston
Monash University
Surface plasmon coupling in assemblies of metal nanoparticles – building functional superstructures for waveguiding

17 October

Dr Salvatore Pepe
Murdoch Childrens Research Institute
Mitochondrial bioenergetics, redox and heart failure

23 October

Professor Simon Aldridge
University of Oxford
Coordination and activation of B-H bonds

25 October

Dr Heroen Verbruggen
University of Melbourne
The ecology and evolution of seaweed diversification

30 October

Dr Toby Bell
Monash University
Applied single molecule fluorescence detection

31 October

Professor Susan Charman
Monash University
Genesis of the antimalarial OZ439: from preclinical studies to clinical trials

NOVEMBER

14 November

Dr Helen Thomas
St Vincent's Medical Research Institute
Apoptosis and necrosis of pancreatic beta cells in diabetes

20 November

Dr Ekaterina Pas
2011 RACI Physical Chemistry lecturer
First principles approaches to studying ionic liquids

DECEMBER

18 December

Dr Alister Page
University of Newcastle
Theoretical insights into chirality-controlled carbon nanotube growth

Publications

BIOCHEMISTRY

Book chapters

Dogovski C, Atkinson S, Dommaraju S, Downton M, Hor L, Moore S, Paxman J, Peverelli M, Qiu T, Reumann M, Siddiqui T, Taylor N, Wagner J, Wubben J, **Perugini M** (2012) Enzymology of bacterial lysine biosynthesis, *Biochemistry*, 225 – 262.

Mathias R, **Ji H**, **Simpson R** (2012) Proteomic profiling of the epithelial-mesenchymal transition using 2D DIGE, *Difference Gel Electrophoresis (DIGE): Methods and Protocols*, 269 – 286.

Stevens J, **Dunse K**, **Fox J**, **Evans S**, **Anderson M** (2012) Biotechnological approaches for the control of insect pests in crop plants, *Pesticides-Advances in Chemical and Botanical Pesticides*, 269 – 308.

Journal articles

Adda C, Macraild C, Reiling L, Wycherley K, Boyle M, Kienzle V, Masendycz P, **Foley M**, Beeson J, Norton R, **Anders R** (2012) Antigenic characterization of an intrinsically unstructured protein, *Plasmodium falciparum* merozoite surface protein 2, *Infection and Immunity*, 80: 4177 – 4185.

Appleby S, Cockshell M, Pippal J, Thompson E, Barrett J, Tooley K, Sen S, Sun W, Grose R, Nicholson I, **Levina V**, **Cooke I**, **Talbo G**, Lopez A, Bonder C (2012) Characterization of a distinct population of circulating human non-adherent endothelial forming cells and their recruitment via intercellular adhesion molecule-3, *PLoS One*, 7: e46996, doi:10.1371/journal.pone.0046996.

Ash M, **Maher M**, Mitchell G, Jormakka M (2012) The cation-dependent G-proteins: in a class of their own, *FEBS Letters*, 586: 2218 – 2224.

Atkinson S, **Dogovski C**, Dobson R, **Perugini M** (2012) Cloning, expression, purification and crystallization of dihydrodipicolinate synthase from *Agrobacterium tumefaciens*, *Acta Crystallographica. Section F: Structural Biology and Crystallization Communications Online*, 68: 1040 – 1047.

Atkinson S, **Dogovski C**, Downton M, Pearce F, Reboul C, Buckle A, Gerrard J, Dobson R, Wagner J, **Perugini M** (2012) Crystal, solution and *in silico* structural studies of dihydrodipicolinate synthase from the common grapevine, *PLoS One*, 7: e38318, doi:10.1371/journal.pone.0038318.

Baker M, **Mooga V**, Guiard B, Langer T, **Ryan M**, **Stojanovski D** (2012) Impaired folding of the mitochondrial small TIM chaperones induces clearance by the i-AAA protease, *Journal of Molecular Biology*, 424: 227 – 239.

Barclay V, Sim D, Chan B, Nell L, Rabaa M, Bell A, **Anders R**, Read A (2012) The evolutionary consequences of blood-stage vaccination on the rodent malaria *Plasmodium chabaudi*, *PLoS Biology*, 10: e1001368, doi:10.1371/journal.pbio.1001368.

Bernabeu M, Lopez F, Ferrer M, Martin-Jaular L, Razaname A, Corradin G, **Maier A**, Del Portillo H, Fernandez-Becerra C (2012) Functional analysis of *Plasmodium vivax* VIR proteins reveals different subcellular localizations and cytoadherence to the ICAM-1 endothelial receptor, *Cellular Microbiology*, 14: 386 – 400.

Bilardi R, Kimura K, **Phillips D**, **Cutts S** (2012) Processing of anthracycline-DNA adducts via DNA replication and interstrand crosslink repair pathways, *Biochemical Pharmacology*, 83: 1241 – 1250.

Bohnert M, Wenz L, Zerbes R, Horvath S, **Stroud D**, Von Der Malsburg K, Muller J, Oeljeklaus S, Perschil I, Warscheid B, Chacinska A, Veenhuis M, Van Der Klei I, Daum G, Wiedemann N, Becker T, Pfanner N (2012) Role of mitochondrial inner membrane organizing system in protein ogenesis of the mitochondrial outer membrane, *Molecular Biology of the Cell*, 23: 3948 – 3956.

Bottinger L, Gornicka A, Czerwik T, Bragoszewski P, Loniewska-lwowska A, Schulze-Specking A, **Truscott K**, Guiard B, Milenkovic D, Chacinska A (2012) *In vivo* evidence for cooperation of Mia40 and Erv1 in the oxidation of mitochondrial proteins, *Molecular Biology of the Cell*, 23: 3957 – 3969.

Boyd S, Nair B, Ng S, Keith J, **Orian J** (2012) Computational characterization of 3' splice variants in the GFAP isoform family, *PLoS One*, 7: e33565, doi:10.1371/journal.pone.0033565.

Brand I, **Civciristov S**, **Taylor N**, **Talbo G**, **Pantaki D**, **Levina V**, Clem R, **Perugini M**, **Kvansakul M**, **Hawkins C** (2012) Caspase inhibitors of the P35 family are more active when purified from yeast than bacteria, *PLoS One*, 7: e39248, doi: 10.1371/journal.pone.0039248.

Caria S, **Chugh S**, Nhu D, Lessene G, **Kvansakul M** (2012) Crystallization and preliminary X-ray characterization of Epstein-Barr virus BHRF1 in complex with a benzoylurea peptidomimetic, *Acta Crystallographica. Section F: Structural Biology and Crystallization Communications Online*, 68: 1521 – 1524.

Conlan B, Colgrave M, **Gillon A**, **Guarino R**, Craik D, **Anderson M** (2012) Insights into processing and cyclization events associated with biosynthesis of the cyclic peptide kalata B1, *Journal of Biological Chemistry*, 287: 28037 – 28046.

PUBLICATIONS

Conlan B, **Gillon A**, **Barbeta B**, **Anderson M** (2012) Subcellular targeting and biosynthesis of cyclotides in plant cells, *American Journal of Botany*, 98: 2018 – 2026.

Damgaard R, Nachbur U, Fiil B, Yabal M, Wong W, Kastirr, M, Rieser E, Rickard J, Bankovacki A, Peschel C, Ruland J, Bekker-Jensen S, Mailand N, Kaufmann T, Strasser A, Walczak H, **Silke J**, Jost P (2012) The ubiquitin ligase XIAP recruits LUBAC for NOD2 signaling in inflammation and innate immunity, *Molecular Cell*, 46: 746 – 758.

Deakin J, **Graves J**, Rens W (2012) The evolution of marsupial and monotreme chromosomes, *Cytogenetic and Genome Research*, 137: 113 – 129.

Dearnley M, **Yeoman J**, Hanssen E, Kenny S, Turnbull L, Whitchurch C, Tilley L, **Dixon M** (2012) Origin, composition, organization and function of the inner membrane complex of *Plasmodium falciparum* gametocytes, *Journal of Cell Science*, 125: 2053 – 2063.

Dogovski C, Atkinson S, Dommaraju S, Downton M, Hor L, Moore S, Paxman J, Peverelli M, Qiu T, Reumann M, Siddiqui T, Taylor N, Wagner J, Wubben J, **Perugini M** (2012) Enzymology of bacterial lysine biosynthesis, *Biochemistry*, 225 – 262.

Dogovski C, Dommaraju S, Small L, **Perugini M** (2012) Comparative structure and function analyses of native and his-tagged forms of dihydrodipicolinate reductase from methicillin-resistant *Staphylococcus aureus*, *Protein Expression and Purification*, 85: 66 – 76.

Dougan D, **Micevski D**, **Truscott K** (2012) The N-end rule pathway: from recognition by N-recognins, to destruction by AAA+ proteases, *Molecular Cell Research*, 1823: 83 – 91.

Ebert L, MacRaild SE, Zanker D, Davis I, Cebon J, **Chen W** (2012) A cancer vaccine induces expansion of NY-ESO-1-specific regulatory T cells in late stage melanoma patients, *PLoS One*, 7(10): e48424, doi:10.1371/journal.pone.0048424.

Faou P, **Hoogenraad N** (2012) Tom34: a cytosolic cochaperone of the Hsp90/Hsp70 protein complex involved in mitochondrial protein import, *BBA – Molecular Cell Research*, 1823: 348 – 357.

Farg M, **Soo K**, **Walker A**, **Pham H**, **Orian J**, Horne M, Warraich S, Williams K, Blair I, **Atkin J** (2012) Mutant FUS induces endoplasmic reticulum stress in amyotrophic lateral sclerosis and interacts with protein disulfide-isomerase, *Neurobiology of Aging*, 33: 2855 – 2868.

Feltham R, **Khan N**, **Silke J** (2012) IAPs and ubiquitylation, *IUBMB Life*, 64: 411 – 418.

Fhaner C, Liu S, **Ji H**, **Simpson R**, Reid G (2012) Comprehensive lipidome profiling of isogenic primary and metastatic colon adenocarcinoma cell lines, *Analytical Chemistry*, 84: 8917 – 8926.

Forrest R, **Swift L**, Rephaeli A, Nudelman A, Kimura K, **Phillips D**, **Cutts S** (2012) Activation of DNA damage response pathways as a consequence of anthracycline-DNA adduct formation, *Biochemical Pharmacology*, 83: 1602 – 1612.

Fowkes F, McGready R, Cross N, Hommel M, Simpson J, Elliott S, Richards J, Lackovic K, Viladpai-Nguen J, Narum D, Tsuboi T, **Anders R**, Nosten F, Beeson J (2012) New insights into acquisition, boosting, and longevity of immunity to malaria in pregnant women, *The Journal of Infectious Diseases,* 206: 1612 – 1621.

Gangoda L, **Doerflinger M**, **Lee Y**, **Rahimi A**, Etemadi N, Chau D, **Milla L**, **O'connor L**, **Puthalakath H** (2012) Cre transgene results in global attenuation of the cAMP/PKA pathway, *Cell Death and Disease*, 3: e365, doi: 10.1038/cddis.2012.110.

Gibert B, Eckel B, Fasquelle L, **Moulin M**, Bouhallier F, Gonin V, Mellier G, Simon S, Kretz-Remy C, Arrigo A, Diaz-Latoud C (2012) Knock down of heat shock protein 27 (hspb1) induces degradation of several putative client proteins, *PLoS One*, 7: e29719, doi:10.1371/journal.pone.0029719.

Griffin M, Billakanti J, Wason A, Keller S, Mertens H, Atkinson S, Dobson R, **Perugini M**, Gerrard J, Pearce F (2012) Characterisation of the first enzymes committed to lysine biosynthesis in Arabidopsis thaliana, *PLoS One*, 7: e40318, doi:10.1371/journal.pone.0040318.

Hanssen E, Knoechel C, **Dearnley M**, **Dixon M**, Le Gros M, Larabell C, Tilley L (2012) Soft X-ray microscopy analysis of cell volume and hemoglobin content in erythrocytes infected with asexual and sexual stages of *Plasmodium falciparum*, *Journal of Structural Biology*, 177: 224 – 232.

He Y, Sutcliffe E, Bunting K, Li J, **Goodall K**, **Poon I**, **Hulett M**, Freeman C, Zafar A, Mcinnes R, Taya T, Parish C, Rao S (2012) The endoglycosidase heparanase enters the nucleus of T lymphocytes and modulates H3 methylation at actively transcribed genes via the interplay with key chromatin modifying enzymes, *Transcription*, 3: 130 – 145.

Hodder A, Czabotar P, Uboldi A, Clarke O, Lin C, Healer J, **Smith B**, Cowman A (2012) Insights into duffy binding-like domains through the crystal structure and function of the merozoite surface protein MSPDBL2 from *Plasmodium falciparum*, *Journal of Biological Chemistry*, 287: 32922 – 32939.

Ishii H, **Hulett M**, Li J, Santiago F, Parish C, Khachigian L (2012) Yin Yang-1 inhibits tumor cell growth and inhibits p21 WAF1/Cip1complex formation with cdk4 and cyclin D1, *International Journal of Oncology*, 40: 1575 – 1580.

Iwata M, Lee Y, Yamashita T, Yagi T, Iwata S, Cameron A, **Maher M** (2012) The structure of the yeast NADH dehydrogenase (Ndi1) reveals overlapping binding sites for water- and lipid-soluble substrates, *Proceedings of the National Academy of Sciences*, 109: 15247 – 15252.

Kalra H, **Simpson R**, **Ji H**, Aikawa E, Altevogt P, Askenase P, Bond V, Borras F, Breakefield X, Budnik V, Buzas E, Camussi G, Clayton A, Cocucci E, Falcon-Perez J, Gabrielsson S,

PUBLICATIONS

Gho Y, Gupta D, Harsha H, Hendrix A, Hill A, Inal J, Jenster G, Kramer-Albers E-M, Lim S, Llorente A, Lotvall J, Marcilla A, Mincheva-Nilsson L, Nazarenko I, Nieuwland R, Nolte-Hoen E, Pandey A, Patel T, Piper M, Pluchino S, Prasad T, Rajendran L, Raposo G, Record M, Reid G, Sanchez-Madrid F, Schiffelers R, Siljander P, Stensballe A, Stoorvogal W, Taylor D, Thery C, Valadi H, Van Balkom B, Vazquez J, Vidal M, Wauben M, Yanez-Mo M, Zoeller M, **Mathivanan S** (2012) Vesiclepedia: A compendium for extracellular vesicles with continuous community annotation, *PLoS Biology*, 10: e1001450, doi:10.1371/journal.pbio.1001450.

Ke B, Pepe S, Grubb D, Komen J, Laskowski A, Rodda F, Hardman B, Pitt J, **Ryan M**, **Lazarou M**, Koleff J, Cheung M, Smolich J, Thorburn D (2012) Tissue-specific splicing of an Ndufs6 gene-trap insertion generates a mitochondrial complex I deficiency-specific cardiomyopathy, *Proceedings of the National Academy of Sciences*, 109: 6165 – 6170.

King N, Sakinc T, Ben Zakour N, Totsika M, **Heras B**, Simerska P, Shepherd M, Gatermann S, Beatson S, Schembri M (2012) Characterisation of a cell wall-anchored protein of *Staphylococcus saprophyticus* associated with linoleic acid resistance, *BMC Microbiology*, 12:8, doi:10.1186/1471-2180-12-8.

Lackovic J, Howitt J, Callaway J, **Silke J**, Bartlett P, Tan S (2012) Differential regulation of Nedd4 ubiquitin ligases and their adaptor protein Ndfip1 in a rat model of ischemic stroke, *Experimental Neurology*, 235: 326 – 335.

Laming E, McGrath A, Guss J, Kappler U, **Maher M** (2012) The X-ray crystal structure of a pseudoazurin from Sinorhizobium meliloti, *Journal of Inorganic Biochemistry*, 115: 148 – 154.

Lay F, **Mills G**, **Hulett M**, **Kvansakul M** (2012) Crystallization and preliminary X-ray crystallographic analysis of the plant defensin NaD1, *Acta Crystallographica. Section F: Structural Biology and Crystallization Communications Online*, 68: 85 – 88.

Lay F, **Mills G**, **Poon I**, Cowieson N, Kirby N, **Baxter A**, **Van Der Weerden N**, **Dogovski C**, **Perugini M**, **Anderson M**, **Kvansakul M**, **Hulett M** (2012) Dimerization of plant defensin NaD1 enhances its antifungal activity, *Journal of Biological Chemistry*, 287: 19961 – 19972.

Lay F, **Veneer P**, **Hulett M**, **Kvansakul M** (2012) Recombinant expression and purification of the tomato defensin TPP3 and its preliminary X-ray crystallographic analysis, *Acta Crystallographica. Section F: Structural Biology and Crystallization Communications*, 68: 314 – 316.

Layton M, Church N, Faux M, **Ji H**, Goode R, Kapp E, Burgess A, **Simpson R** (2012) Solubilisation of the armadillo-repeat protein ß-catenin using a zwitterionic detergent allows resolution of phosphorylated forms by 2DE, *Electrophoresis*, 33: 1804 – 1813.

Layton M, Faux M, Church N, Catimel B, Kershaw N, Kapp E, Nowell C, Coates J, Burgess A, **Simpson R** (2012) Identification of a Wnt-induced protein complex by affinity proteomics using an antibody that recognizes a sub-population of ß-catenin, *BBA–Proteins and Proteomics*, 1824: 925 – 937.

Leong D, Komen J, Hewitt C, Arnaud E, McKenzie M, Phipson B, Bahlo M, Laskowski A, Kinkel S, Davey G, Heath W, Voss A, Zahedi R, Pitt J, Chrast R, Sickmann A, **Ryan M**, Smyth G, Thorburn D (2012) Proteomic and metabolomic analyses of mitochondrial complex I-deficient mouse model generated by spontaneous B2 short interspersed nuclear element (SINE) insertion into NADH dehydrogenase (ubiquinone) Fe-S protein 4 (Ndufs4) gene, *Journal of Biological Chemistry*, 287: 20652 – 20663.

Lim J, Mathias R, Kapp E, Layton M, Faux M, Burgess A, **Ji H**, **Simpson R** (2012) Restoration of full-length APC protein in SW480 colon cancer cells induces exosome-mediated secretion of DKK-4, *Electrophoresis*, 33: 1873 – 1880.

Liu T, Peng L, Yu P, Zhao Y, Shi Y, Mao X, **Chen W**, Cheng P, Wang T, Chen N, Zhang J, Liu X, Li N, Guo G, Tong W, Zhuang Y, Zou Q (2012) Increased circulating Th22 and Th17 cells are associated with tumor progression and patient survival in human gastric cancer, *Journal of Clinical Immunology*, 32: 1332 – 1339.

Lowth B, Kirstein-Miles J, **Saiyed T**, Brotz-Oesterhelt H, Morimoto R, **Truscott K**, **Dougan D** (2012) Substrate recognition and processing by a Walker B mutant of the human mitochondrial AAA+ protein CLPX, *Journal of Structural Biology*, 179: 193 – 201.

Macraild C, Pedersen M, **Anders R**, Norton R (2012) Lipid interactions of the malaria antigen merozoite surface protein 2, *BBA – Biomembranes*, 1818: 2572 – 2578.

Maiorca M, Hanssen E, Kazmierczak E, **Maco B**, Kudryashev M, Hall R, Quiney H, Tilley L (2012) Improving the quality of electron tomography image volumes using pre-reconstruction filtering, *Journal of Structural Biology*, 180: 132 – 142.

Mathivanan S (2012) Quest for cancer biomarkers: Assaying mutant proteins and RNA that provides the much needed specificity, *Journal of Proteomics & Bioinformatics*, 5: 11.

Mathivanan S (2012) Exosomes and shedding microvesicles are mediators of intercellular communication: how do they communicate with the target cells? *Journal of Biotechnology & Biomaterials*, 2: e110, doi:10.4172/2155 – 952X.1000e110.

Mathivanan S, Fahner C, Reid G, **Simpson R** (2012) ExoCarta 2012: database of exosomal proteins, RNA and lipids, *Nucleic Acids Research*, 40: 1241 – 1244.

Mathivanan S, **Ji H**, **Tauro B**, Chen Y, **Simpson R** (2012) Identifying mutated proteins secreted by colon cancer cell lines using mass spectrometry, *Journal of Proteomics*, 76: 141 – 149.

PUBLICATIONS

Mimaki M, **Wang X**, McKenzie M, Thorburn D, **Ryan M** (2012) Understanding mitochondrial complex I assembly in health and disease, *BBA – Bioenergetics*, 1817: 851 – 862.

Moujalled D, **Cook W**, **Duquez J**, **Khan N**, **Ahmed A, Callus B**, **Vaux D** (2012) In mouse embryonic fibroblasts, neither caspase-8 nor cellular FLICE-inhibitory protein (FLIP) is necessary for TNF to activate NF-kB, but caspase-8 is required for TNF to cause cell death, and induction of FLIP by NF-kB is required to prevent it, *Cell Death & Differentiation*, 19: 808 – 815.

Moulin M, **Carter H**, Voss A, Thomas T, **Wong W**, **Bankovacki A**, **Feltham R**, **Chau D**, **Cook W**, **Silke J**, **Vaux D** (2012) IAPs limit activation of RIP kinases by TNF receptor 1 during development, *The EMBO Journal,* 31: 1679 – 1691.

Nicholls C, Pinto A, Li H, Li N, Wang L, **Simpson R**, Liu J (2012) Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) induces cancer cell senescence by interacting with telomerase RNA component, *Proceedings of the National Academy of Sciences*, 109: 13308 – 13313.

Ntumngia F, **Schloegel J**, Barnes S, Mchenry A, Singh S, King C, Adams J (2012) Conserved and variant epitopes of *Plasmodium vivax* duffy binding protein as targets of inhibitory monoclonal antibodies, *Infection and Immunity*, 80: 1203 – 1208.

Okamoto T, Campbell S, Mehta N, Thibault J, Colman P, Barry M, Huang D, **Kvansakul M** (2012) Sheeppox virus SPPV14 encodes a Bcl-2-like cell death inhibitor that counters a distinct set of mammalian proapoptotic proteins, *Journal of Virology*, 86: 11501 – 11511.

Pettikiriarachchi A, Gong L, **Perugini M**, Devenish R, Prescott M (2012) Ultramarine, a chromoprotein acceptor for förster resonance energy transfer, *PLoS One*, 7: e41028, doi:10.1371/journal.pone.0041028

Poon S, Heath R, **Clarke A** (2012) A chimeric arabinogalactan protein promotes somatic embryogenesis in cotton cell culture, *Plant Physiology*, 160: 684 – 695.

Rath E, Berger E, Messlik A, Nunes T, Liu B, Kim S, **Hoogenraad N**, Sans M, Sartor R, Haller D (2012) Induction of dsRNA activated protein kinase links mitochondrial unfolded protein response to the pathogenesis of intestinal inflammation, *Gut*, 61:1269 – 78.

Rautureau G, Yabal M, Yang H, Huang D, **Kvansakul M**, Hinds M (2012) The restricted binding repertoire of Bcl-B leaves Bim as the universal BH3-only prosurvival Bcl-2 protein antagonist, *Cell Death and Disease*, 3: e443, doi: 10.1038/cddis.2012.178.

Reboul C, Porebski B, Griffin M, **Dobson R**, **Perugini M**, Gerrard J, Buckle A (2012) Structural and dynamic requirements for optimal activity of the essential bacterial enzyme dihydrodipicolinate synthase, *PLoS Computational Biology*, 8: e1002537, doi:10.1371/journal.pcbi.1002537.

Reddy S, **Anders R**, Beeson J, Farnert A, Kironde F, Berenzon S, Wahlgren M, Linse S, Persson K (2012) High affinity antibodies to *Plasmodium falciparum* merozoite antigens are associated with protection from malaria, *PLoS One*, 7: e32242, doi:10.1371/journal.pone.0032242.

Ryan M, **Stojanovski D** (2012) Mitofusins 'bridge' the gap between oxidative stress and mitochondrial hyperfusion, *EMBO Reports*, 13: 870 – 871.

Sakamoto H, Takeo S, **Maier A**, Sattabongkot J, Cowman A, Tsuboi T (2012) Antibodies against a *Plasmodium falciparum* antigen PfMSPDBL1 inhibit merozoite invasion into human erythrocytes, *Vaccine*, 30: 1972 – 1980.

Siddiqui A, Xainli J, **Schloegel J**, Carias L, Ntumngia F, Shoham M, **Casey J**, **Foley M**, Adams J, King C (2012) Fine specificity of *Plasmodium vivax* duffy binding protein binding engagement of the duffy antigen on human erythrocytes, *Infection and Immunity*, 80: 2920 – 2928.

Simpson R, Kalra H, **Mathivanan S** (2012) ExoCarta as a resource for exosomal research, *Journal of Extracellular Vesicles*, 1: 18374, doi.org/10.3402/jev.v1i0.18374.

Simpson R, **Mathivanan S** (2012) Extracellular microvesciles: the need for internationally recognised nomenclature and stringent purification criteria, *Journal of Proteomics and Bioinformatics*, 5: ii.

Siriwardena G, **Cooke I**, Sutherland W (2012) Landscape, cropping and field boundary influences on bird abundance, *Ecography*, 35: 162 – 173.

Sivaraman K, Oellig C, Huynh K, Atkinson S, Poreba M, **Perugini M**, Trenholme K, Gardiner D, Salvesen G, Drag M, Dalton J, Whisstock J, Mcgowan S (2012) X-ray crystal structure and specificity of the *Plasmodium falciparum* malaria aminopeptidase PfM18AAP, *Journal of Molecular Biology*, 422: 495 – 507.

Soo K, **Atkin J**, **Farg M**, **Walker A**, Horne M, Nagley P (2012) Bim links ER stress and apoptosis in cells expressing mutant SOD1 associated with amyotrophic lateral sclerosis, *PLoS One*, 7: e35413, doi:10.1371/journal.pone.0035413.

Stojanovski D, Bohnert M, Pfanner N, Van Der Laan M (2012) Mechanisms of protein sorting in mitochondria, *Cold Spring Harbor Perspectives in Biology*, 4: a011320, doi:10.1101/cshperspect.a011320.

Stojanovski D, Bragoszewski P, Chacinska A (2012) The MIA pathway: a tight bond between protein transport and oxidative folding in mitochondria, *BBA – Molecular Cell Research*, 1823: 1142 – 1150.

Stylli S, **Stacy T**, Kaye A, **Lock P** (2012) Prognostic significance of Tks5 expression in gliomas, *Journal of Clinical Neuroscience*, 19: 436 – 442.

Tarasenko N, **Cutts S**, **Phillips D**, Inbal A, Nudelman A, Kessler-Icekson G, Rephaeli A (2012) Disparate impact of butyroyloxymethyl diethylphosphate (AN-7), a histone deacetylase inhibitor, and doxorubicin in mice bearing a mammary tumor, *PLoS One*, 7: e31393, doi:10.1371/journal.pone.0031393.

Tarasenko N, Kessler-Icekson G, Boer P, Inbal A, Schlesinger H, **Phillips D**, **Cutts S**, Nudelman A, Rephaeli A (2012) The histone deacetylase inhibitor butyroyloxymethyl diethylphosphate (AN-7) protects normal cells against toxicity of anticancer agents while augmenting their anticancer activity, *Investigational New Drugs*, 30: 130 – 143.

Tauro B, **Greening D**, **Mathias R**, **Ji H**, **Mathivanan S**, Scott A, **Simpson R** (2012) Comparison of ultracentrifugation, density gradient separation, and immunoaffinity capture methods for isolating human colon cancer cell line LIM1863-derived exosomes, *Methods*, 56: 293 – 304.

Tucker E, **Mimaki M**, Crompton A, McKenzie M, **Ryan M,** Thorburn D (2012) Next-generation sequencing in molecular diagnosis: NUBPL mutations highlight the challenges of variant detection and interpretation, *Human Mutation*, 33: 411 – 418.

Walden P, **Heras B**, Chen K, Halili M, Rimmer K, Sharma P, Scanlon M, Martin J (2012) The 1.2 A resolution crystal structure of TcpG, the *Vibrio cholerae* DsbA disulfide-forming protein required for pilus and cholera-toxin production, *Acta Crystallographica. Section D: Biological Crystallography*, 68: 1290 – 1302.

Wierer S, Peter S, **Elgass K**, Mack H, Bieker S, Meixner A, Zentgraf U, Schleifenbaum F (2012) Determination of the in vivo redox potential by one-wavelength spectro-microscopy of roGFP, *Analytical and Bioanalytical Chemistry*, 403: 737 – 744.

Ye M, Khoo K, Xu S, Zhou M, Boonyalai N, **Perugini M**, Shao X, Chi C, Galea C, Wang C, Norton R (2012) A helical conotoxin from *Conus imperialis* has a novel cysteine framework and defines a new superfamily, *Journal of Biological Chemistry*, 287: 14973 – 14983.

Zhang X, **Adda C**, Low A, Zhang J, Zhang W, Sun H, Tu X, **Anders R**, Norton R (2012) Role of the helical structure of the N-terminal region of *Plasmodium falciparum* merozoite surface protein 2 in fibril formation and membrane interaction, *Biochemistry*, 51: 1380 – 1387.

Zhao R, Mifsud N, Xaio K, Chan K-F, Oveissi S, Jackson H, Dimopoulos N, Guillaume P, Knights A, Lowen T, Robson N, Russell S, Scotet E, Davies I, Maraskovsky E, Cebon J, Luescher I, **Chen W** (2012) A novel HLA-B18 restricted CD8+ T cell epitope is efficiently cross-presented by dendritic cells from soluble tumor antigen, *PLoS One*, 7: e44707, doi:10.1371/journal.pone.0044707.

CHEMISTRY

Book chapter

Spencer M (2012) Density functional theory modeling of ZnO for gas sensor applications, *Chemical Sensors: Simulation and Modeling: Volume 1: Microstructural Characterization and Modeling,* 163 – 216.

Journal articles

Abrahams B, **Abrahams C**, Haywood M, Hudson T, Moubaraki B, Murray K, Robson R (2012) 3d-Metal derivatives of the [Cu I(SO 3) 4] 7- ion: structure and magnetism, *Dalton Transactions*, 41: 4091 – 4099.

Aprile A, **Wilson D**, **Richards A** (2012) The synthesis and characterization of mono and dinuclear group 13 complexes derived from a Schiff base, *Dalton Transactions*, 41: 8550 – 8555.

Asghari-Khiavi M, Wood B, Hojati-Talemi P, Downes A, McNaughton D, **Mechler A** (2012) Exploring the origin of tip-enhanced Raman scattering, preparation of efficient TERS probes with high yield, *Journal of Raman Spectroscopy*, 43: 173 – 180.

Beavers C, **Richards A** (2012) Synthesis and structures of a pentanuclear Al(III) phosphonate cage, an In(III) phosphonate polymer, and coordination compounds of the corresponding phosphonate ester with GaI_3 and $InCl_3$, *Dalton Transactions*, 41: 11305 – 11309.

Beheshti A, Zafarian H, Khorramdin R, Fattahi M, **Abrahams C** (2012) Novel silver(I) pyrazole-based coordination polymers: synthetic and structural studies, *Polyhedron*, 48: 245 – 252.

Benheim D, **Rochfort S**, **Robertson E**, **Potter I**, Powell K (2012) Grape phylloxera (Daktulosphaira vitifoliae): a review of potential detection and alternative management options, *Annals of Applied Biology*, 161: 91 – 115.

Browne E, Langford S, **Abbott B** (2012) Peptide nucleic acid monomers: a convenient and efficient synthetic approach to Fmoc/Boc monomers, *Australian Journal of Chemistry*, 65: 539 – 544.

Conway R, Valant C, Christopoulos A, Robertson A, Capuano B, **Crosby I**, Robertson A (2012) Synthesis and SAR study of 4-arylpiperidines and 4-aryl-1,2,3,6-tetrahydropyridines as 5-HT 2C agonists, *Bioorganic & Medicinal Chemistry Letters*, 22: 2560 – 2564.

Doeven E, Zammit E, Barbante G, Barnett N, Francis P, **Hogan C** (2012) A potential-controlled switch on/off mechanism for selective excitation in mixed electrochemiluminescent systems, *Chemical Science*, doi:10.1039/C2SC21707D.

Doeven E, Zammit E, Barbante G, **Hogan C**, Barnett N, Francis P (2012) Selective excitation of concomitant electrochemiluminophores: tuning emission color by electrode potential, *Angewandte Chemie (International Edition)*, 51: 4354 – 4357.

Domazetis G, **James B**, Liesegang J, **Raoarun M**, Kuiper M, **Potter I**, **Oehme D** (2012) Experimental studies and molecular modelling of catalytic steam gasification of brown coal containing iron species, *Fuel*, 93: 404 – 414.

PUBLICATIONS

Dryza V, Sanelli J, **Robertson E**, Bieske E (2012) Electronic spectra of gas-phase polycyclic aromatic nitrogen heterocycle cations: Isoquinoline + and quinoline +, *The Journal of Physical Chemistry Part A: Molecules, Spectroscopy, Kinetics, Environment and General Theory,* 116: 4323 – 4329.

Dube J, Hanninen M, **Dutton J**, Tuononen H, Ragogna P (2012) Homoleptic pnictogen-chalcogen coordination complexes, *Inorganic Chemistry*, 51: 8897 – 8903.

Dutton J, **Wilson D** (2012) Lewis base stabilized dicarbon: Predictions from theory, *Angewandte Chemie (International Edition)*, 51: 1477 – 1480.

Fraser S, Mulet X, Martin L, Praporski S, **Mechler A**, Hartley P, Polyzos A, Separovic F (2012) Surface immobilization of bio-functionalized cubosomes: sensing of proteins by quartz crystal microbalance, *Langmuir*, 28: 620 – 626.

Fukazawa A, **Dutton J**, Fan C, Mercier L, Houghton A, Wu Q, Piers W, Parvez M (2012) Reaction of pentaarylboroles with carbon monoxide: an isolable organoboron carbonyl complex, *Chemical Science*, 3: 1814 – 1818.

Godfrey P, **Robertson E** (2012) Microwave spectrum, structure, tautomeric, and conformational composition of 4-vinylimidazole, *Journal of Chemical Physics*, 137: 064306.

Hodder A, Czabotar P, Uboldi A, Clarke O, Lin C, Healer J, **Smith B**, Cowman A (2012) Insights into duffy binding-like domains through the crystal structure and function of the merozoite surface protein MSPDBL2 from Plasmodium falciparum, *Journal of Biological Chemistry*, 287:32922 – 32939.

Hughes A, Verdon C, White J (2012) Diastereoselectivity in unusual intermolecular tandem Michael reactions, *Tetrahedron*, 68: 1979 – 1987.

Joshi T, Barbante G, Francis P, **Hogan C**, Bond A, Gasser G, Spiccia L (2012) Electrochemiluminescent monomers for solid support syntheses of Ru(II)-PNA bioconjugates: multimodal biosensing tools with enhanced duplex stability, *Inorganic Chemistry*, 51: 3302 – 3315.

Lobo I, **Wilson D**, Bieske E, **Robertson E** (2012) A sting in the tail of flexible molecules: spectroscopic and energetic challenges in the case of p-aminophenethylamine, *Physical Chemistry Chemical Physics*, 14: 9219 – 9229.

Marchesan S, Easton C, **Kushkaki F**, Waddington L, Hartley P (2012) Tripeptide self-assembled hydrogels: unexpected twists of chirality, *Chemical Communications*, 48: 2195 – 2197.

Medcraft C, Fuss W, Appadoo D, McNaughton D, Thompson C, **Robertson E** (2012) Structural, vibrational, and rovibrational analysis of tetrafluoroethylene, *Journal of Chemical Physics*, 137: 214301, doi.org / 10.1063 / 1.4768417.

Medcraft C, McNaughton D, Thompson C, Appadoo D, Bauerecker S, **Robertson E** (2012) Size and temperature dependence in the far-ir spectra of water ice particles, *The Astrophysical Journal*, 758: 17, doi:10.1088 / 0004 – 637X / 758 / 1 / 17

Medcraft C, Thompson C, **Robertson E**, Appadoo D, McNaughton D (2012) The far-infrared rotational spectrum of ethylene oxide, *The Astrophysical Journal,* 753: 18, doi:10.1088 / 0004 – 637X / 753 / 1 / 18.

Nguyen H, Miyazaki H, Hoshi N, **Smith B**, Nukina N, Goldin A, Chandy K (2012) Modulation of voltage-gated K^+ channels by the sodium channel Î²1 subunit, *Proceedings of the National Academy of Sciences*, 109: 18577 – 18582.

Nguyen N, Sleebs B, White J, **Hughes A** (2012) Diastereoselective synthesis of highly functionalized ß2,2,3-substituted amino acids from 4-substituted-1,3-oxazinan-6-ones, *Tetrahedron*, 68: 4745 – 4756.

Oehme D, **Brownlee R**, **Wilson D** (2012) Can cyclic HIV protease inhibitors bind in a non-preferred form? An *ab initio*, DFT and MM-PB(GB) SA study, *Journal of Molecular Modeling*, 1: 1 – 18.

Oehme D, **Brownlee R**, **Wilson D** (2012) Effect of atomic charge, solvation, entropy, and ligand protonation state on MM-PB(GB) SA binding energies of HIV protease, *Journal of Computational Chemistry*, 33: 2566 – 2580.

Pell T, **Couchman S**, **Ibrahim S**, **Wilson D**, **Barnard P**, **Smith B**, **Dutton J** (2012) Diverse reactions of PhI(OTf)2 with common 2-electron ligands: complex formation, oxidation, and oxidative coupling, *Inorganic Chemistry*, 51: 13034 – 13040.

Richards A, **Aprile A**, **Hogan C** (2012) A 1D Schiff base zinc polymer as a versatile metallo-ligand for the synthesis of polynuclear zinc cages, *Dalton Transactions*, 41: 8361 – 8367.

Richards A, Beavers C (2012) Synthesis and structures of a pentanuclear Al(III) phosphonate cage, an In(III) phosphonate polymer, and coordination compounds of the corresponding phosphonate ester with GaI3 and InCl3, *Dalton Transactions*, 41: 11305 – 11310.

Rivadehi S, **Reid E**, **Hogan C**, Bhosale S, Langford S (2012) Fluoride-selective optical sensor based on the dipyrrolyl-tetrathiafulvalene chromophore, *Organic & Biomolecular Chemistry*, 10: 705 – 709.

Smith B (2012) PS – A program for the analysis of helix geometry, *Journal of Molecular Graphics and Modelling*, 33: 52 – 60.

Spencer M (2012) Gas sensing applications of 1D-nanostructured zinc oxide: insights from density functional theory calculations, *Progress in Natural Science*, 57: 437 – 486.

Spencer M, Morishita T, Snook I (2012) Reconstruction and electronic properties of silicon nanosheets as a function of thickness, *Nanoscale*, 4: 2906 – 2913.

Spencer M, Wong K, Yarovsky I (2012) Surface defects on ZnO nanowires: implications for design of sensors, *Journal of Physics: Condensed Matter*, 24: 305001.

Wedlock L, Aitken J, Berners-Price S, **Barnard P** (2012) Bromide ion binding by a dinuclear gold(I) N-heterocyclic carbene complex: a spectrofluorescence and X-ray absorption spectroscopic study, *Dalton Transactions*, doi: 10.1039/c2dt31817b.

Wilson D, Beavers C, **Richards A** (2012) Di-, tetra-, penta- and polynuclear zinc complexes supported by a flexible tetradentate Schiff base ligand, *European Journal of Inorganic Chemistry*, 1: 1130–1138.

Wilson D, **Couchman S**, **Dutton J** (2012) Are N-heterocyclic carbenes "better" ligands than phosphines in main group chemistry? A theoretical case study of ligand-stabilized E 2 molecules, L-E-E-L (L = NHC, phosphine, E = C, Si, Ge, Sn, Pb, N, P, As, Sb, Bi), *Inorganic Chemistry*, 51: 7657–7668.

Wong K, Field M, Ou J, Latham K, **Spencer M**, Yarovsky I, Kalantar-Zadeh K (2012) Interaction of hydrogen with ZnO nanopowders – evidence of hydroxyl group formation, *Nanotechnology*, 23: 015705.

Zammit E, Barbante G, Carlson B, **Doeven E**, Barnett N, **Hogan C**, Richter M, Francis P (2012) Chemiluminescence from osmium(ii) complexes with phenanthroline, diphosphine and diarsine ligands, *The Analyst,* 137: 2766–2769.

GENETICS

Journal articles

Albertin C, Bonnaud L, Brown C, Crookes-Goodson W, Da Fonseca R, Di Cristo C, Dilkes B, Edsinger-Gonzales E, Freeman R, Hanlon R, Koenig K, Lindgren A, Martindale M, Minx P, Moroz L, Nodl M-T, Nyholm S, Ogura A, Pungor J, Rosenthal J, Schwarz E, Shigeno S, **Strugnell J**, Wollesen, Zhang G, Ragsdale C (2012) Cephalopod genomics: a plan of strategies and organization, *Standards in Genomic Sciences*, 7: 175–188.

Allcock A, **Strugnell J** (2012) Southern ocean diversity: paradigms from molecular ecology, *Trends in Ecology & Evolution*, 27: 520–528.

Ballantyne K, Van Oven M, Ralf A, Stoneking M, **Mitchell R**, Van Oorschot R, Kayser M (2012) MtDNA SNP multiplexes for efficient inference of matrilineal genetic ancestry within Oceania, *Forensic Science International: Genetics*, 6: 425–436.

Braby M, Eastwood R, **Murray N** (2012) The subspecies concept in butterflies: has its application in taxonomy and conservation biology outlived its usefulness? *Linnean Society Biological Journal*, 106: 699–716.

Ezaz T, **Graves J** (2012) Foreword: sex and sex chromosomes-new clues from nonmodel species, *Chromosome Research*, 20: 1–5.

Goray M, **Mitchell R**, Van Oorschot R (2012) Evaluation of multiple transfer of DNA using mock case scenarios, *Legal Medicine*, 14: 40–46.

Goray M, Van Oorschot R, **Mitchell R** (2012) DNA transfer within forensic exhibit packaging: potential for DNA loss and relocation, *Forensic Science International: Genetics*, 6: 158–166.

Guzik M, Adams M, **Murphy N**, Cooper S, Austin A (2012) Desert springs: deep phylogeographic structure in an ancient endemic crustacean (*Phreatomerus latipes*), *PLoS One*, 7: e37642, doi:10.1371/journal.pone.0037642.

Krajewski C, Anderson F, **Woolley P**, **Westerman M** (2012) Molecular evidence for a deep clade of dunnarts (Marsupiolia: Dasyuridae: Sminthopsis), *Journal of Mammalian Evolution*, 19: 265–276.

Ma G, Rahman M, **Grant W**, Schmidt O, Asgari S (2012) Insect tolerance to the crystal toxins Cry1Ac and Cry2Ab is mediated by the binding of monomeric toxin to lipophorin glycolipids causing oligomerization and sequestration reactions, *Developmental & Comparative Immunology*, 37: 184–192.

Muirhead K, **Murphy N**, Sallam N, Donnellan S, Austin A (2012) Phylogenetics and genetic diversity of the *Cotesia flavipes* complex of parasitoid wasps (Hymenoptera: Braconidae), biological control agents of lepidopteran stemborers, *Molecular Phylogenetics and Evolution*, 63: 904–914.

Murphy N, Breed M, Guzik M, Cooper S, Austin A (2012) Trapped in desert springs: phylogeography of Australian desert spring snails, *Journal of Biogeography*, 39: 1573–1582.

Peeters L, Janssen T, De Haes W, Beets I, Meelkop E, **Grant W**, Schoofs L (2012) A pharmacological study of NLP-12 neuropeptide signaling in free-living and parasitic nematodes, *Peptides*, 34: 82–87.

Stasiuk S, Scott M, **Grant W** (2012) Developmental plasticity and the evolution of parasitism in an unusual nematode, *Parastrongyloides trichosuri*, *EvoDevo*, 3: 1–14.

Strugnell J, Watts P, Smith P, Allcock A (2012) Persistent genetic signatures of historic climatic events in an Antarctic octopus, *Molecular Ecology*, 21: 2775–2787.

Taylor D, Nagle N, Ballantyne K, Van Oorschot R, Wilcox S, Henry J, Turakulov R, **Mitchell R** (2012) An investigation of admixture in an Australian Aboriginal Y-chromosome STR database, *Forensic Science International: Genetics*, 6: 532–538.

Westerman M, Kear B, Aplin K, Meredith R, Springer M (2012) Phylogenetic relationships of living and recently extinct bandicoots based on nuclear and mitochondrial DNA sequences, *Molecular Phylogenetics and Evolution*, 62: 97–108.

Research laboratory

PHARMACY AND APPLIED SCIENCE

Journal articles

Agatonovic-Kustrin S, **Morton D**, **Singh R** (2012) Hybrid neural networks as tools for predicting the phase behavior of colloidal systems, *Colloids and Surfaces A: Physicochemical and Engineering Aspects*, 415: 59 – 67.

Comarmond M, Payne T, Collins R, **Palmer G**, Lumpkin G, **Angove M** (2012) Inhibition of uranium(VI) sorption on titanium dioxide by surface iron(III) species in ferric oxide / titanium dioxide systems, *Environmental Science and Technology*, 46: 11128 – 11134.

Evans T, **Seviour R** (2012) Estimating biodiversity of fungi in activated sludge communities using culture-independent methods, *Microbial Ecology*, 63: 773 – 786.

Johnson B, Quill E, **Angove M** (2012) An investigation of the mode of sorption of inositol hexaphosphate to goethite, *Journal of Colloid and Interface Science*, 367: 436 – 442.

Ihmaid S, Al-Rawi J, Bradley C, Angove M, Robertson M (2012) Synthesis, DNA-PK inhibition, anti-platelet activity studies of 2-(*N*-substituted-3-aminopyridine)-substituted-1,3-benzoxazines and DNA-PK and PI3K inhibition, homology modeling studies of 2-morpholino-(7, 8-di and 8-substituted)-1,3-benzoxazines, European Journal of Medicinal Chemistry, 57: 85 – 101.

Kustrin S, **Morton D** (2012) The use of UV-visible reflectance spectroscopy as an objective tool to evaluate pearl quality, *Marine Drugs*, 10: 1459 – 1475.

McKerrow J, Al-Rawi J, Brooks P (2012) Synthesis of some n-aryl α-amino acids using diaryliodonium salts, Asian Journal of Chemistry, 24: 1227 – 1236.

Petrovski S, **Dyson Z**, **Seviour R**, **Tillett D** (2012) Small but sufficient: the *Rhodococcus* Phage RRH1 has the smallest known *Siphoviridae* genome at 14.2 kilobases, *Journal of Virology*, 86: 358 – 363.

Petrovski S, **Tillett D**, **Seviour R** (2012) Genome sequences and characterization of the related *gordonia* phages GTE5 and GRU1 and their use as potential biocontrol agents, *Applied and Environmental Microbiology*, 78: 42 – 47.

Spark M, **Willis J** (2012) Systematic review of progesterone use by midlife and menopausal women, *Maturitas*, 72: 192 – 202.

Spark M, **Willis J**, **Byrne G** (2012) Compounded progesterone: why is it acceptable to Australian women? *Maturitas*, 73: 318 – 324.

External funding

AdAlta ($1,953,774)

AMSI Intern Program (M Foley, 1 year, $20,000)

Development of new diagnostic and therapeutic approaches to infectious diseases (M Foley, 7 years, $1,933,774)

ANZ ($23,189)

Dangerous liaisons: understanding the scaffolding function of scribble in normal and cancer cell signalling (M Kvansakul, 1 year, $23,189)

ARC ($11,508,072)

Advanced Fluorescence Characterisation Facility (C Hogan, 1 year, $150,000)

Apoptotic signalling in virally infected and normal cells (C Hawkins, 5 years, $788,800)

Bacteriophages for foam control in wastewater processing (administered by Melbourne University) (D Tillett, 3 years, $45,000)

Base stabilized dicarbon as a new building block for supramolecular organometallic chemistry (J Dutton, 3 years, $375,000)

Centre for Excellence in Coherent X-ray Science (M Ryan & L Tilley, 9 years, $2,930,880)

Discovery and application of circular proteins (M Anderson, 4 years, $305,130)

Disulfide Catalysis and Protein Folding in Bacterial Virulence (B Heras, 1 year, $20,000)

Identification of the molecular targets on filamentous fungi that lead to specific recognition and killing by an antifungal plant defensin NaD1 (M Anderson, 3 years, $330,000)

Improvement of anthracycline chemotherapy by enhancement of apoptotic responses and tumour targeted activation (S Cutts, 5 years, $686,400)

Laser Spectroscopy of Functional Molecules (E Robertson, 3 years, $200,000)

Melbourne and La Trobe Rapid Integrated X-ray Diffraction Facility (M Kvansakul, 1 year, $360,000)

Mitochondrial proteases and their contribution to protein homeostasis (K Truscott, 4 years, $686,400)

Molecular Archaeology: Carbon isotope analysis of amino acids as a means to investigate diets, physiology, metabolism and paleo environment (C Smith, 4 years, $686,400)

Molecular Mechanisms of cyclic AMP induced apoptosis (H Puthalakath, 3 years, $300,000)

Molecular mechanisms of regulatory proteolysis in Escherichia coli (D Dougan, 5 years, $425,000)

Molecular evolution of a model oligomeric enzyme from bacterial extremophiles (M Perugini, 4 Years, $686,400)

Paper fluidics - A novel approach to low cost printable microsensors (C Hogan, 4 years, $125,440)

Rapid integrated X-ray diffraction facility (M Kvansakul, 1 year, $360,000)

Stress transcriptomics: development of tests to reduce the incidence of summer mortality in abalone (J Strugnell, 3 years, $225,000)

Studies on the regulation of the pro-apoptotic protein Bim in mammalian development and cancer (H Puthalakath, 4 years, $788,800)

The systematic development of fundamentally important group 15 compounds: their applications to innovative industrial and environmental processes (A Richards, 4 years, $704,622)

Transporting proteins to and within mitochondria (D Stojanovski, 3 years, $328,800)

CRC ($6,000,000)

Cooperative Research Centre for Biomarker Translation (N Hoogenraad, 7 years, $6,000,000)

Hexima ($7,214,525)

To investigate the potential human therapeutic effects of Hexima's molecules (M Anderson, M Hulett, 2 years, $7,214,525)

NHMRC ($8,591,707)

Cellular transport dysfunction and motor neuron disease (J Atkin, 3 years, $419,925)

Colorectal Cancer - molecular basis to targeted therapeutics (R Simpson, 3 years, $1,177,717)

Investigating mechanisms of dementia and motor neuron disease - Salary component $68,723. (A Walker, 4 years, $303,924)

Investigating the role of Kaposi sarcoma herpes virus Bcl-2 in tumourigenesis (M Kvansakul, 4 years, $414,615)

Mitochondrial mediated cell death (D Stojanovski, 3 years, $296,175)

Molecular mechanisms of apoptotic cell clearance (I Poon, 4 years, $307,524)

Multi Targeted Inhibition of an essential tetrameric enzyme from Drug Resistant Streptococcus pneumonie (M Perugini, 1 year, $153,900)

NHMRC Investigating the role of Kaposi sarcoma herpes virus Bcl-2 in tumourigenesis (M Kvansakul, 3 years, $414,615)

Pluripotent Stem Cells from the mouse testis (A Hart, 3 years, $538,500)

Protecomics and bioinformatics analyses of exosomes and secretome for the detection of colorectal cancer biomarkers (S Mathivanan, 4 years, $255,531)

Protein Disulphide Isomerase and Neurodegeneration in Motor Neuron Disease (J Atkin, 3 years, $307,524)

Sirtuins and Pathogenesis of Human Cytomegalovirus (R Mathias, 4 years, $332,484)

Snail family proteins regulate stem cell differentiation (W Somers, 4 years, $279,000)

Structure and interactions of a disordered malaria surface protein: Implications for antigenicity (R Anders, $60,000)

Targeting viral Bcl-2 proteins for therapy (M Kvansakul, 3 years, $300,750)

The role of assembly factors in mitochondrial Complex I biogenesis and their defects in disease (M Ryan, 3 years, $586,875)

Understanding and controlling influenza (W Chen, 3 years, $840,098)

Understanding and Controlling Influenza (W Chen, 3 years, $295,393)

Viral caspase inhibitors (C Hawkins, 3 years, $686,400)

Other ($2,059,805)

A central role for ER-Golgi trafficking in MND (J Atkin, 1 year, $48,635)

Are direct apoptosis inducers less mutagenic than chemotherapy drugs? (C Hawkins, 3 years, $297,450)

Australian Biological Resources Study Student Travel Bursary (J Strugnell, 1 year, $1,000)

Blood brain barrier dynamics in early EAE (J Orian, 4 years, $400,780)

Failure of ER-Golgi trafficking as a central mechanism of toxicity in ALS (J Atkin, 1 year, $99,870)

Genographic research on migration of humans: Oceania and pacific node of international collaboration (J Mitchell, 6 years, $420,684)

Investigation of the immunomodulatory function of FTY720 in the experimental autoimmune encephalomyelitis (EAE) model for multiple sclerosis (MS) (J Orian, 2 years, $156,800)

Investigation of the role of the tetraspanin MS4A8B in asthma (M Hulett, 1 year, $25,000)

Markets for invermectin response (W Grant, 1 year, $36,145)

Molecular dissection of Mycrobacteria ClpP: assembly, activation, cofactors and physiological targets (D Dougan, 3 years, $90,000)

Programmed cell death (W Cook, 1 year, $136,085)

Removal of toxic chemical species from contaminated soils and industrial wastes (M Angove, 4 years, $103,000)

Resolving the blue-ringed octopus fauna of Australia: taxonomy, phylogeny and human health hazards of the genus *Hapalochlaena* (Family Ocyopodidae) (J Strugnell, 2 years, $24,000)

Shape, form and function of the human malaria parasites sexual stages (M Dixon, 2 years, $61,888)

The Tumour Microenvironment and Cellular Stress: Signalling, Metabolism, Imaging and Therapeutic Targets Conference (D Greening, 1 year, $2,500)

Travel application to attend The Cephalapod International Advisory Council Symposium 2012, Florianopolis, Santa Cataria, Brazil (J Strugnell, 1 year, $3,000)

Walnut Health Benefit Attributes Project (M Angove, 1 year, $5,000)

Whole genome sequencing of the Blue Ringed octopus (J Strugnell, 1 year, $48,500)

VLSCI ($485,000)

A new experimental model for analysis of human globin genes switching during embryonic stem cell differentiation (A Hart, 3 years, $15,000)

Life Sciences Computation Centre (L O'Connor, 2 years, $470,000)

CS31307 05/13

CONTACT

General enquiries
La Trobe Institute for Molecular Science
La Trobe University
Victoria 3086 Australia

T +61 3 9479 2160
F +61 3 9479 1266
E LIMSEnquiries@latrobe.edu.au

latrobe.edu.au/lims