



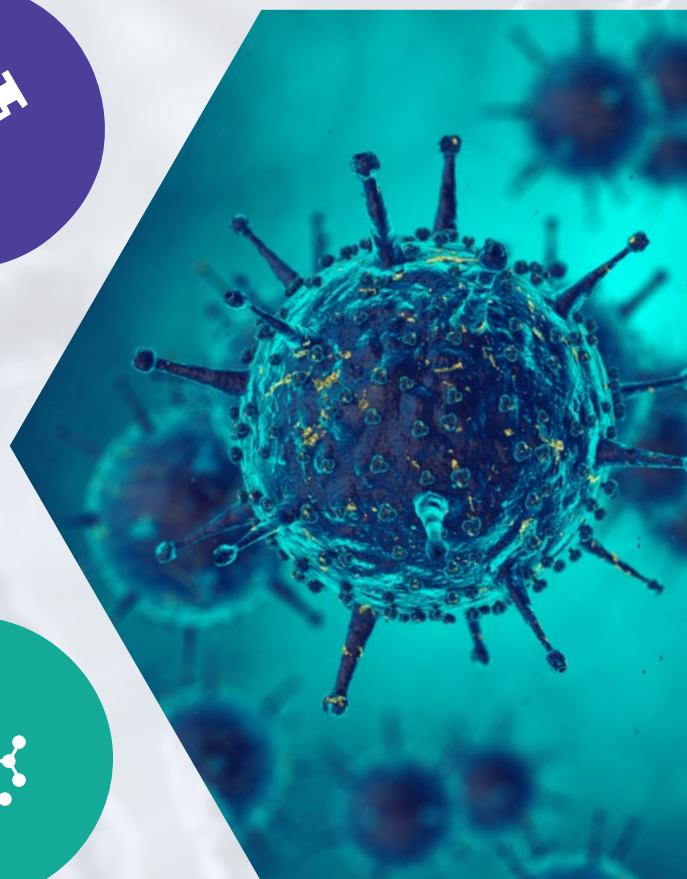
**LA TROBE**  
UNIVERSITY



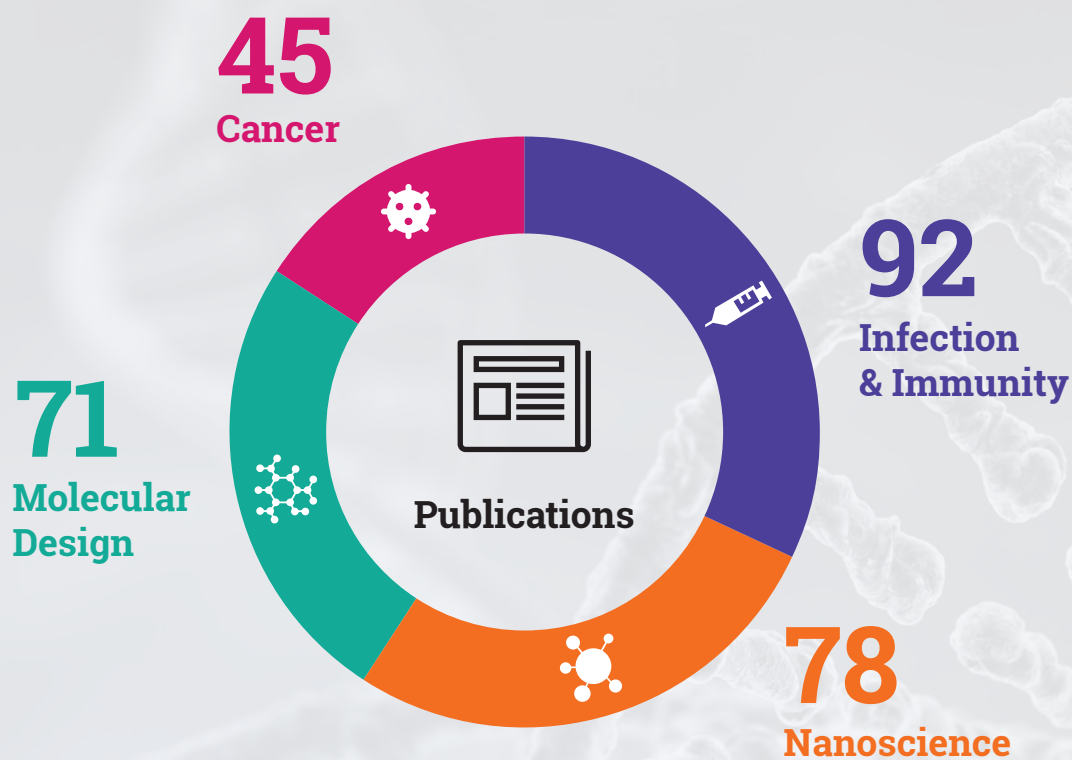
LA TROBE  
INSTITUTE FOR  
MOLECULAR SCIENCE

# LIMS ANNUAL REPORT 2020

La Trobe Institute for  
Molecular Science



# LIMS 2020



  
**2359**  
Followers

  
**748**  
Followers

  
**2715**  
Followers

Printed on Hanno Silk

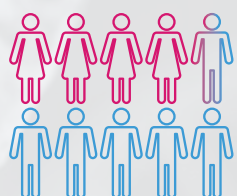
Hanno Silk is manufactured using low environmental impact FSC certified pulps in a facility that is ISO 14001 Environmental Management System accredited.





# #1

for Gender Equality <sup>1</sup>



# 43%

Women  
lab heads



Workplace  
Gender Equality  
Agency

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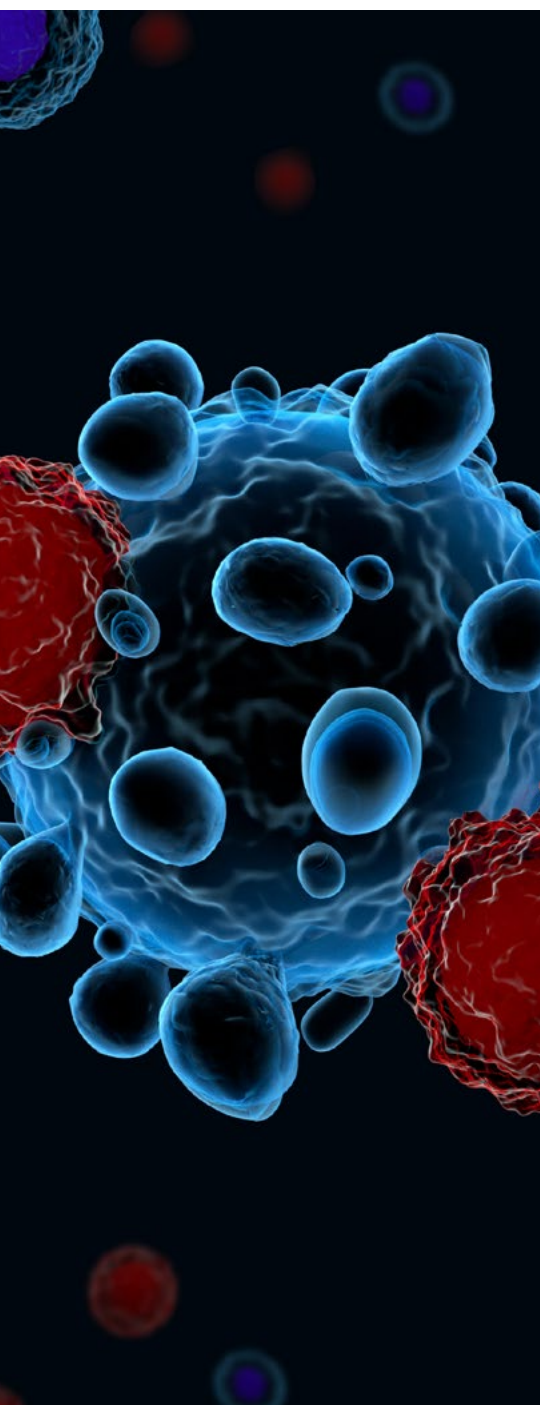
34 Publications

**Disclaimer:** Every effort has been made to ensure the information contained in this publication is accurate and current at the date of printing.

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<sup>1</sup> Times Higher Education Impact Ranking for La Trobe University

# TRANSLATABLE MOLECULAR DISCOVERIES



THE LA TROBE INSTITUTE FOR MOLECULAR SCIENCE (LIMS) BRINGS TOGETHER LA TROBE UNIVERSITY'S LEADING RESEARCHERS. THROUGH RESEARCH AND EDUCATION, WE ARE WORKING TOWARDS SOLVING SOME OF THE WORLD'S MOST CRITICAL PROBLEMS AT THE INTERFACE OF HEALTH AND SCIENCE.

The La Trobe Institute for Molecular Science vision of excellence is achieved through four thematic areas of research strength: Cancer, Infection and Immunity, Molecular Design and Nanoscience.

The research agenda of LIMS is supported by a collaborative culture and modern facilities, where scientists in diverse disciplines work together to achieve remarkable outcomes that would not be possible in traditional academic settings. Our high impact research generates collaborations and partnerships across the globe.

Within LIMS are two embedded biotech companies. Hexima is a biotech company with a novel topical treatment for fungal nail infections in Phase IIb clinical trials. AdAlta is an innovative, clinical stage biotech company developing a unique range of new drug treatments.

LIMS has outstanding links with the Australian Synchrotron. Several of the Institute's physicists design and build synchrotron components to extend the synchrotron's capabilities.

And an important collaboration with the Olivia Newton-John Cancer Research Institute facilitates the sharing of knowledge, skills, training and facilities in the area of cancer research.

These mutually beneficial partnerships raise our research capabilities to new levels of national and international significance.

# LIMS AT A GLANCE

**>400**

ACADEMIC STAFF  
AND POSTGRADUATE  
STUDENTS



**>60**

LABORATORY HEADS

**>\$44M**

EQUIPMENT ACROSS  
3 CAMPUSES



**>900**

INDIVIDUAL PIECES  
OF EQUIPMENT

**3**

ARC FUTURE FELLOWS  
4 DECRA FELLOWS



**2**

NHMRC FELLOWS

**1**

VCA MID-CAREER  
FELLOWSHIP



**1**

TRACEY BANIVANUA  
MAR FELLOW

**259**

WEB OF SCIENCE  
PUBLICATIONS (2020)



**1.72**

SCOPUS FIELD WEIGHTED  
CITATION IMPACT

ERA RANKINGS:

**5**

BIOCHEMISTRY AND CELL  
BIOLOGY; ANALYTICAL  
CHEMISTRY; OPTICAL  
PHYSICS; CONDENSED  
MATTER PHYSICS;  
GENETICS; MEDICINAL AND  
BIOMOLECULAR CHEMISTRY



**4**

INORGANIC CHEMISTRY;  
PHYSICAL CHEMISTRY

LIMS RESEARCH THEMES:

CANCER  
INFECTION AND IMMUNITY



MOLECULAR DESIGN  
NANOSCIENCE

FACILITIES:

HISTOLOGY  
COMPREHENSIVE  
PROTEOMICS PLATFORM



BIOIMAGING PLATFORM  
STORE

RESEARCH CENTRES:

MATERIALS AND  
SURFACE SCIENCE  
MOLECULAR CANCER  
PREVENTION



EXTRACELLULAR  
VESICLES  
BIOMEDICAL AND  
ENVIRONMENTAL  
SENSOR TECHNOLOGY

EMBEDDED BIOTECHNOLOGY COMPANIES:

HEXIMA LTD



ADALTA LTD





The LIMS Building, Bundoora



# DIRECTOR'S REPORT

WHEN HISTORY LOOKS BACK AT 2020, IT'S HARD TO IMAGINE IT WILL BE REMEMBERED FOR ANYTHING OTHER THAN THE COVID-19 PANDEMIC, YET THIS WAS A YEAR LIKE NO OTHER.

The Victorian and New South Wales bushfires at the beginning of the year and the global support for its victims, the international Black Lives Matter protests, and the quashing by the High Court of Cardinal George Pell's convictions, are but a few of 2020's significant events. COVID-19 impacted every one of us even though, in Australia, we were fortunate to have far fewer illnesses and fatalities than in other countries.

From late March, unlike many other research institutes, LIMS was subject to the restrictions placed on tertiary education providers. Under direction from the Department of Health, our ability to attend campus and to continue our research was considerably hampered. Despite these restrictions and the need for masks and social distancing, and following a limited timetable for on campus activity, our researchers have achieved their usual high standard of output. With travel curtailed, collaborators embraced Zoom meetings; and LIMS continued its support for conference attendance, albeit virtual, for our ECR researchers.

In January, Dr Donna Whelan moved from the Bruce Stone Fellowship to a well-deserved ARC DECRA – the first to be awarded to a researcher in Bendigo. Donna continues her development of LIMS' next-generation single molecule microscope to enable her research in exploring DNA damage and repair pathways.

In November we welcomed Dr Sarah Stewart, who returned to Australia to take up an ARC DECRA in 2021. Upon arrival at LIMS, Sarah completed her BBSRC (Biotechnology and Biological Sciences Research Council) Future Leader Fellow. Sarah had commenced this position in the Wellcome-MRC Institute of Metabolic Science Metabolic Research Laboratories of Dr Kevin Moreau at the University of Cambridge in the UK. Sarah's research, in collaboration with LIMS Professor Suresh Mathivanan, investigates how extracellular vesicles facilitate cell-to-cell communication.

Professor Stephanie Gras moved her lab from Monash University to LIMS in December 2020, ready to embark on the next stage of her career in 2021. Stephanie works on the T-cell response towards infections, with a primary focus on HIV, influenza and SARS-CoV-2. Stephanie joins the LIMS Infection and Immunity theme.

In 2021 and beyond, I have no doubt we will continue to face challenges brought upon us by the COVID-19 pandemic, as well as those from a myriad of other sources. However, LIMS researchers are passionate about delivering a difference to those problems facing our world and I have no doubt they will continue to face up to the challenge. As an institute with a vision to translate our molecular discoveries, we will continue our exceptional research into the basic sciences that underpin all research. We will explore all opportunities where these discoveries can lead to an impact on the communities we serve. And we will continue our focus on providing exceptional training for upcoming generations of scientists.

Everything in the physical world has a molecular origin. Those talented people who seek to understand our world at the molecular level have the greatest capacity to influence our future. LIMS researchers are poised to make a difference with their passion, curiosity, and integrity, to ensure a positive future for all.



**Professor Brian Smith**  
Director

# LIMS ADVISORY BOARD

THE LIMS ADVISORY BOARD PROVIDES STRATEGIC ADVICE ON THE INSTITUTE'S RESEARCH AGENDA.

## **Professor Fiona Cameron (Chair)**

Professor Cameron is a molecular geneticist with a PhD from Macquarie University. A 20-year career with the CSIRO encompassed gene regulation, gene delivery, drug formulation and gene therapy. Professor Cameron has held management roles with the CSIRO Nanotechnology Centre and the National Flagship for Food Futures, as well as running the Innovation and Consulting unit at the University of Western Sydney. Her subsequent roles were Executive Director for Biological Sciences and Biotechnology, and Senior Executive Director at the Australian Research Council.

## **Professor Marilyn Anderson AO**

Professor Marilyn Anderson AO FAA FTSE is Professor of Biochemistry at La Trobe University and the Chief Scientist of Hexima Limited. She is a Fellow of the Australian Academy of Science and the Australian Academy of Technological Sciences and Engineering. She was awarded the Lemberg Medal from the Australian Society of Biochemistry and Molecular Biology in 2014 and the Leach Medal from the Lorne Protein Society in 2017.

## **Professor Susan Dodds**

Professor Dodds is the Deputy Vice-Chancellor (Research and Industry Engagement) and Professor of Philosophy at La Trobe University. A La Trobe University alumnus, having completed her PhD in 1993, she has held senior roles at multiple institutions including the University of New South Wales. Professor Dodds is recognised internationally for her leadership in research ethics and public policy development related to emerging medical technologies, and is an active researcher in applied ethics and political philosophy.

## **Professor Matthias Ernst**

Professor Ernst is the Head of the School of Cancer Medicine at La Trobe University and the Director of the Olivia Newton-John Cancer Research Institute. He obtained his PhD from the ETH Zurich (Switzerland), is a member of the Ludwig Institute for Cancer Research and an Investigator of the NHMRC.

## **Dr Megan Fisher**

Dr Fisher is the Pro Vice-Chancellor (Industry Engagement) at La Trobe University. She has over 20 years experience in executive management and leadership positions in higher education and research-based organisations in the public and private sector, most recently as Director of Research, Innovation and Commercial Engagement at the University of Melbourne. Dr Fisher has a PhD in Organic Chemistry and a Bachelor of Science (First Class Honours) from the University of Sydney, as well as qualifications in business and executive management. Megan has extensive experience in leading and advising on a broad range of commercial transactions.

## **Professor Andrew Hill**

Professor Hill was Director of LIMS from 2017 to 2019 before moving to Associate Provost Research and Industry Engagement for the College of Science Health and Engineering. He obtained his PhD at Imperial College London in 1998. He joined La Trobe University in 2015 as Head of the Department of Biochemistry and Genetics. His research specialises in molecular studies of neurodegenerative diseases and in the application of extracellular vesicles for diagnostics and therapeutics.



### Professor Helen Irving

Professor Irving is the Director of the Understanding Disease Research Focus Area at La Trobe University. Professor Irving obtained her PhD in Biochemistry from the University of Melbourne and conducted post-doctoral work at Vanderbilt University (USA) and the University of Kentucky (USA) before returning to Australia to take up an ARC Post-Doctoral Fellowship at La Trobe University. For most of her career she has been a teaching/research academic based at the Faculty of Pharmacy and Pharmaceutical Sciences at Monash University. Helen moved to the La Trobe Institute for Molecular Sciences in 2017.

### Mr Stephen May

Stephen May has more than 20 years experience working in strategic marketing and development roles across the higher education, not for profit and healthcare sectors. He has an MBA from Mt Eliza/ Melbourne Business School and a Bachelor of Education from Deakin University and brings extensive expertise and knowledge around philanthropy and international alumni programs. Stephen is currently the Chief Advancement Officer at La Trobe University where he is responsible for delivering the \$100M Make the Difference Campaign.

### Professor Andrew Peele

Professor Peele is the Director of ANSTO's Australian Synchrotron. He is an adjunct Professor of Physics at La Trobe University and was seconded to the Australian Synchrotron from La Trobe University in 2011. He is a Fellow of the Australian Academy of Technological Sciences and Engineering and a past president of the Australian Institute of Physics. His research improves the versatility and quality of x-ray imaging.

### Professor Robert Pike

Professor Pike is Provost of the College of Science, Health and Engineering at La Trobe University. He has extensive experience in academic and research leadership roles, and is a former Director of LIMS. Professor Pike is a biochemist specialising in enzymes.

### Dr Tony Radford AO

Dr Radford AO is a Director of Ellume Limited and ASX listed Genetic Signatures Ltd. He was previously Director of Nucleus Networks and CEO of ASX listed Cellestis, from its founding until its acquisition by QIAGEN NV in 2011. For his contributions to tuberculosis diagnosis and enterprise, he received the Clunies Ross Award for the application of technology and is a Distinguished Alumnus of La Trobe University.

### Professor Brian Smith

Professor Brian Smith is Director of LIMS and Head of the School of Molecular Sciences. After completing his PhD in Chemistry at the University of Melbourne he held various research positions before being appointed as La Trobe's inaugural LIMS Principal Research Fellow in 2011. Professor Smith is a Fellow of the Royal Australian Chemical Institute and a Fellow of the Royal Society of Chemistry. He specialises in the determination of protein structure by X-ray crystallography.

# LEADERSHIP TEAM

LIMS IS LED BY AN EXPERIENCED TEAM THAT UNDERSTANDS THE IMPORTANCE OF SCIENTIFIC INNOVATION AND TRANSLATABLE RESEARCH OUTCOMES.



**Professor Brian Smith**

Professor Brian Smith is the Director of LIMS and Head of the School of Molecular Sciences.



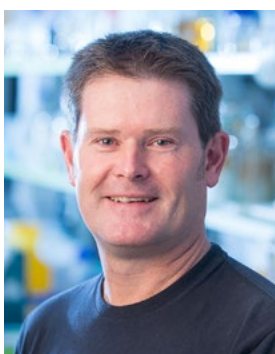
**Professor Brian Abbey**

Professor Brian Abbey is Deputy Director of La Trobe Institute for Molecular Science and the school's Research Director.



**Associate Professor Michael Angove**

Associate Professor Michael Angove is Head of the Department of Pharmacy and Biomedical Sciences, and Academic Director of Transnational Education for PSB Academy.



**Professor Mark Hulett**

Professor Mark Hulett is Head of the Department of Biochemistry and Genetics.



**Associate Professor David Wilson**

Associate Professor David Wilson is Head of the Department of Chemistry and Physics.



**Mrs Denise Strong**

Mrs Denise Strong is School Manager for the School of Molecular Sciences. Mrs Strong holds a ACMA and CGMA.

# LIMS FELLOWS

THE LIMS ENDOWMENT FUND WAS ESTABLISHED TO CREATE NEW AND SUSTAINABLE OPPORTUNITIES FOR SCIENTISTS WITH OUTSTANDING POTENTIAL.

The inaugural Bruce Stone Fellowship in Chemical Biology and the Nicholas Hoogenraad Fellowship in Molecular Sciences were awarded in 2015.

Both fellowships are named after two long-serving leaders: Professor Bruce Stone was the foundation professor of Biochemistry from 1972-1989, succeeded by Professor Nicholas Hoogenraad, who later became the first Director of LIMS. Professor Hoogenraad AO retired in 2014.

## Nicholas Hoogenraad Fellowship

### Dr Nick Reynolds

Dr Nick Reynolds graduated with a PhD from the University of Sheffield in 2009 before undertaking postdoctoral fellowships and research positions at the University of Zurich, CSIRO and the ARC Training Centre for Biodevices (Swinburne University of Technology). His research focuses on the design, discovery and characterisation of self-assembled nanomaterials. These materials have applications in tissue engineering, biosensing, drug delivery and understanding the molecular origins of disease.

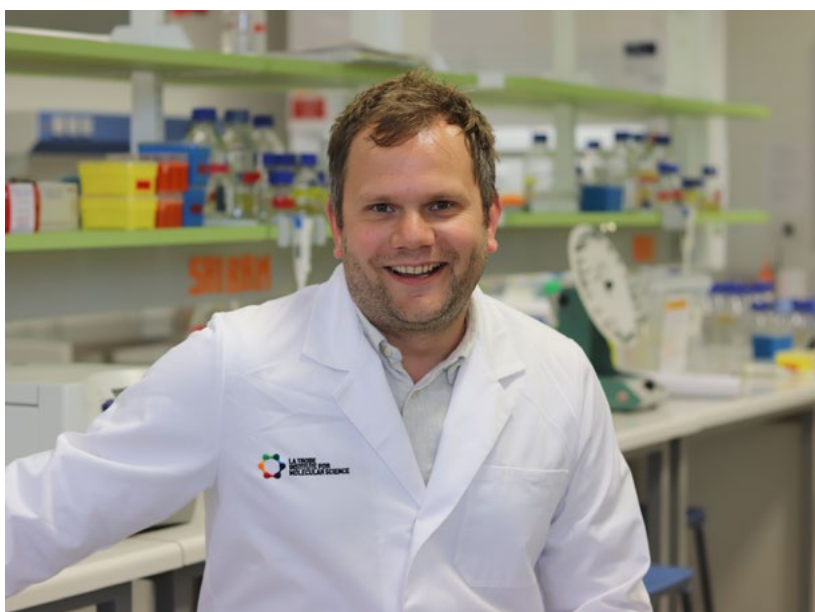
Dr Reynolds works closely with biotech companies and hospitals to promote the translation of fundamental research into devices and commercial products that have real-world impact. Dr Reynolds has published 35 research papers (12 first, 10 corresponding author, > 940 citations) in high impact journals including *Nature Communications*, *Chemical Society Reviews*, *The Journal of the American Chemical Society* and *ACS Nano*. He joined LIMS in 2019.

### Donations

For over a decade LIMS has been supporting mid-career scientists to bring their research to the next level. The LIMS fellowships provide the security and support our elite scientists require in advancing research within their specialist fields including cancer and disease prevention. We are actively seeking to broaden the number of fellowships we offer.

If you would like to find out how you can help by way of a donation or bequest visit [www.latrobe.edu.au/lims/about/support-us](http://www.latrobe.edu.au/lims/about/support-us)

or please get in touch for more information.

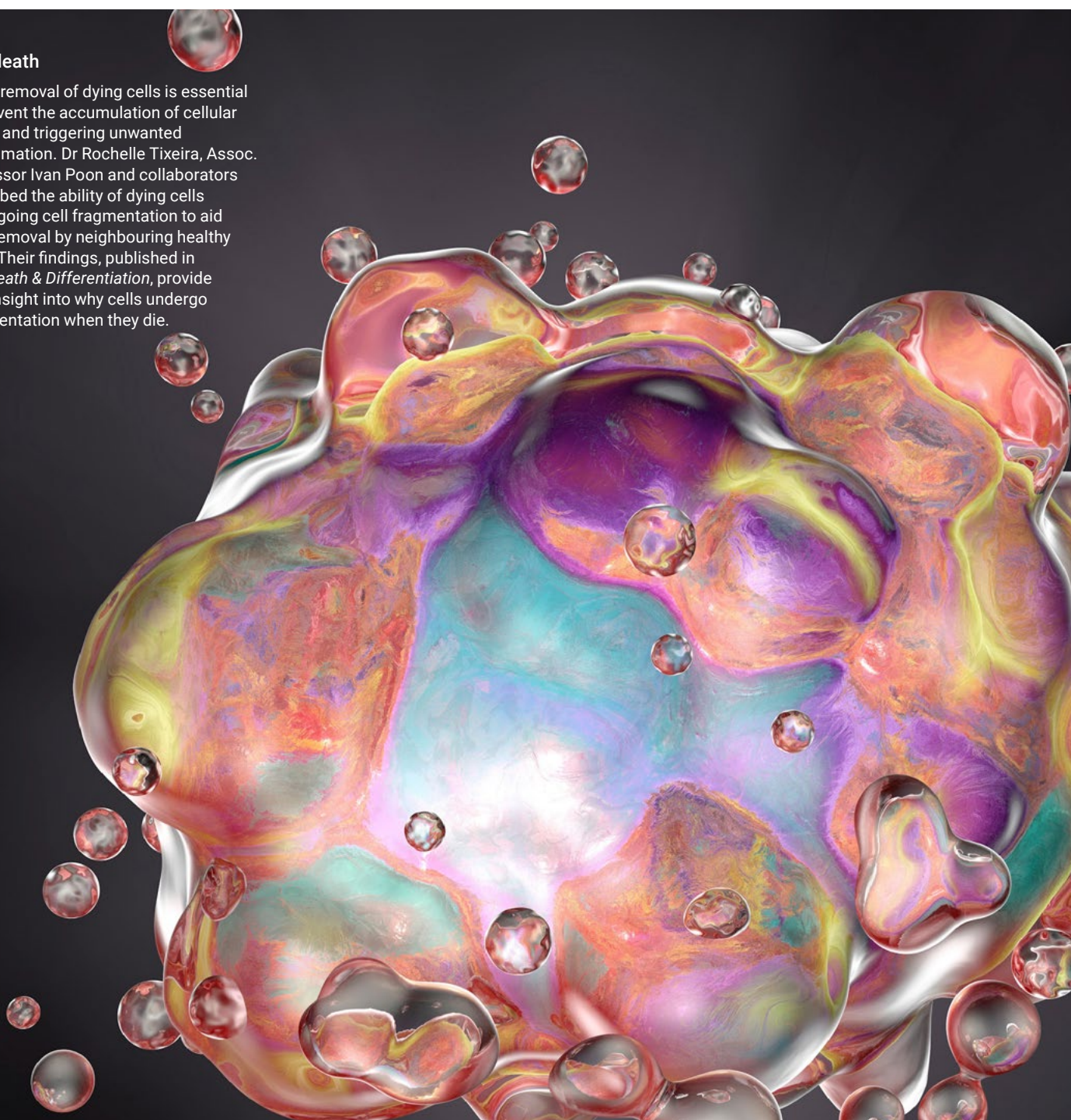




# DISCOVERY HIGHLIGHTS

## Cell death

Rapid removal of dying cells is essential to prevent the accumulation of cellular waste and triggering unwanted inflammation. Dr Rochelle Tixeira, Assoc. Professor Ivan Poon and collaborators described the ability of dying cells undergoing cell fragmentation to aid their removal by neighbouring healthy cells. Their findings, published in *Cell Death & Differentiation*, provide new insight into why cells undergo fragmentation when they die.

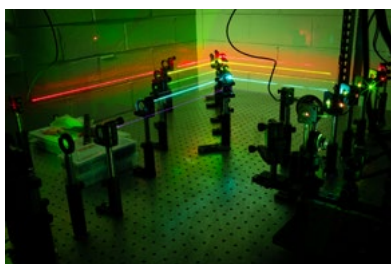


LIMS SCIENTISTS PUBLISH IN HIGH IMPACT JOURNALS INCLUDING *NATURE*, *ANGEWANDTE CHEMIE INTERNATIONAL*, *NUCLEIC ACIDS RESEARCH* AND *APPLIED PHYSICS LETTERS*.



### Necroptosis hope

Chemotherapy drugs damage DNA with the aim to initiate the death of cancer cells. However this can increase the risk of 'therapy-related' secondary cancers. Dr Mark Miles and Associate Professor Christine Hawkins have determined that a version of cell death, known as 'necroptosis,' fails to damage DNA or mutate cells. Their findings in *Cell Death Discovery* imply anti-cancer drugs that activate necroptotic cell death may reduce the risk of therapy-related cancers.



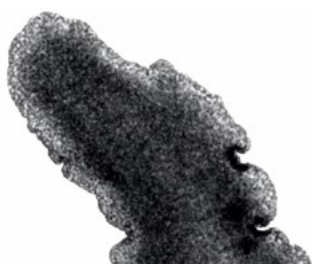
### DNA repair

Investigating DNA repair has long been constrained by the limits of conventional microscopy. Dr Donna Whelan developed assays that use single molecule super-resolution microscopy to capture the moment of an individual DNA double strand break. Findings, published in *PLoS Genetics*, unravel how cells work to avoid and mitigate damage, revealing new pathways and proteins and their key roles in maintaining genomic stability. In the future these assays will produce the most comprehensive picture of DNA repair pathways.



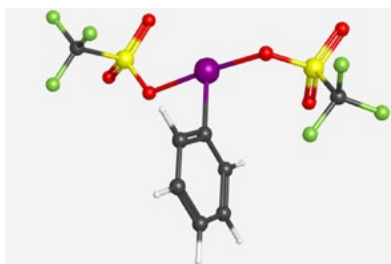
### Molecular chameleon

The folding state of the proteins in live cells often reflect the cell's general health. A team from LIMS including the Heras and Hong labs have developed a molecular probe that senses the state of the proteome by measuring the polarity of the protein environment. As demonstrated in their *Angewandte Chemie* paper, the fluorescence signal of the probe quantifies unfolding and its chameleon-like colour shift maps the cellular regions of enhanced misfolding.



### Ancient rituals

The similarities between altruistic cell death in *Trichoplax adhaerens*, a tiny marine invertebrate, and a similar but defective process in human cancer cells, provides unexpected insights into the workings of a crucial cell survival pathway. The international research team, including Professors Marc Kvasnakul and Patrick Humbert from the La Trobe Institute for Molecular Science, used the Australian Synchrotron to image this ancient mechanism of cell self-sacrifice at the atomic level. Their research was published in *Science Advances*.



### Non-existent chemical

The chemical  $\text{PhI}(\text{OTf})_2$  has long been used in organic chemistry as a strong oxidant but a LIMS team, led by Associate Professor Jason Dutton, has demonstrated that it does not exist at all. Knowing the actual identity of the iodine compounds responsible for these transformations will allow for better prediction and explanation of the outcomes of organic chemistry using the mixtures that were previously misidentified as  $\text{PhI}(\text{OTf})_2$ . Findings were published in *Chemistry – A European Journal*.



### Brilliant diamonds

Diamonds can withstand high-voltage, high-power operations, extreme conditions and hold the promise to enable next-generation technologies. The Atom Scale Research Group, led by Professor Chris Pakes and Dr Alex Schenk, has developed a method of growing silicon carbide on diamond. Findings, in *ACS Applied Electronic Materials*, create a pathway to better thermal management in traditional power electronics and is the first demonstration of a new pathway for forming epitaxial semiconductor heterojunctions with diamond.

# LOCKED-DOWN BUT NOT OUT

IT WAS ON 24 JANUARY 2020 THAT COMMUNICATION FROM LA TROBE UNIVERSITY TO ITS STAFF AND ACADEMICS FIRST WARNED OF A NEW CORONAVIRUS IN WUHAN. LESS THAN TWO MONTHS LATER THE WORLD HEALTH ORGANISATION HAD DECLARED A PANDEMIC, LA TROBE STAFF WERE WORKING FROM HOME, THE VICTORIAN PREMIER HAD DECLARED A STATE OF EMERGENCY AND INTERNATIONAL TRAVEL WAS EFFECTIVELY SUSPENDED.

As we now know, this was just the beginning.

Yet through all of this, the research output at LIMS exceeded that of the previous year in both citation impact score and in the total number of published papers. It was a year to remember, and not just for the wrong reasons.

Six of our research teams seized the once-in-a-lifetime opportunity to work on a completely new virus, contributing their molecular investigations into SARS-CoV-2 to the global research effort.

Other LIMS academics capitalised on their time out of the laboratory by writing up their past research. Many of our labs published in excess of ten papers in 2020.

Our HDR students took advantage of having more time at home by finessing their literature review and planning the next phase of their research. And whilst a handful of students deferred their degree, the vast majority of LIMS Honours, Masters and PhD students remained committed to their studies.

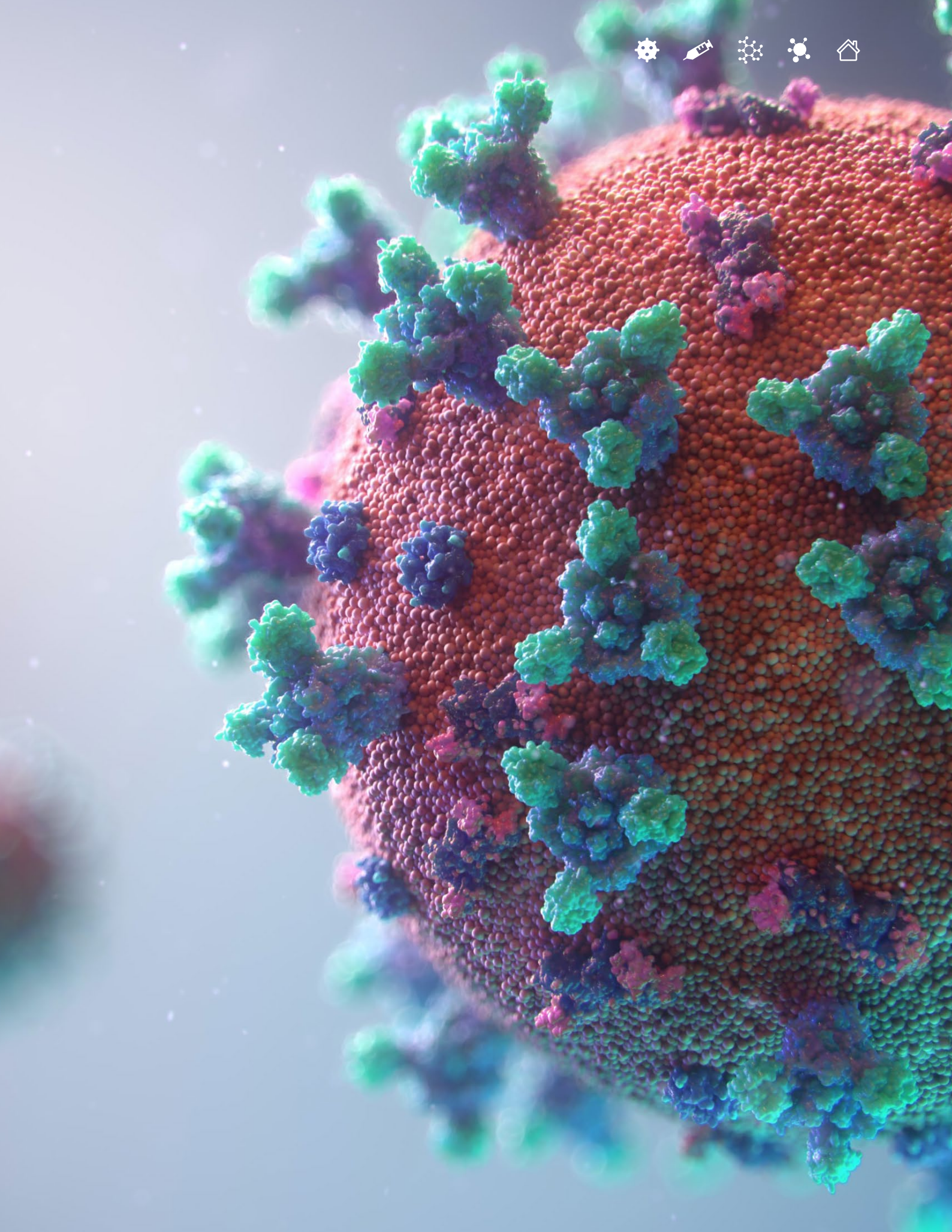
"We saw a lot of positives and real highlights coming from what was a challenging year," says LIMS Director Professor Brian Smith.

Two international PhD students, Ruitao and Sitong, had returned to China for Chinese New Year in January 2020. Pandemic related restrictions saw them unable to return to Australia. Yet through the efforts of La Trobe University and his supervisor, Ruitao was able to complete his PhD in molecular modelling in 2020. And with access to her supervisor and La Trobe Research facilities, Sitong remains strongly connected and on track to complete her PhD in 2021.

Masters student, Tania, spent much of 2020 locked out of the lab yet made the switch to computational chemistry and completed her degree remotely. Working with two PhD students who had onsite lab access, the research team was able to debunk the science behind a long-held chemistry practice and publish in a high impact journal.

"These are just two examples of how LIMS academics, students and staff remained locked-down but not out. I am immensely proud of the way our people rose to the many challenges of lock-down, lab lock-outs and remote teaching," said Professor Smith.





# CANCER



The Cancer theme investigates the mechanisms of cancer initiation and progression, the crosstalk between cancer cells and the surrounding environment, and the discovery of new therapeutic approaches to combat the disease.

## Theme leader

**Erinna Lee**

Senior Lecturer

**Apoptosis, autophagy, cancer, drug discovery, cell biology, biochemistry, structural biology**

Examines cell death/survival by apoptosis and autophagy, using biochemistry, cell biology and structural biology approaches. Uses this information to understand normal physiology and to develop therapeutics targeting these pathways.

## Members

**Suzanne Cutts**

Senior Lecturer

**Cellular responses to anticancer drugs**

Develops new therapeutic strategies for cancer treatment. Examines the mechanism of action of anticancer drugs. Works to restrict the killing properties of these drugs to cancerous cell types to minimise their toxic side effects.

**Doug Fairlie**

Associate Professor

**Apoptosis, autophagy, cancer, drug development and peptides**

Uses biochemical, cell biology, structural biology and medicinal chemistry approaches to understand the molecular mechanisms that control apoptosis. Develops new reagents, including drugs that could target and inhibit the actions of the key pro-survival proteins that keep cancers alive.

**David Greening**

Senior Research Fellow

**Functional proteomics, extracellular vesicles, cell reprogramming, nanotechnology**

Specialises in quantitative proteomics, secreted factors and extracellular vesicles in cardiometabolic disease and normal physiology. Investigates the molecular basis of cell signalling, identifies new deliverable therapeutic targets for cell-free therapy, and engineers nano-carriers for targeted delivery.

**Christine Hawkins**

Associate Professor

**Cell death regulation in cancer and viral infection**

Studies apoptotic regulation in normal, cancerous and virally-infected cells. Explores the potential for molecularly targeted therapies to improve outcomes for patients with the bone cancer osteosarcoma.

**Nick Hoogenraad AO**

Emeritus Professor

**Development of therapeutic antibodies against cachexia**

Specialises in cancer cachexia, a serious wasting condition and a major complication of cancer. Investigates the molecular basis of this condition and therapeutic intervention using monoclonal antibodies, with the aim of discovering biomarkers for early diagnosis and monitoring the outcome of treatment.

**Patrick Humbert**

Professor

**Cancer biology, cell polarity and tissue architecture**

Determines how cell asymmetry and tissue organisation can regulate cancer initiation, progression and metastasis. Examines how the cell polarity genetic program may be involved in tissue regeneration as well as developmental processes such as blood cell production and function.





### **Mihwa Lee**

**Tracey Banivanua Mar Fellow**

#### **Structural biology in gene regulation and DNA damage repair pathway**

Uses a multidisciplinary approach combining molecular biology, protein chemistry, cell biology and X-ray crystallography. Characterises the macromolecular complexes (protein-protein and protein-nucleic acid complexes) in the nucleus to understand their fundamental roles in gene regulation and the DNA damage repair pathway.

### **Suresh Mathivanan**

**Professor and ARC Future Fellow**

#### **Exosomes, secretome and systems biology**

Explores the role of extracellular matrix components (soluble secreted proteins and extracellular vesicles) in cancer and intercellular communication using proteomic, genomic and bioinformatics methodologies. Undertakes basic science projects including the biogenesis of exosomes and the role of exosomes in intercellular communication.

### **Helena Richardson**

**Associate Professor**

#### **Cell polarity, cell signalling and cancer lab**

Uses the vinegar fly, *Drosophila*, to determine how regulators of cell shape (polarity) and the cell skeleton (actin cytoskeleton) impact on cell signalling and cancer initiation and progression, and to identify novel pathways that cooperate with the Ras oncogene in cancer.

### **Richard Simpson**

**Distinguished Professor**

#### **Extracellular vesicles, exosomes, shed midbody remnants and cancer biology**

Uses an integrated proteomic, RNA profiling, bioinformatics and live-cell imaging strategy to understand the seminal role of extracellular vesicles in cell-cell communication in the extracellular environment during cancer progression and cancer plasticity.

### **Sarah Stewart**

**ARC DECRA Fellow**

#### **Unconventional protein secretion, extracellular vesicles and intercellular communication**

Investigates alternative pathways for protein secretion from mammalian cells. Focuses on describing mechanisms of unconventional protein secretion including secretion of extracellular vesicles and their role in cellular homeostasis and disease.

### **Kaye Truscott**

**Senior Lecturer**

#### **Mitochondrial protein homeostasis**

Studies the function of proteins engaged in the biogenesis and maintenance of mitochondria, the cell's power plant and manufacturer of essential biomolecules. At a molecular level investigates mitochondrial factors contributing to the development of human diseases including rare neuroendocrine tumours.

### **Donna Whelan**

**ARC DECRA Fellow**

#### **Biophysics, DNA damage, fluorescence, single molecule imaging**

Applies state-of-the-art techniques to biological questions. Uses microscopic and spectroscopic methods to visualise the compositions and ultrastructures of individual cells and their subcomponents.



# THE CURSE OF THE NEMATODE WORM

NEMATODE WORMS ARE THE MOST DIVERSE AND UBIQUITOUS ORGANISMS ON EARTH. THERE ARE MANY MORE VARIETIES OF NEMATODES, OFTEN REFERRED TO AS ROUNDWORMS, THAN THERE ARE DAYS IN A DECADE. AND IF YOU HEAD OUT INTO YOUR GARDEN YOU'LL FIND THOUSANDS OF INDIVIDUAL NEMATODES WITHIN JUST A SMALL HANDFUL OF SOIL.

The sheer abundance of nematode worms, and their ability to adapt, are causes for concern. The worms are responsible for countless diseases in humans, livestock and plants. Yet good can arise from bad. There are learnings scientists can forge from studying nematodes.

In 2002, Nobel prize-winning work in the model nematode species *C. elegans* laid the foundation for the field of research that investigates how cells live or die. This has had a significant impact beyond worms as the process that dictates cell fate is a critical factor in the development of cancer and how patients respond to anti-cancer treatments.

In 2020, researchers from the La Trobe Institute for Molecular Science including Associate Professor Doug Fairlie and Dr Erinna Lee (with collaborators at the University of Melbourne and WEHI) identified and characterised key cell survival/death molecules in over 80 nematode species. The research team point to a greater diversity in numbers and potential regulatory mechanisms than previously believed present.

The findings, published in *Communications Biology*, provide unexpected insights into the evolution of how cells survive. Importantly, the results pave the way for the repurposing of anti-cancer drugs that work by triggering cell death as new anti-infectives, and the team has just published another study in *ACS Infectious Diseases* reporting the first of these compounds.

"It's exciting that we have been able to go from a fundamental evolutionary study to the creation of new compounds targeting these pathways in diverse organisms," said Associate Professor Fairlie.

"Our hope is that we can now develop these further and generate drugs that could have a real impact against infectious diseases caused by nematodes and other parasitic worms."

For more information on this research or other Cancer related discoveries please contact the La Trobe Institute for Molecular Science.



Dr Erinna Lee and Associate Professor Doug Fairlie

# INFECTION AND IMMUNITY

The Infection and Immunity theme studies the molecules used by viruses, bacteria, parasites and fungi to infect humans, animals and plants, and the immune response associated with this.

## Theme leader

**Begoña Heras**  
Associate Professor

### Structural Biology of Bacterial Pathogenesis

Studies the molecular mechanisms underlying Gram-negative bacterial infections. Uses a multidisciplinary approach combining X-ray crystallography, molecular biology and biochemistry to investigate the structure-function relationships in proteins involved in bacterial pathogenesis and develop antibacterial drugs with novel modes of action.

## Members

**Marilyn Anderson AO, FAA, FTSE**  
Professor

### Plant innate immunity proteins

Specialises in protection of humans and crops from pathogens by studying natural defences of plants and the biology of the pathogens themselves. Identifies insecticidal and antifungal molecules in Australian native plants for commercial applications in crop protection and human antifungal therapeutics. Chief Science Officer of the biotechnology company Hexima, which is embedded in LIMS and involved in the R&D of plant derived proteins and peptides.

**Amy Baxter**  
NHMRC Peter Doherty Fellow

### Extracellular vesicles in cell death

Focuses on the role of endothelial cell derived apoptotic bodies in intercellular communication and clearance during vascular inflammation, using both *in vitro* and *in vivo* models of disease.

**Katrina Binger**  
Lecturer

### Macrophage metabolism in biology and disease

Investigates the role of the physical and chemical composition of the tissue microenvironment on immune cell function. Focuses on innate immune cells, macrophages, and how metabolites and electrolytes modulate metabolic pathways to identify new targets for treating inflammatory diseases and infection.

**Weisan Chen**  
Professor

### Cellular immunity to influenza A virus and transplant antigens

Specialises in CD8+ T cell biology and antigen processing and presentation in the development of cross-protective immune responses to the influenza virus and the initiation of transplant immunity. Investigates interactions between T cells and antigen-presenting cells, such as dendritic cells, macrophages and monocytes.

**Mick Foley**  
Professor

### Use of single domain antibodies as therapeutics in fibrosis and other chronic diseases

Uses a library of single domain antibodies derived from sharks to identify antibodies that bind and block the function of proteins shown to be involved in human pathological conditions such as fibrosis of the lung, kidney and eye as potential therapies for these diseases. Chief Scientific Officer of AdAlta, a LIMS embedded company.

**Andrew Hill**  
Professor and Associate Provost  
(Research and Industry Engagement)

### Neurodegenerative diseases, extracellular vesicles and noncoding RNA's

Uses *in vitro* and *in vivo* models to look at how abnormal proteins and RNA travel from cell to cell and are involved in neurodegenerative diseases. Studies the biology of extracellular vesicles and their potential use as diagnostics in neurological and infectious diseases.

**Di Hughes**  
Lecturer

### Oxidative stress, erythrocyte morphology and haemorheology

Researches peripheral oxidative stress in Parkinson's disease and rheumatoid arthritis. Studies erythrocyte morphology and haemorheology parameters to mark peripheral oxidative stress and whole blood antioxidant capacity.

**Mark Hulett**  
Professor and Head of Biochemistry and Genetics

### Innate defence and inflammation

Investigates molecular mechanisms that drive inflammatory disease, innate immunity and tumour progression. Focuses on the function of innate defence peptides and the heparan sulphate-degrading enzyme heparanase in order to develop novel therapeutics to treat infection, inflammatory disease and cancer.





### **Helen Irving**

**Professor and Director of Understanding Disease Research Focus Area**

#### **Proteins in the innate immune system**

Studies unusual mechanisms that proteins in the innate immune system use to signal processes in cells to control inflammatory responses. Uses a multidisciplinary approach involving protein molecular, cell biology and protein chemistry supplemented by bioinformatics and systems approaches.

### **Cristina Keightley**

**Senior Lecturer**

#### **Myeloid development and disease**

Seeks to discover and understand molecular pathways controlling myeloid cell development and disease. Focuses on haematopoietic stem cells and the innate immune response. Informs the design of pharmaceuticals, including stem cell therapies.

### **Christine Kettle**

**Lecturer**

#### **Autonomic and central nervous system regulation of metabolism**

Examines the physiology of metabolism to find novel drug targets that activate brown adipose tissue (BAT) thermogenesis. Activation of BAT is a possible pathway to target obesity.

### **Marc Kvsanakul**

**Professor**

#### **Structural biology of cell death and host pathogen interactions**

Examines how viruses hijack cellular defence systems to ensure their own proliferation and survival. Understands the role of small proteins that act as a first line of defence against microbial targets and the mechanisms they use to destroy target cell membranes.

### **Ronan O'Toole**

**Associate Professor**

#### **Infectious diseases and antimicrobial resistance**

Applies genomic epidemiology to track the origin and spread of healthcare-associated pathogens such as *Enterococcus faecium*, to map the acquisition of antibiotic resistance by *Mycobacterium tuberculosis* in relation to treatment outcomes and to correlate genotypes of non-typeable *Haemophilus influenzae* strains with chronic obstructive pulmonary disease presentations.

### **Jacqueline Orian**

**Senior Research Fellow**

#### **Neurodegenerative diseases**

Investigates mechanisms underlying blood brain barrier damage and neuronal loss in Multiple Sclerosis (MS). Uses the experimental autoimmune encephalomyelitis (EAE) MS model to generate proof of concept for pathological and molecular neurodegenerative mechanisms. The long-term view is to develop novel therapeutics that will delay entry into progressive MS.

### **Ivan Poon**

**Associate Professor and NHMRC EL2 Fellow**

#### **Apoptotic cell disassembly and clearance**

Studies the machinery that controls how dying cells can disassemble into smaller pieces. Specialises in the importance of cell disassembly in disease settings, such as influenza A infection and atherosclerosis to identify new drugs to control this process.

### **Hamsa Puthalakath**

**Associate Professor**

#### **Regulation of apoptosis by Bcl-2 family proteins**

Studies apoptosis regulation by Bcl-2 family proteins in different pathophysiologicals using *in vitro* and *in vivo* models. This includes death of immune cells during polymicrobial sepsis leading to immune paralysis, and the death of heart muscle cells leading to cardiomyopathy and heart failure.

### **Joseph Tucci**

**Associate Professor**

#### **Bacteriophage as alternatives to antibiotics, pharmacogenomics and pharmacy practice**

Examines the personalisation of medicine to fit a patient's genetic profile, particularly in traditional and Indigenous populations. Studies the use of bacteriophage as an alternative to antibiotics and how these can be delivered clinically.

### **James Van Dyke**

**Senior Lecturer**

#### **Integrative Physiology**

Studies how vertebrate physiology interacts with environment to determine reproductive success. Focuses in particular on the physiology and evolution of placentation as a model for complex trait evolution. Also applies physiological approaches to solving environmental problems in the Murray-Darling catchment.

### **Lakshmi Wijeyewickrema**

**Lecturer**

#### **Proteases, inhibitors and receptors: relationship to disease states**

Without enzymes human life would be impossible. Enzymes play an essential role in the immune system, including the reduction of inflammation. Understanding how enzymes work is integral in understanding how we can prevent and fight disease.

# THE FIGHT AGAINST SEPSIS

SCIENTISTS ARE ONE STEP CLOSER TO WINNING THE FIGHT AGAINST SEPSIS, A DISEASE THAT EACH YEAR KILLS ONE IN FIVE OR 11 MILLION PEOPLE WORLDWIDE.

Sepsis is caused by the immune system going into over-drive in response to infection. It leads to extreme inflammation that can cause blood clots and block oxygen from reaching vital organs, resulting in tissue death and multiple organ failure.

Researchers from the La Trobe Institute for Molecular Science have identified and characterised the gene responsible for immune cell death and inflammation during sepsis.

This significant finding, published in *Nature Immunology*, reveals that removal of protein receptor TREML4 in cell based and in-vivo experiments leads to almost absolute protection from sepsis, sepsis-induced pneumonia and blood-born *Candida* infection commonly associated with invasive medical procedures.

Lead researcher Dr Christina Nedeva from LIMS said sepsis is characterised by two deadly stages.

"The initial inflammatory phase, or septic shock, is followed by a prolonged immunosuppression phase, which commonly leads to pneumonia. While the shock accounts for about 15 per cent of sepsis-related deaths, the immunosuppression phase accounts for 85 per cent," Dr Nedeva said.

"Excitingly, we've discovered the TREML4 gene regulates both of these phases."

Lead supervisor of the study at LIMS, Associate Professor Hamsa

Puthalakath, said current therapies aimed at controlling inflammation such as the use of steroids, help reduce the time that sepsis patients spend in intensive care units, but do not reduce the overall deaths.

"Steroids reduce inflammation, but they also wipe out the immune system, preventing our body from fighting both mild and serious infections," Associate Professor Puthalakath said.

"The removal of TREML4 can be described as the 'Goldilocks' approach, in that it leaves the body with some inflammation, but the immune system remains uncompromised and is healthy enough to fight off infection."

The researchers have already identified the human equivalents of the TREML4 receptor.

"There have been more than 100 clinical trials for sepsis-related therapies in the last 25 years, none of which have proved successful," Associate Professor Puthalakath said.

"LIMS is on the forefront of potentially life-saving research. We hope to secure new funding for the next stage of our study, which will focus on the development of therapeutic antibodies against the TREML4 receptor."

For more information on this research or other Infection and Immunity related discoveries please contact the La Trobe Institute for Molecular Science.





Associate Professor Hamsa Puthalakath and Dr Christina Nedeva



# MOLECULAR DESIGN

The Molecular Design theme uses molecules to solve real world problems from computational studies on the interaction of drugs with proteins, to molecular synthesis, and surface and material science.

## Theme leader

**Yuning Hong**

Senior Lecturer

**Fluorescent probes, cell imaging, protein misfolding and neurodegenerative diseases**

Develops fluorescence-based tools for understanding and manipulating fundamental biological processes. Designs and synthesises new luminescent molecules in combination with advanced fluorescence spectroscopy and microscopy for monitoring protein conformational transitions associated with neurodegenerative diseases.

## Members

**Belinda Abbott**

Senior Lecturer

**Medicinal chemistry and synthetic organic chemistry**

Uses synthetic organic chemistry to make novel compounds for testing in biological assays in order to study the structure-activity relationships of how the compounds interact with the target. Develops treatments for bacterial infection, malaria, cardiomyopathy and motor neurone disease.

**Carmel Abrahams**

Senior Lecturer

**Supramolecular chemistry and single crystal X-ray diffraction characterisation of small molecules**

Investigates the design, synthesis and characterisation of supramolecular systems. Studies the use of the biodegradable porous compound Zn saccharate and its ability to act as a host for molecules such as small aromatic hydrocarbons.

**Jasim Al-Rawi**

Senior Lecturer

**Heterocyclic compounds such as PNA-PK, PI3K PDE3 inhibitors for cancer treatment**

Synthesis of novel benzoxazines as DNA-PK, PI3K inhibitors for more effective treatment of cancer. Studies PI3K isoform selectivity as well as DNA-PK selectivity over PI3K. Uses molecular modelling to explain drug-receptor optimum interaction.

**Peter Barnard**

Senior Lecturer

**Synthetic organic and inorganic chemistry**

Synthesises coordination complexes for diagnostic imaging applications and sensor development. Specialises in small molecule organic and inorganic synthesis in combination with analytical techniques for the generation and characterisation of new compounds.

**Jason Dutton**

Associate Professor

**Organic, organometallic and inorganic chemistry from synthetic and theoretical perspectives**

Examines the fundamental chemistry of a wide variety of systems (literally spanning the periodic table from beryllium to iodine) using both synthetic and computational approaches. Discovers new structures, bonding and reactivity for a variety of elements.

**Cathryn Hogarth**

Senior Lecturer and

Head of Campus Albury-Wodonga

**Sperm development and maturation**

Investigates the role that retinoic acid plays in the differentiation and maturation of sperm within the testis and epididymis. Focuses on how the production of retinoic acid is controlled within these organs and the downstream molecular targets of retinoic acid signalling. The ultimate goal is to develop new strategies for the treatment of male infertility and novel male contraceptives.

**John Moses**

Professor and ARC Future Fellow

**Design and synthesis of new functional molecular entities**

Designs and synthesises new functional molecular entities and develops new methodologies for challenging and useful chemical reactions/transformations. Specialises in click chemistry, natural product synthesis and chemical biology.

**Matthew Perugini**

Associate Professor

**Rational drug design targeting infection and age-related diseases**

Studies the structure, function, regulation and inhibition of essential oligomeric enzymes such as dihydrodipicolinate synthase from the lysine biosynthesis pathway of bacteria. Characterises the role of apolipoprotein E in cardiovascular and Alzheimer's diseases.

**Pallavi Sharma**

Senior Lecturer

**Synthetic organic chemistry**

Develops new synthetic methodology that delivers structurally diverse and complex chemical entities via rapid fusion of short lived reactive species. Using under-represented reagents, explores their latent reactivity for heterocycles, spirocycles, natural products and analogue synthesis.

**Brian Smith**

Professor, Director of LIMS and Head of the School of Molecular Sciences

**Modelling molecular interactions**

Uses quantum-mechanical methods to understand enzyme mechanism, molecular mechanical methods to explore the dynamics of proteins, and a variety of tools to predict how molecules interact. Uses X-ray crystallography to determine the structures of complexes of proteins, polypeptides and small molecules.

**Tatiana Soares da Costa**

ARC DECRA Fellow

**Antibiotic and Herbicide Discovery**

Examines the structure, function and regulation of essential proteins in bacteria and plants to guide the development of novel classes of antibiotics and herbicides. Focuses on targets involved in cell wall and amino acid syntheses and employs techniques encompassing biochemistry, bacteriology, biophysics, chemistry and plant biology.

**David Wilson**

Associate Professor and Head of Chemistry and Physics

**Computational chemistry and quantum chemistry**

Uses computational quantum chemistry to model molecular structures, properties and spectroscopies, as well as the energetics of reactions. Focuses on understanding the fundamental properties of chemical bonding and electronic structure in the design of new chemistry and new materials.

**David Winkler**

Professor

**Computational molecular design and AI**

Uses computational methods to study the interaction of molecules and complex materials. Expertise in the application of AI, machine learning and evolutionary computational methods to design bespoke materials with novel properties. Designs small molecules and peptides as drug leads, novel 2D hybrid materials for energy applications, biomaterials and coatings to control immunity and cell behaviour, and advanced informatics methods for surface science.

# CHALLENGING MOLECULAR DOGMAS

OFTEN IT IS THE WORK OF RESEARCHERS STUDYING “BASIC” OR “FUNDAMENTAL” SCIENCE, SUCH AS ION CHANNELS, THAT LEADS THE WAY TO DISCOVERING THERAPEUTIC TREATMENTS FOR SOME OF HUMANKINDS MOST DEBILITATING AND DESTRUCTIVE DISEASES.

Ion channels are proteins contained within the plasma membrane. A primary function of ion channels is to mediate the cell interaction with its environment, providing a passageway through which charged ions can pass.

While structures of many ion channels have been determined, their mechanism at an atomic detail remains elusive.

Some ion channels, including potassium channels, are best known for propagating the electrical signals that drive the central nervous system and vital organs. The failing of this system can cause diseases such as epilepsy, depression, multiple sclerosis, Huntington’s disease, and the invasiveness of gliomas – to name but a few.

Potassium channels allow potassium ions to cross cell membranes with exquisite selectivity. Conventional wisdom dictated that these structures underwent significant change to allow these ions to traverse the path linking the two sides of the membrane.

However a study co-led by LIMS Director, Professor Brian Smith and published in *Nature Communications*, shows that these ions can pass one of the restrictions along the path with very little structural deformation of the channel structure.

According to Professor Smith, “These findings question the long unchallenged dogma relating to the mechanism of ion conduction.”

Current drug design strategies rely heavily on understanding the structure and mechanism of disease related proteins and there are few therapeutics currently on the market that target these channels.

“This varied awareness of channel mechanism provides a new strategy for the design of drugs that target channelopathies, which are diseases caused by dysfunctional ion channels,” said Professor Smith.

For more information on this research or other Molecular Design related discoveries please contact the La Trobe Institute for Molecular Science.

*This project is a long-standing collaboration between Professor Brian Smith at LIMS and Dr Jacqui Gulbis at WEHI.*





Professor Brian Smith

# NANOSCIENCE

The Nanoscience theme uses a broad range of methods to characterise molecular structure and function, and to identify and quantitate key chemical and biochemical species in the environment and in the human body.

## Theme leader

### Grant van Riessen

#### Senior Lecturer

Experimental condensed matter and materials physics, and coherent X-ray imaging development

Develops new ways of characterising and manipulating materials using coherent synchrotron light sources, with the aims of realising *in situ* imaging of nanoscale dynamics and enabling the next generation of lithographic patterning technology.

## Members

### Brian Abbey

#### Professor, Deputy Director of LIMS and Director of Research, School of Molecular Sciences

##### Coherent X-ray science and optics

Combines elements of optics, nanofabrication and X-ray free-electron lasers to develop new approaches to imaging materials and structures at the atomic, molecular and cellular level. Develops techniques for interpreting patterns of coherently scattered light.

### Russell Anderson

#### Senior Lecturer

##### Quantum enhanced sensing based on atom-light interactions

Develops next-generation quantum technologies with defence, medical and commercial applications. These include quantum-assured position, navigation and timing (PNT), and new perspectives on optical atomic magnetometry. Is also a leader in software control and automation of quantum technologies.

### Michael Angove

#### Associate Professor and Head of Pharmacy and Biomedical Sciences

##### Colloid, environmental and pharmaceutical science

Uses colloid chemistry to research environmental and agricultural soil systems so that we are better placed to manage soil environments and even rehabilitate damaged or contaminated soils. Studies pharmaceutical products that utilise colloidal particles and systems.

### Narelle Brack

#### Associate Professor and Associate Head of the School of Molecular Sciences

##### Surface modification and

##### characterisation of advanced materials

Creates materials at the nanometer scale. Explores chemical and molecular properties and processes at surfaces and at interfaces. Develops surface modification strategies for material systems including next generation aircraft materials and carbon nanofibers.

### Conor Hogan

#### Associate Professor

##### Electrochemistry, photochemistry, chemical sensing and biosensing

Conducts fundamental and applied multidisciplinary research with the aim of expanding the bounds of analytical science and translation for real-world applications. A world leader in ultrasensitive electrochemiluminescence (ECL) based detection and the use of mobile phones and other personal electronic devices for low-cost chemical / biochemical analysis.

### David Hoxley

#### Lecturer

##### Biosensing applications of wide bandgap semiconductors

Studies the surfaces of semiconductor crystals, particularly diamond, and how they react to the world around and within us. Researches ways of making coaching possible in the tertiary education system, primarily through combining modern educational psychology with information technology.

**Shanshan Kou**  
Lecturer

**Bio-imaging and bio-photonics, optical micro- and nano-scopy, and biomedical instrumentation**

Studies the interactions between light and biological matter to explore and discover the complex mechanisms behind cellular and sub-cellular events and processes. Develops novel bio-imaging modalities and instrumentation to be used in new diagnostic and therapeutic tools.

**Adam Mechler**  
Associate Professor

**Bioinspired self-assembling nanostructures**

Studies the mechanism of antimicrobial peptide-membrane interactions, the formation of metallosupramolecular assemblies and the reaction pathways of antioxidant activity. Applies principles of self-assembly in the development of novel peptide antibiotics, antivirals and the design of oligoamide-based metamaterials.

**Chris Pakes**  
Professor and Pro Vice-Chancellor (Graduate and Global Research)

**Quantum materials for quantum computing, low-power spintronics and biosensing**

Examines the functionalisation of diamond via chemical modification of the surface and surface transfer doping. Focuses on atom-scale engineering of diamond devices for next-generation digital technologies enabling low-power and secure information processing.

**Paul Pigram**  
Professor

**Interactions at surfaces**

Creates, understands and controls materials at the nanometer scale. Focuses on surface science, in particular exploring chemical and molecular properties and processes at surfaces and at interfaces, understanding molecular interactions at surfaces, and bio-surface characterisation.

**Ian Potter**  
Senior Lecturer

**Analytical and environmental chemistry**

Prepares polymer inclusion membranes and polymer-based microspheres for use as small-scale chemical reactors and sensors for biological, environmental and industrial applications. Develops methods to analyse plant biomarkers. Develops forensic analysis methods to determine the production method and source of dangerous chemicals.

**Nick Reynolds**  
Nicholas Hoogenraad Fellow

**Self-assembled nanomaterials**

Translational research into the design, discovery and characterisation of self-assembled nanomaterials with applications in fields including tissue engineering, drug delivery, antibacterial materials, biosensing and understanding disease.

**Evan Robertson**  
Associate Professor

**Optical spectroscopy of atmospheric and biological molecules**

Uses powerful light sources, such as lasers and the Australian Synchrotron's infrared beamline, to study the shape of neurotransmitter molecules relevant to pharmaceuticals, greenhouse gas molecules, ice cloud particles and even molecules in the interstellar medium.

**Chanh Tran**  
Lecturer

**Interactions of X-rays with matter, optical coherence and X-ray imaging**

Specialises in various forms of X-ray imaging, precision determination of the interaction cross-sections between X-rays and a range of elements and compounds. Developing phase spectroscopy and imaging of dynamic systems.



# UNDERSTANDING THE ROLE OF CHOLESTEROL AT THE NANOSCALE

IT IS WELL KNOWN THAT CHOLESTEROL IS ASSOCIATED WITH AN INCREASED RISK OF HEART ATTACK OR STROKE WHEN IT IS PRESENT IN OUR BLOOD AT HIGH LEVELS. HOWEVER, WHEN NOT PRESENT IN EXCESS QUANTITIES, CHOLESTEROL PLAYS A POSITIVE ROLE IN OUR HEALTH.

The molecule is a key component of the outer layer of our cells, known as the cell membrane, and contributes to important biological processes like cell communication.

The interdisciplinary LIMS team coordinated by Dr Shanshan Kou, Associate Professor Adam Mechler, Professor Brian Abbey and Dr Arif Siddiquee have used a new scientific technique to examine the composition of synthetic cell membranes at the nanoscale.

Their findings have identified where cholesterol is found in synthetic cell membranes, and why.

"Scientists have been unable to determine the specific location of cholesterol in the cell membrane, or how it might influence membrane structure and function," explained Dr Kou.

"The main challenge is that it's a very small molecule. It has been virtually impossible to investigate its role without affecting its function."

The research team used a technique called spectroscopic scanning near-field optical microscopy to image the synthetic membranes without disrupting them. This type of microscopy captures three-dimensional images of materials at the nanoscale, along with new chemical data.

"By examining cholesterol in this way, we discovered that it is not evenly distributed in the synthetic membrane, but instead forms localised, cholesterol-rich islands. Islands like these have been identified in natural cell membranes and play a role in natural and pathogenic membrane processes," said Dr Kou.

The team also identified molecular-scale interactions between cholesterol and the main membrane components, which offer insight into how the islands form in synthetic membranes. "The islands form spontaneously, which indicates that such processes are key to membrane development in biological cells," said Dr Kou.

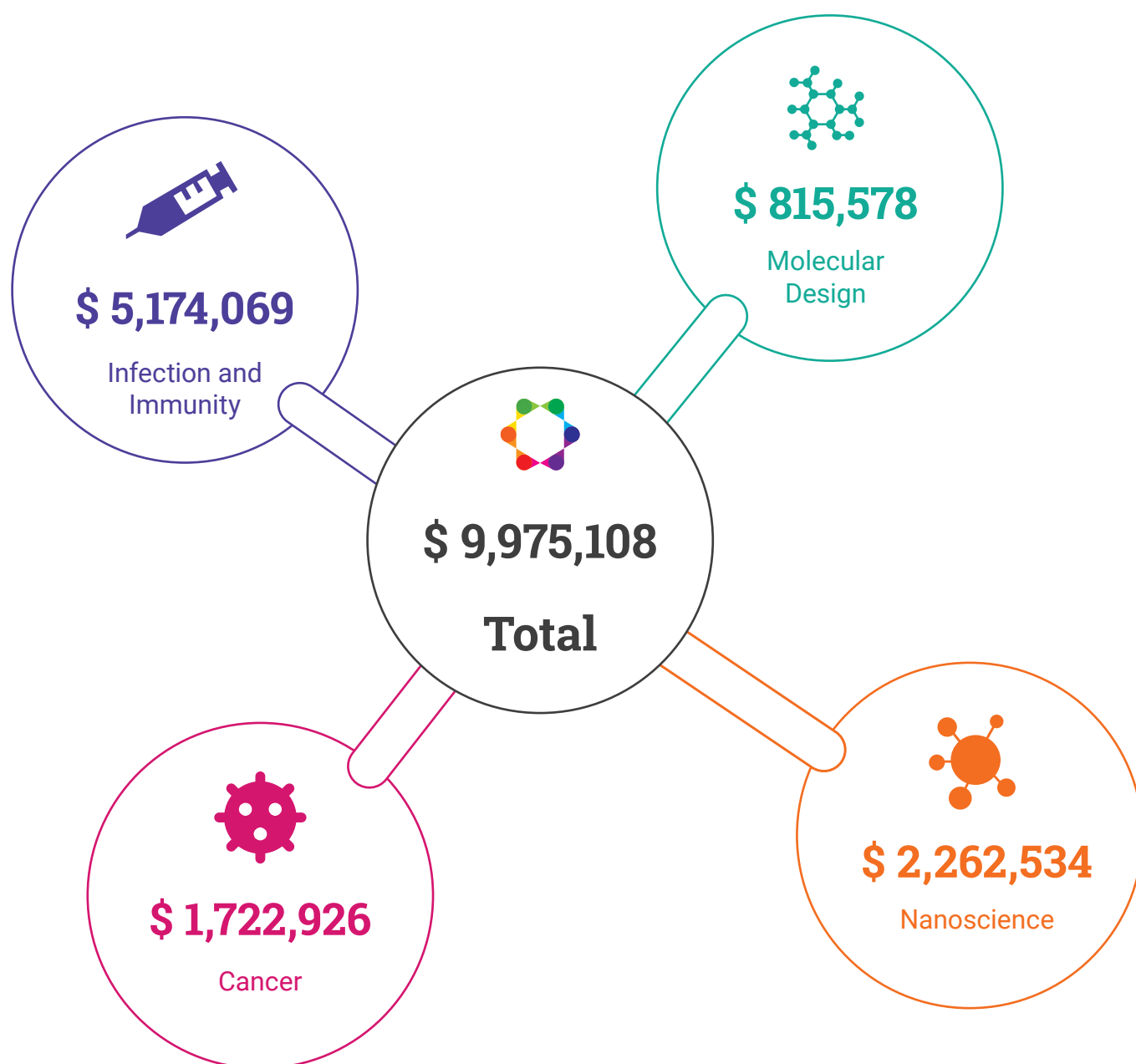
"Cholesterol is important to our health, so it is vital that we understand its role in our body. Our findings point towards a better understanding of how cell membranes function and the biochemical machinery of life."

For more information on this research or other Nanoscience related discoveries please contact the La Trobe Institute for Molecular Science.



Dr Shanshan Kou, Associate Professor Adam Mechler and Professor Brian Abbey

# EXTERNAL FUNDING





- Cancer
- Infection and Immunity
- Molecular Design
- Nanoscience

Project		2020 Revenue
<b>AdAlta</b>		
Provision of Research Services for AdAlta Pty Ltd (Michael Foley)	<span style="color: #3f51b5;">●</span>	970,417.40
<b>Australian Research Council</b>		
C-H to C-F using electrochemistry and gold catalysis (Jason Dutton)	<span style="color: #00bcd4;">●</span>	114,107.52
Design and Fabrication of 2D Hybrid Materials (David Winkler)	<span style="color: #00bcd4;">●</span>	5,000.00
Developing Next Generation Click Chemistry (John Moses)	<span style="color: #00bcd4;">●</span>	251,143.27
Discovering New Organic Chemistry using an Inorganic Touch (Jason Dutton)	<span style="color: #00bcd4;">●</span>	109,952.99
DNA Replication Stress: Characterizing ground zero for genomic instability (Donna Whelan)	<span style="color: #e91e63;">●</span>	147,688.37
Extracellular vesicles in the pathogenesis of fungal plant disease (Marilyn Anderson)	<span style="color: #3f51b5;">●</span>	155,601.21
How autotransporter proteins mediate bacterial interactions (Begoña Heras)	<span style="color: #3f51b5;">●</span>	172,643.37
How did the red blood cell lose its nucleus? (Patrick Humbert)	<span style="color: #e91e63;">●</span>	175,834.52
How do extracellular vesicles fuse with cells to deliver messages? (Sarah Stewart)	<span style="color: #e91e63;">●</span>	147,688.34
Laws of attraction and repulsion: a novel family of bacterial chemosensors (Brian Smith)	<span style="color: #00bcd4;">●</span>	15,000.00
Mechanisms by which Beclin1 regulates intestinal homeostasis (Erinna Lee)	<span style="color: #e91e63;">●</span>	128,453.96
Molecular Mechanisms of Novel Bacterial Copper Defense Proteins (Begoña Heras)	<span style="color: #3f51b5;">●</span>	123,333.00
New biosensing strategies based on bipolar electrochemiluminescence (Conor Hogan)	<span style="color: #ff9800;">●</span>	134,854.35
Recombinant protein expression of poxviral virulence factors (Marc Kvensakul)	<span style="color: #3f51b5;">●</span>	32,481.60
The Structural Basis For Defensin-Mediated Membrane Attack (Marc Kvensakul)	<span style="color: #3f51b5;">●</span>	148,459.06
Towards herbicide cocktails with a new mode of action to avert resistance (Tatiana Soares da Costa)	<span style="color: #00bcd4;">●</span>	147,730.47
Understanding the biogenesis of exosomes (Suresh Mathivanan)	<span style="color: #e91e63;">●</span>	230,651.20
X-Ray Nanolithography Facility: Towards the ultimate resolution (Grant van Riessen)	<span style="color: #ff9800;">●</span>	425,000.00
<b>Australian Research Council Centre of Excellence</b>		<b>875,182.20</b>
ARC Centre of Excellence in Advanced Molecular Imaging (Brian Abbey)	<span style="color: #ff9800;">●</span>	875,182.20
<b>Hexima</b>		
Antifungal activity implant defensins; discovery of novel insecticidal proteins; interaction between matriptase and proteinase inhibitors (Marilyn Anderson)	<span style="color: #3f51b5;">●</span>	1,617,052.63

# EXTERNAL FUNDING

Project		2020 Revenue
<b>National Health and Medical Research Council</b>		
Biomarkers to aid clinical trials for neurodegenerative disease (Andrew Hill)	●	426,088.40
Conologues: Ultra-fast-acting therapeutic insulins based on cone snail venom insulin principles (Brian Smith)	●	51,123.00
Defining the molecular regulators of apoptotic cell disassembly and their role in cell clearance and lupus-like autoimmune disease (Ivan Poon)	●	255,285.88
Dissecting the pathogenic triad of enteric pathogens: Assembly, structure and function of autotransporter proteases (Begoña Heras)	●	175,556.87
Dissecting the pathogenic triad of enteric pathogens: Assembly, structure and function of autotransporter proteases (Lakshmi Wijeyewickrema)	●	39,925.39
DsbA foldases from multidrug resistant pathogens as targets for new antimicrobials (Begona Heras)	●	30,000.00
DsbA foldases from multidrug resistant pathogens as targets for new antimicrobials (Begoña Heras)	●	101,457.00
Elucidating the mechanism and function of cell disassembly during apoptosis (Ivan Poon)	●	112,449.60
Elucidating the mechanism and function of extracellular vesicle formation during cell death (Amy Baxter)	●	84,041.60
Molecular basis of apoptotic cell disassembly and the function of this process in infection and chronic inflammation (Ivan Poon)	●	152,100.00
Reappraisal of the mechanisms underlying implantation success or failure (David Greening)	●	14,489.51
Regulation of cell signalling and tumourigenesis by Lgl (Helena Richardson)	●	276,166.06
The metastability of proteome foldedness in neurodegenerative disease (Yuning Hong)	●	31,824.52
<b>Other</b>		
A novel strategy to combat high-risk neuroblastoma (Pamali Fonseka)	●	50,000.00
ANATARA: Characterisation of pineapple cysteine proteases with therapeutic potential (Lakshmi Wijeyewickrema)	●	45,826.50
ANTSO: A fast soft X-ray detector system for advanced biological and materials imaging (Grant van Riessen)	●	37,372.26
Australia-China Joint Research Centre for Personal Health Technologies (JRC Collaboration) (Yuning Hong)	●	39,000.00
Australian National Fabrication Facility (ANFF) - Victoria Node (Paul Pigram)	●	125,000.00
Baker IDI: Understanding Extracellular Vesicles in Human Embryo Implantation (David Greening)	●	13,798.00
Boosting the cancer-killing capacity of immune cells with dying cell fragments (Georgia Atkin-Smith)	●	25,000.00
Ceramic Oxide Fabricators (Aust): Fabrication and characterisation of novel coatings for low temperature oxygen sensors (Brian Abbey)	●	30,200.00
Characterisation of pineapple cysteine proteases with therapeutic potential (Lakshmi Wijeyewickrema)	●	105,000.00
Controlling immune responses in blood cells (Helen Irving)	●	45,347.78
CSIRO-La Trobe Early Research Career Postdoctoral Fellowship (Paul Pigram)	●	127,155.60

- Cancer
- Infection and Immunity
- Molecular Design
- Nanoscience

Project		2020 Revenue
Developing a framework for sustainable labs at La Trobe University (Eduard Willms)	<span style="color: blue;">●</span>	30,086.00
DNA damage by Idronoxil in Monotherapy and in Combination with Radiation (Paul Pigram)	<span style="color: orange;">●</span>	51,431.80
Evaluating Smac mimetic treatment for metastatic osteosarcoma (Christine Hawkins)	<span style="color: red;">●</span>	50,000.00
Fighting Superbugs with Novel Drugs to Tackle Resistance (Tatiana Soares da Costa)	<span style="color: green;">●</span>	15,000.00
GDRC Research scholarship: Emily Mackie (Tatiana Soares Da Costa)	<span style="color: green;">●</span>	35,697.00
Holsworth Wildlife Research Endowment postgraduate research grant (James Van Dyke)	<span style="color: blue;">●</span>	6,375.00
Is stroke neurodegenerative? A longitudinal study of changes in brain volume and cognition following stroke (Andrew Hill)	<span style="color: blue;">●</span>	9,000.00
Megan Verinder CCV studentship (Christine Hawkins)	<span style="color: red;">●</span>	1,800.00
Mid-Career Research Fellowship (Erinna Lee)	<span style="color: red;">●</span>	296,351.00
Pre-clinical evaluation of IAP antagonists for osteosarcoma treatment (Christine Hawkins)	<span style="color: red;">●</span>	91,754.00
Research Services for Amcor AFAP Moorabbin (Paul Pigram)	<span style="color: orange;">●</span>	14,700.00
Research Services for CSL Behring (Paul Pigram)	<span style="color: orange;">●</span>	18,450.00
Research Services for Dulux (Paul Pigram)	<span style="color: orange;">●</span>	24,000.00
Research Services for Robert Bosch (Australia) Pty Ltd (Paul Pigram)	<span style="color: orange;">●</span>	8,400.00
Research Services: Geneworks (Patrick Humbert)	<span style="color: red;">●</span>	71,451.36
Research Services: XRD Analysis (Paul Pigram)	<span style="color: orange;">●</span>	969.50
Roche: New Project: Is B cell targeting neuroprotective in multiple sclerosis? (Jacqueline Orian)	<span style="color: blue;">●</span>	15,000.00
Specificity testing and cross-laboratory validation of a blood test for AD (Lesley (Sim) Cheng)	<span style="color: blue;">●</span>	18,825.00
Targeting tumour metabolic reprogramming by Fn14 as a driver of cancer cachexia (Laura Murray-Rust)	<span style="color: red;">●</span>	25,000.00
Understanding the role of exosomes in the transfer of chemoresistance between cancer cells (Suresh Mathivanan)	<span style="color: red;">●</span>	1,800.00
Unlocking a more robust immune system (Cristina Keightley)	<span style="color: blue;">●</span>	15,000.00
Vivazome: Enabling Exosome Therapy: Developing an Advanced Manufacturing Process (Andrew Hill)	<span style="color: blue;">●</span>	122,588.50
Werai forest turtle monitoring project (James Van Dyke)	<span style="color: blue;">●</span>	39,750.00
Wintermute: Next-generation antibiotics to fight antimicrobial resistance (Andrew Hill)	<span style="color: blue;">●</span>	99,377.73
X-Ray Nanolithography Facility: Towards the ultimate resolution (Grant van Riessen)	<span style="color: orange;">●</span>	300,000.00
<b>Total</b>		<b>9,975,108.12</b>



# PUBLICATIONS

Abad, I.P.L., Fam, R.L., Nguyen, D.-T., Nowell, C.J., Trinh, P.N.H., Manallack, D.T., Freihat, L.A., Chakrabarti, J., Jamil, A., Exintaris, B., Yaakob, N.S. & Irving, H.R. (2020). Visualising functional 5-HT<sub>3</sub> receptors containing A and C subunits at or near the cell surface. *Biomedicine and Pharmacotherapy*, 132. [I]

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 Infection and Immunity [I]  
 Nanoscience [N]  
 Molecular Design [M]

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La Trobe University acknowledges that our campuses are located on the lands of many Traditional Custodians in Victoria and New South Wales. We recognise their ongoing connection to the land and value their unique contribution to the University and wider Australian society.

La Trobe University is committed to providing opportunities for Aboriginal and Torres Strait Islander people, both as individuals and communities, through teaching and learning, research and community partnerships across all our campuses.

The wedge-tailed eagle (*Aquila audax*) is one of the world's largest, and the Wurundjeri people – Traditional Owners of the land where our Melbourne campuses are located – know the wedge-tailed eagle as Bunjil, the creator spirit of the Kulin Nations.

There is a special synergy between Bunjil and the La Trobe University logo of an eagle. The symbolism and significance for both La Trobe and for Aboriginal people challenges us all to gamagoen yarrbat – to soar.



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