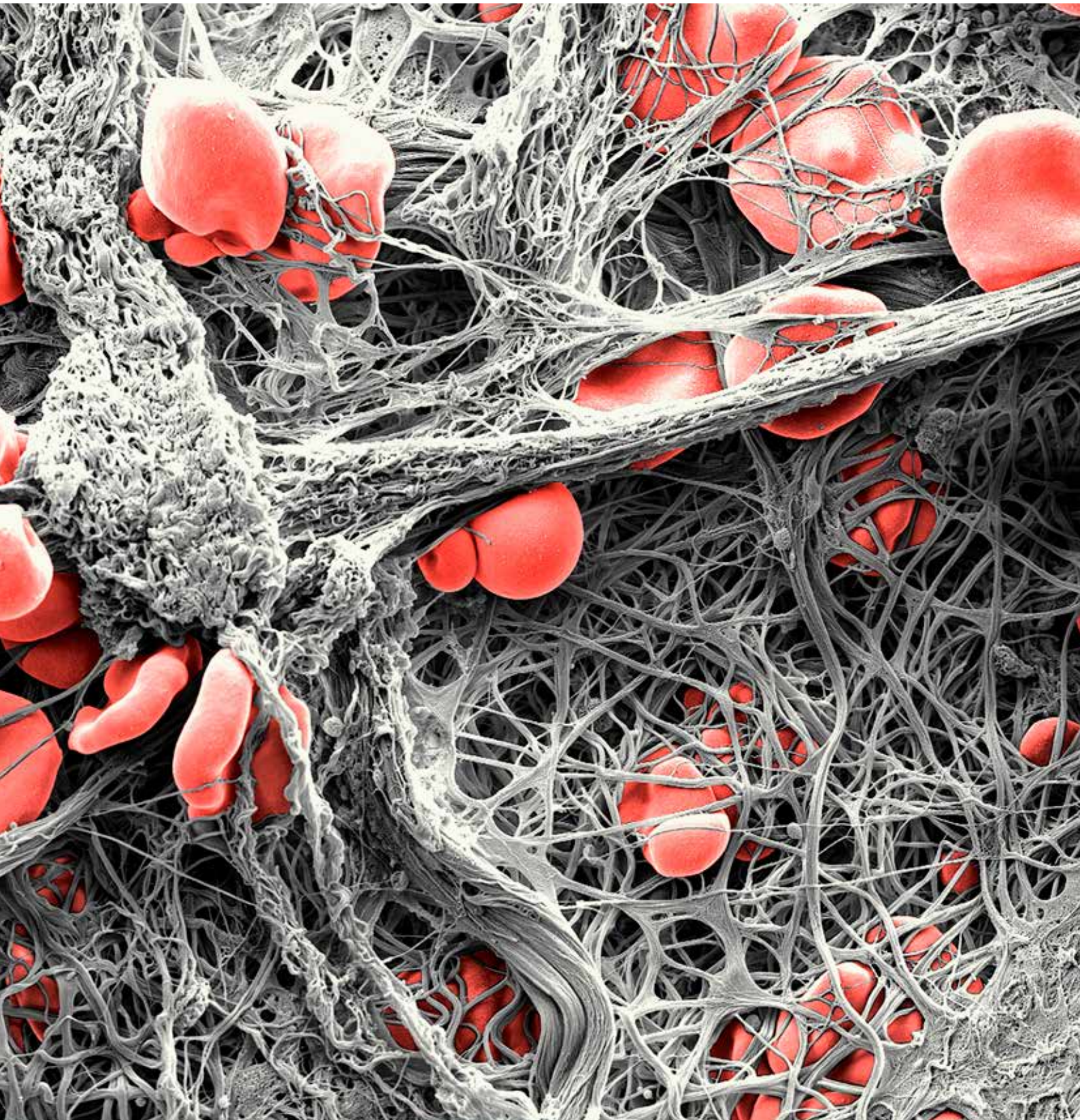
2017
Annual Report

Centre for Cancer Biology



Centre for Cancer Biology Members

Members
Professor Michael Brown
Professor Richard D'Andrea
Professor Greg Goodall
Professor Sharad Kumar AM
Professor Angel Lopez AO
Professor Stuart Pitson
Professor Paul Reynolds
Professor Hamish Scott
Professor Vinay Tergaonkar
Associate Professor Claudine Bonder
Associate Professor Susan Branford
Associate Professor Natasha Harvey
Associate Professor Yeesim Khew-Goodall
Associate Professor Michael Samuel
Associate Professor Quenten Schwarz

Associate Members
Professor Leanne Dibbens
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Dr Cameron Bracken
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Dr Loretta Dorstyn
Dr Guillermo Gomez
Dr Philip Gregory
Dr Christopher N Hahn
Dr Jason Powell
Dr Nirmal Robinson
Dr Nico Voelcker

Clinical Affiliates
Associate Professor Harshita Pant
Dr Janice Fletcher
Dr Karin Kassahn
Dr David Ross

Centre for Cancer Biology
An alliance between
SA Pathology and the
University of South Australia

UniSA Building
Corner North Terrace
and Morphett Street Bridge
Adelaide, South Australia 5001
Australia

Postal Address
GPO Box 2471
Adelaide South Australia 5001
Australia

T +61 8 8302 7916
F +61 8 8302 9246
E info@centreforcancerbiology.org.au

www.centreforcancerbiology.org.au

Publication Coordination
Angela Ziaei
Centre for Cancer Biology

Design and Production
Catherine Buddle
Buddle Design

Photography, unless otherwise credited
Peter Dent and Peta Grant
SA Pathology Photo and Imaging

cover image Electron microscopy image of coagulated human blood inside a medical grade metallic stent. Red blood cells were individually tinted in Adobe Photoshop to distinguish them from the strings of polymerised proteins that trap them. The image was captured on the Future Industries Institute's (FII) Zeiss Merlin Ultra-High Resolution Field-Emission Gun Scanning Electron Microscope thanks to the interdisciplinary collaboration between the CCB and FII.
Image captured by Dr Eli Moore

2017
Annual Report

Centre for Cancer Biology

Organisation

The Honourable John Hill

Chairman's Report

The Honourable John Hill
Former Member for Kaurna and former Minister for Health

It gives me great satisfaction to report on the Centre for Cancer Biology's performance for 2017.

As a medical research institute that focuses squarely on cancer, the CCB has continued its discovery and translation programs seeking to bring better health outcomes to cancer patients. The alliance between SA Health and the University of South Australia continues to provide excellent conditions for the growth and impact of the CCB. The close interactions of medical researchers with clinical services is already providing more rapid and advanced tests in the areas of genomics and genetic testing thanks to our two Australian Cancer Research Foundation-funded facilities.

The integration of research and services that epitomises the CCB is at the core of new national and international initiatives best represented by the Medical Research Future Fund. These are exciting times as we continue to build on existing collaborations with other interstate cancer Institutes to form meaningful Australia-wide alliances that can bring new approaches to help alleviate the burden of cancer to the community and to each patient.

It is pleasing to reflect that we continue to be strongly supported by an exceptional Scientific Advisory Board chaired by Professor Ian Frazer AC (University of Queensland) which includes Professor Joseph Trapani (Director, Peter MacCallum Cancer Centre), Professor Michelle Haber AM (Executive Director, Children's Cancer Institute), Professor Brendan Crabb AC (Executive Director, Burnet Institute) and Professor Christina Mitchell (DVCR, Monash University). The exceptional expertise in science and governance brought by this group of national leaders has been greatly appreciated over the course of 2017.

The alliance between Health and the University of South Australia continues to underpin much of the medical research activity of the CCB membership. It is pleasing to report that this confidence has borne fruit in 2017 with CCB members achieving an outstanding success rate in funding by the premier funding agency in Australia, the National Health and Medical Research Council. Particularly pleasing was the success of several collaborative initiatives between the CCB and other organisations in the new Adelaide BioMed City.

Which brings me to comment on the final touches being applied to the new facility to accommodate the CCB in the Adelaide BioMed City from 2018 onwards. An outstanding building, erected with major contributions from the Federal Government and the University of South Australia and carefully planned to service the functional needs of the CCB, will be occupied and opened by the time this report goes to press. An aesthetically beautiful facility, thoughtfully planned and at the heart of the Adelaide BioMed City next to our collaborators at the new Royal Adelaide Hospital, SAHMRI and the University of Adelaide places the CCB in an excellent position to achieve further success in the future.

The Honourable John Hill

Professors Angel Lopez AO and Sharad Kumar AM

2017 AGM Keynote speaker Professor Michelle Haber AM

Associate Professor Sue Branford, Professor Sharad Kumar AM, Former Minister for Health the Hon Jack Snelling, Mr Joel Geoghegan, Professor Angel Lopez AO, Professor Hamish Scott, Adjunct Associate Professor Julie Hartley-Jones, Professor Greg Goodall

Directors' Report

Professor Angel Lopez AO MBBS PhD FRCPA FAA FAHMS
Professor Sharad Kumar AM MSc PhD FAA FAHMS

As we write this report we enter our tenth year as the Centre for Cancer Biology. This is a good time to reflect with pride on how far we have come since April 2009: we have developed a national and international identity as a preeminent cancer-focussed Australian Medical Research Institute, with a culture of excellence and collaboration and a vision to find causes and cures for cancer.

The passion and personal investment made by everybody in the Centre for Cancer Biology (CCB) gives us plenty of confidence in its future. This optimism is backed by our performance in 2017 which has been an immensely successful year for the CCB. We are proud to highlight that the CCB was awarded 14 project grants from the National Health and Medical Research Council of Australia (NHMRC) with a total value in excess of $10 million over the next 3–4 years. At a time when the national success rate is about 16.4% (of submitted projects achieving funding), a CCB success rate of 40% is truly remarkable.

It was pleasing to see that our younger investigators were particularly successful, with Associate Professor Natasha Harvey receiving an impressive three NHMRC grants to study the development of the lymphatic network, a key system responsible for cancer metastases. Associate Professor Quenten Schwarz received two NHMRC grants and an ARC discovery project grant to continue his research into the origins and treatment of common birth defects and childhood cancers. We are also pleased with our more established investigators such as Associate Professor Yeesim Khew-Goodall and Professor Hamish Scott who continue with their excellent research on receptor signalling in cancer and inherited and sporadic hematological cancers respectively. Professor Scott's success is very timely too as he leads Genomics Health Alliances seeking to bring precision medicine to many patients with both cancers and inherited diseases. We are both humbled to have recently received the honour of being appointed to the Order of Australia; Angel as an Officer (AO) and Sharad as a Member (AM). These honours are certainly in recognition of the highly regarded research carried out by the CCB.

One of the hallmarks of the CCB is its spirit of collaboration. We were delighted to see that several of these grants involved CCB cancer researchers working closely with other institutes. One of the grants involved a collaboration between Professor Paul Reynolds (Royal Adelaide Hospital, University of Adelaide and CCB) and Associate Professor Claudine Bonder (CCB) to study how blood vessels contribute to lung cancer. Another collaboration between Associate Professor Sue Branford (CCB) and Professor Tim Hughes (SAHMRI and Adelaide University) promises to reveal how best to treat (and when to stop treating) patients with chronic myeloid leukaemia. Another hallmark of the CCB is its strength in enthusiastic and high achieving students and early career researchers who won awards for their oral presentations at conferences and fellowships, both here and abroad.

In 2017 we continued to communicate our research with over 120 publications in some of the best medical and scientific journals such as *Nature Communications*, *Cell Reports*, *Leukaemia*, *J Exp Med*, *Cancer Research*, *New England Journal of Medicine*, *PNAS*, *Nature*, *Cell Death and Differentiation*, *EMBO Journal* and *Blood*. The quality of these journals underlines the significance and impact of our work and is one of the reasons that our researchers are appreciated and sought after.

Bringing our discoveries closer to tangible patient benefit is important for our mission, and 2017 saw the CCB making significant advances, sometimes through commercialisation with long-term partners and occasionally through new ventures. Associate Professor Claudine Bonder's work with the Cell Therapy Manufacturing Cooperative Research Centre has paved the way for the future emergence of two companies that will exploit the immune system to fight cancer, and develop new types of stents to overcome vascular blockage.

Another major effort in translation has focused on 'genomics'. Professor Hamish Scott is the South Australian leader of Australian Genomics, a national research collaboration of clinicians, researchers and diagnostic geneticists working together to provide evidence for the equitable, effective and sustainable delivery of genomic medicine in healthcare. In partnership with SA Pathology (Drs Janice Fletcher and Karin Kassahn among others), they and the CCB ACRF Cancer Genomics Facility are rapidly shaping the genomics testing and research scene in SA. Recent successes can be seen in national and international collaboration on programs including 'Genomics Autopsy' in perinatal (stillbirth) genetic testing and Familial Haematological Cancer Studies bringing hope for healthy children and healthy lives to many families worldwide.

Our collaboration with A*STAR and the National University of Singapore is going from strength to strength with several high profile publications, exchange of personnel and knowhow, and, active participation in joint grant applications. A highlight for this program is the recruitment of Dr Nirmal Robinson from the University of Cologne who brings complementary expertise in infection and inflammation and with Professor Tergaonkar will jointly lead the CCB Inflammation and Ailments Laboratory.

To have a focus in improving patient's wellbeing and to ensure that we do not lose sight of the important mission, we are being aided by a strong and dedicated group of 'consumers'. Associate Professors Claudine Bonder and Michael Samuel, together with Professors Michael Brown, Greg Goodall and Dr Sarah Boyle have formed a group of consumer advocates which includes Paula Nagel AM, Desi Heliotis, Paul Murray, Belen Mansford and Trish Fuss, who constantly help us in our endeavours.

In August the CCB held its AGM and we were fortunate to have Professor Michelle Haber AM, Director of the Children's Cancer Institute (CCI) in Sydney, as our keynote speaker. Professor Haber spoke about the importance of creating a personalised approach to cancer treatment and the huge value of collaboration. The Zero Childhood Cancer initiative, led by the CCI and the Sydney Children's Hospitals Network, brings together all major Australian clinical and research groups working in childhood cancer to offer Australia's first ever personalised medicine program for children with high-risk or relapsed cancer. The CCB is proud to be part of this initiative. As the descendent of the Hanson Centre for Cancer Research, the CCB prides itself on continuing the tradition of excellence in cancer research and it puts us in good stead to formalise national alliances with like-minded research institutes, such as the CCI. Professor Haber was also kind enough to join other members of our Scientific Advisory Board, Christina Mitchell and Joe Trapani, and our Alliance partners' representatives, for helpful and constructive discussions about strengthening the CCB.

In November, under the leadership of Professor Stuart Pitson, we hosted the biennial Science Amongst the Vines™ series of meetings with the 8th Barossa Meeting on the theme of Cell Signalling in Cancer Medicine. At this meeting, the Clifford Prize for Cancer Research, which recognises outstanding international achievement in cancer research, was awarded to Professor Joseph Schlessinger of Yale University, USA. Professor Schlessinger's work has elucidated the structure and function of receptor tyrosine kinases and has provided the foundation of profound advances in targeted cancer therapies being applied worldwide. The award was presented by Ms Jenny Richter, CEO of the Central Adelaide Local Health Network, and was followed by a celebratory dinner at Chateau Tanunda. We are proud of these biennial scientific and medical meetings, which are now well entrenched in the Australian calendar and present an international window to the world into the quality of the lifestyle and medical research scene in South Australia.

As we look back with pride over the last ten years we cannnot avoid a sense of optimism and excitement about our future, joining forces with our colleagues and friends in neighbouring institutions in an open spirit of collaboration that is essential to energise and bring the best out of the new Biomedical Precinct.

We would like to recognise the strong support we continue to receive from SA Pathology and the University of South Australia in their efforts to strengthen and grow the CCB. We are indebted to South Australian patients for allowing us to use their samples through the South Australian Cancer Research Biobank (SACRB) to advance cancer research, and for the support of the SA public who continue to donate generously to accelerate the work of the CCB. We are grateful to The Hospital Research Foundation (THRF) team led by Mr Paul Flynn for promoting our work and for steadily increasing their support to the CCB. The philanthropic support of THRF and every individual donor who generously contributes to our fight against cancer is gratefully acknowledged from the bottom of our hearts.

Professors Angel Lopez AO and **Sharad Kumar AM**
Co-Directors, Centre for Cancer Biology

Professor Angel Lopez, Ms Jenny Richter, Clifford Prize recipient Professor Joseph Schlessinger and Professor Stuart Pitson

Ms Jenny Richter, CEO of CALHN, introduces Professor Joseph Schlessinger

8th Barossa Meeting

On 14–17 November 2017 we hosted medical researchers from overseas and across Australia in the Barossa Valley for the Eighth Biennial Barossa Meeting on the theme of 'Cell Signalling in Cancer Medicine'. Originating from, and always organised by the Centre for Cancer Biology, these meetings are now established as one of the premier cell signalling conferences on the international scientific calendar.

Meeting highlights included:

Ali Shilatifard (Northwestern University, USA) who described the use of genomics to identify new treatments for diffuse intrinsic pontine gliomas, one of the most devastating forms of pediatric cancers.

Lea Starita (University of Washington, USA) spoke on the use of saturating CRISPR-Cas9 editing combined with functional screens to identify pathogenic variants in the BRCA1 breast cancer susceptibility gene.

Daniel Finley (Harvard Medical School, USA) described his work in identifying regulation and role for the ubiquitin-proteasome system.

Fiona Watt (Kings College London, UK) spoke on the use of the knockout mice consortium to identify new tumour suppressors in skin cancer.

Wanjing Hong (Institute of Molecular and Cell Biology, Singapore) described his work identifying a functional link between Agrin, an extracellular matrix proteoglycan, and the transcriptional regulator YAP.

Lena Claesson-Welsh (Uppsala University, Sweden) presented her recent work in identifying important roles for VEGF signalling in vascular leakage and the passage of metastatic cancer cells through blood vessel walls.

Johannes Bos (Utrecht University, Netherlands) described the development of colorectal cancer organoid cultures in an effort to screen for agents that might inhibit progression of these maligancies.

Maria Sibilia (Medical University of Vienna, Austria) presented her recent discoveries that EGF receptor signalling in tumour-associated myeloid cells plays an important role in tumour growth.

Joseph Schlessinger (Yale University, USA) discussed his recent identification of the structure of the beta-Klotho receptor bound to its primary ligand fibroblast growth factor (FGF) 21, a cytokine that plays key roles in endocrine cell function, and how this information is being utilized for development of potential treatments for obesity and liver disease.

A further 16 interstate invited speakers, 12 local invited speakers, 11 talks from selected abstracts, and 22 posters completed the impressive program. A report of the meeting has been published (Gomez *et al*, *Cell Death and Disease* 9:284, 2018).

The Barossa Meetings also provide the venue for the presentation of the Clifford Prize for Cancer Research, recognising outstanding international achievement in cancer research. In 2017, this was awarded to Professor Joseph Schlessinger of Yale University, USA for his work in elucidating the structure and function of receptor tyrosine kinases that has provided the foundation for profound advances in targeted cancer therapies. The Prize, presented by Ms Jenny Richter, Chief Executive Officer of the Central Adelaide Local Health Network, comprised perpetual and keepsake trophies crafted by South Australian glass artist Nick Mount, and a magnum of Clarenden Hills 'Astralis'. With this award, Professor Schlessinger joins an illustrious group of past winners including Axel Ullrich (Munich), Tony Hunter (San Diego), John Dick (Toronto), Vishva Dixit (San Francisco), Arul Chinnaiyan (Ann Arbor), Jane Visvader (Melbourne) and Inder Verma (San Diego).

The Meeting also included several social events, including the Clifford Prize dinner which was held at Chateua Tanunda, with an exquisite dinner presented by Elli and Saskia Beer, with matched wines introduced by John Leydon.

The Barossa Meetings continue to provide a vehicle for local medical researchers and students to mix and establish collaborations with world class researchers from overseas and interstate, while showcasing the quality of South Australian cancer research.

Professor Stuart Pitson
Convenor, 8th Barossa Meeting

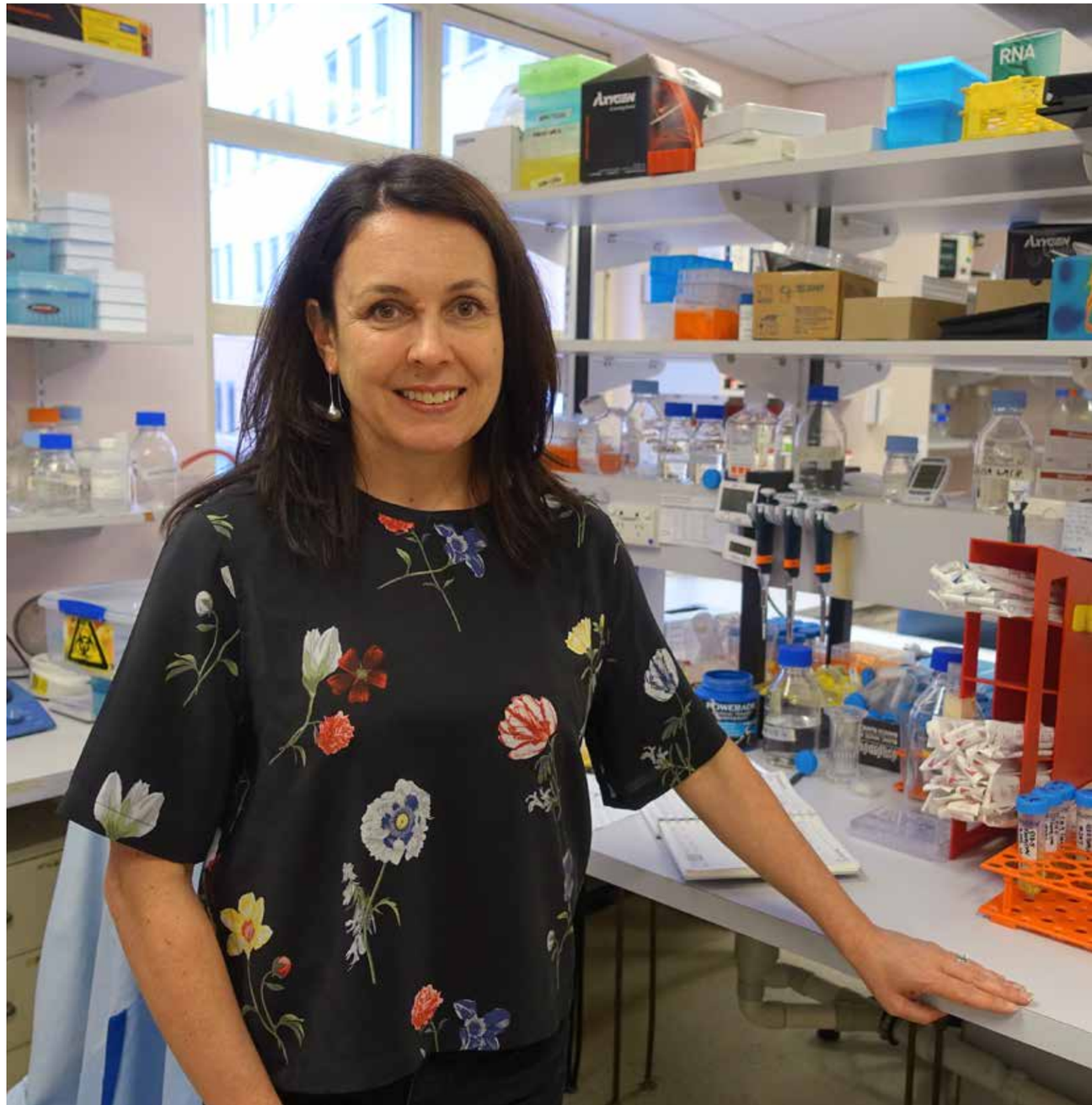
Barossa Meeting photography by Ian Buckland

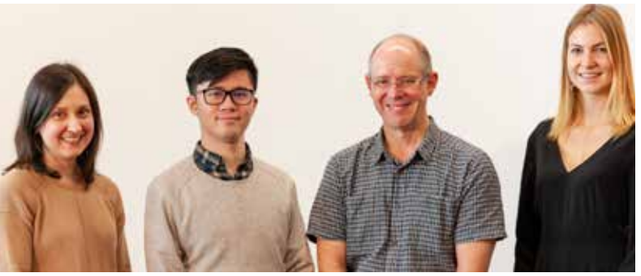
Centre for Cancer Biology
Making News …

In 2017, the CCB continued to be featured in newspaper and online articles focussing on the high quality research we are conducting and how this is leading to better health outcomes for Australians.

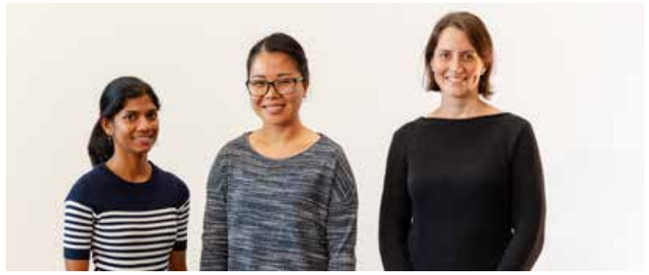
Centre for Cancer Biology
2017 Laboratory Reports

Associate Professor Natasha Harvey and her team want to put the brakes on cancer and in particular, to halt the spread of cancer by preventing the access of cancer cells to the blood and lymphatic vessel 'highways' in our bodies.





Diana Iarossi, Ka Leung Li, Richard D'Andrea, Tatjana Geukens



Saumya Samaraweera, Tran Nguyen, Debora Casolari

Acute Leukaemia Laboratory

Professor Richard D'Andrea PhD
Dr David Ross MBBS PhD FRACP FRCPA

The Acute Leukaemia Laboratory has a fundamental interest in Acute Myeloid Leukaemia (AML) and related diseases such as the Myeloproliferative neoplasms (MPN). AML is the most common form of acute leukaemia in adults. MPN are a group of chronic diseases characterised by high blood cell counts, increased risk of bleeding and clotting, and a propensity to transform to AML. Both AML and MPN show considerable genetic diversity and variable prognostic outcomes.

The research carried out by the Acute Leukaemia Laboratory strives to better understand the mechanisms underlying AML and MPN, with the ultimate goal of improving treatment outcomes. The genetic complexity of AML has hampered progress in the field, with the molecular basis for some subtypes still largely unknown. Overall survival for younger adults with AML is still only 30–40%, and lower still in people aged over 60. New targeted therapies are expected to improve outcomes for some subtypes and for older patients. We are using new technologies to better understand the regulatory pathways that are disrupted and lead to disease initiation and progression.

A significant research focus of the lab is the investigation of the mechanisms that control stem and progenitor cell growth and survival, and which are commonly deregulated in AML and MPN. Our studies have led to new biological insights into the growth and survival pathways that drive continued growth of disease cells, and have identified novel mutations, previously undetected in MPN, allowing for improved diagnosis. Our continued investigations will involve identification and functional characterisation of novel mutations and gene products identified from genetic profiling of panels of AML and MPN samples, leading to improvements in diagnosis and better understanding of these diseases.

Outcomes for the Community

These studies increase fundamental knowledge of AML and MPN disease pathogenesis, and have important implications for diagnosis and treatment. We continue our laboratory and pre-clinical modelling of AML and MPN to validate novel targets, and our ongoing collaborations with other research groups around Australia and overseas to develop new diagnostic tools for these groups of diseases. These studies are tightly linked with efforts to translate our laboratory research findings into the clinic through our collaborative links with SA Pathology and major South Australian hospitals. Ongoing clinical trials are of direct benefit to patients, providing access to novel therapies that may improve outcome for elderly or high-risk AML patients currently facing a dismal prognosis.

Key discoveries 2017

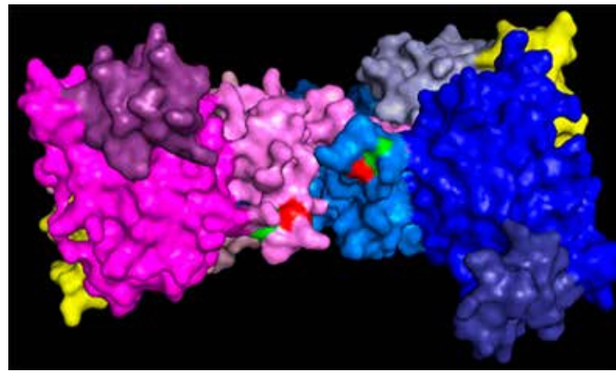
Biology of AML

It is well established that AML is genetically and clinically heterogeneous. Despite findings that recurrent changes to protein-coding genes occur in AML, and are directly linked to pathogenesis, the contribution of non-coding genes to disease biology and treatment is still largely unclear. We are collaborating with other national groups to determine the relationships between non-coding RNA (ncRNA) expression, common AML mutations, disease characteristics and outcome. In a key collaborative study reported in the journal *Leukemia* in 2017 novel data is presented on 1664 long intervening/intergenic non-coding RNAs (lincRNAs), a specific subgroup of ncRNA genes not overlapping with other coding genes. This study revealed that distinct lincRNA expression profiles were associated with recognized subgroups of AML, and furthermore an expression signature composed of just four lincRNAs provided important prognostic information potentially providing a tool for better clinical management. The ncRNAs are emerging as key regulators of an increasing number of molecular processes, with their aberrant expression being correlated with the development of cancers and with clinical outcome, and the data from our ongoing multi-centre study will be important for the adoption of ncRNAs as useful clinical biomarkers to improve AML diagnosis, and will also guide our continuing targeted experimental investigations of novel genes that are deregulated in AML.

In separate studies we have investigated mechanisms that control the expression and function of the key stem cell regulatory molecule CD123 (aka IL-3Ra) in AML. High expression of this cell surface receptor molecule is a hallmark of the AML leukaemic stem cells (LSCs) that maintain the production of disease cells and also represent a pool of cells resistant to therapy. Our collaborative studies reported in *Blood Advances* have shown that high levels of CD123 expression promote proliferation and enhanced survival of LSC, also affecting the way that LSC interact with critical non-leukaemic cells in the bone marrow. We have also shown (*Leukemia Research*, 2017) that increased expression of a particular ncRNA (miR-155) may be an important consequence of increased CD123 levels in AML cells. Given the known functional roles of miR-155 in leukaemia, activation of this CD123-miR155 pathway is likely a novel mechanism whereby elevated CD123 contributes to malignant haematopoiesis.

Improving diagnosis and treatment of MPN: identification of rare driver mutations

While the discovery of key recurrent mutations in MPN has greatly improved diagnosis, further characterisation of novel mutations is important for patients in whom current routine molecular testing is inconclusive, and to improve understanding of the pathways contributing to MPN in these individuals. We have focussed on a group of patients that fit the clinical picture of the MPN, Polycythaemia vera (PV), but for whom molecular analysis has not detected a somatic JAK2 mutation that is the hallmark of this disease, meaning that the diagnosis and best treatment approach for these patients is unclear. Our studies reported in *British Journal of Haematology* identified rare PV patients with novel complex mutations affecting JAK2 that are not detectable by current laboratory testing, and we show further that next generation sequencing (NGS) can help diagnose this subgroup of MPN patients. We thus propose that NGS be performed as a secondary assay in patients suspected of PV, but for whom standard JAK2 testing is negative. Better diagnosis of PV will prevent under-treatment of undiagnosed cases, and reduce unnecessary investigations to rule out secondary causes of erythrocytosis.



The crystal structure of the Epidermal Growth Factor Receptor (EGFR) dimer shows the cysteine pair (C329, red–C333, green) in the dimerization domain. Somatic $EGFR^{C329R}$ variant was observed in a Polycythaemia vera patient.

In a separate study published in *Scientific Reports* we describe a novel mutation in the receptor for epidermal growth factor receptor (EGFR) in a PV patient, and show a potential contribution to disease pathogenesis. This study raises important questions regarding the role of JAK2-independent mechanisms for aberrant activation of signalling pathways in MPN. Activation of the EGFR group of receptors can occur via multiple mechanisms, and given recent reports of cross-talk between EGFR and JAK2 we propose that a dual targeting strategy of combining clinical JAK2 inhibitors with inhibitors of EGFR and/or downstream kinases, may be an effective strategy in MPN patients. Such an approach has been reported to be effective in lung cancer patients resistant to EGFR inhibition.

Clinical trials in AML

The fundamental research in the Acute Leukaemia Laboratory is complemented by a number of laboratory and clinical studies testing new therapies for AML, and carried out in conjunction with the Haematology Clinical Trials Unit in the Royal Adelaide Hospital. The clinical trials provide AML patients with access to new treatments, and allow parallel laboratory studies investigating the effects of novel agents on primary leukaemia cells from patients. Such studies are critical for understanding the mechanism of these drugs in human AML, and for investigation of the specific molecular factors that affect drug response.

Freya Gehling, Ana Lonic, Yeesim Khew-Goodall, Leila Belle, Xiaochun Li

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall PhD

The interest of the Cell Signalling Laboratory is to understand how signals that are normally generated to maintain homeostasis, give rise to disease when dysregulated. Our primary research interest is to understand how a cancer cell progresses from a benign state, with good prognosis, to a malignant state resulting in metastatic disease. In solid cancers, which constitute 80% of human cancers, the main cause of deaths is due to metastasis.

Our two main areas of research are:

The role of protein trafficking in breast cancer

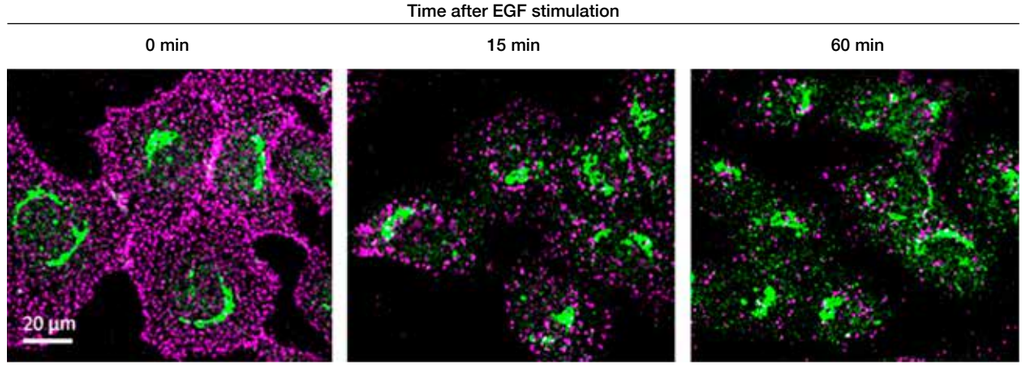
Dysregulation of cell proliferation is a major driver of cancer. Whether a cell grows and divides, remains quiescent, or dies, is determined in large part by its responses to extracellular growth factors, which bind receptors on the cell surface to activate signalling pathways within the cell. We study the signalling pathways that control the amount of growth factor receptors that are displayed on the cell surface, and we have identified a major receptor trafficking regulatory pathway that is dysregulated in multiple solid cancers. We have discovered that the protein tyrosine phosphatase PTPN14 (also called Pez) and its substrate PKCδ regulate the amount of growth factor receptors on the cell surface available for ligand binding and signalling. PTPN14 is mutated in multiple cancers, including breast and colorectal cancers and our studies have shown that it is a suppressor of metastasis. Current studies in the Cell Signalling Laboratory are directed towards understanding the fundamental mechanisms of receptor trafficking regulated by this PTPN14-PKCδ signalling pathway, understanding how dysregulation of this pathway leads to human diseases like cancer, and deciphering how cancers with dysregulation in this pathway and other trafficking abnormalities can be treated.

The role of mir-200 in neuroblastoma (in collaboration with the Gene Regulation Unit)

Neuroblastoma is a childhood cancer usually affecting children under the age of five, with metastasis being the main cause of death. The ability of cancer cells to invade their surrounding tissue is critical for their spread to secondary organs. We have identified novel targets of miR-200 critical for assembly and regulation of the invasive machinery in neuroblastoma, how they act to promote invasion and how they are regulated.

Key discoveries 2017

A particularly exciting development this year is our discovery of a novel set of biomarkers in cohorts of triple negative and Her2+ breast cancer patients that could potentially predict aggressive or drug-resistant cancers. Equally exciting is our discovery of potential therapeutic targets that could be used to treat these cohorts of patients.



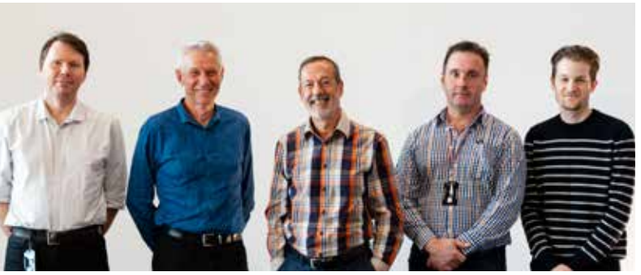
EGFR PTPN14

Dynamic relocalisation of EGFR and PTPN14 after EGF stimulation

Outcomes for the Community

Solid tumours constitute the majority of human cancers whereby the progression to metastasis is the main cause of morbidity and mortality in these patients. Currently, there is little effective treatment for metastatic diseases. Our studies which identified a novel pathway regulating protein trafficking have revealed some potential new biomarkers for identifying triple negative breast cancers that have increased likelihood to metastasise. Current work is aimed at identifying therapeutic targets for this group of cancers.

In addition to our studies on breast cancer, we are also exploring new ways to inhibit metastasis in neuroblastoma, the third most common type of childhood cancer and the leading cause of cancer deaths of children under five, accounting for 15% of all childhood cancer deaths. Aggressive neuroblastoma has not seen a major change in the survival rate in the last ten years. Our studies aim to increase knowledge of the molecules driving metastasis using multiple strategies so that we may identify and open up avenues for new therapeutics to be developed.



Denis Tvorogov, Frank Stomski, Angel Lopez, Tim Hercus, Cameron Bastow
Absent: Dave Yip

Anna Sapa, Mara Dottore, Ceilidh Marchant, Winnie Kan, Emma Barry

Cytokine Receptor Laboratory

Professor Angel Lopez AO MBBS PhD FRCPA FAA FAHMS

Cytokines are small proteins that act as haematopoietic regulators that control blood cell production, immune functions and inflammatory responses. Our laboratory is particularly focussed on an important family of cytokines known as the beta common (βc) family, so named because they all utilise the shared receptor subunit βc and includes the cytokines GM-CSF, IL-3 and IL-5.

Our research program seeks to determine, in atomic detail, the structural and functional properties of these cytokines bound to their receptor, to identify the mechanisms underlying receptor signalling and to develop new tools and ultimately new drugs for use in leukaemia and allergic diseases. Our work is relevant in diseases such as leukaemia that exhibit abnormalities in expression and signalling by βc cytokine receptors, and in allergic inflammation, like asthma, where excessive activation of βc cytokine receptors in myeloid cells in the lung contributes by restricting breathing and promoting lung inflammation.

In collaboration with Professor Michael Parker's laboratory (University of Melbourne Bio21 and SVIMR) we have solved crystal structures of several cytokine receptor complexes including GM-CSF and IL-3 binary complexes with cognate receptor alpha subunits. We have now solved structures of both GM-CSF and IL-3 ternary complexes containing cognate receptor alpha subunits and the βc subunit. These structural studies have revealed the molecular interactions that allow assembly of the GM-CSF and IL-3 receptor signalling complexes and identified key features of receptor assembly that lead to receptor activation in the βc family of cytokines that control distinct signalling pathways.

Some of the studies we are performing have practical and immediate application. In collaboration with Dr Jarrod Sandow, Professor Jeffrey Babon and Dr Andrew Webb from WEHI, Dr Daniel Thomas from Stanford University, and Dr David Ross and Professor Tim Hughes from the Royal Adelaide Hospital and SA Pathology, we have focussed on the Janus kinase JAK2, a key component of signalling by the βc cytokines. The Type I JAK inhibitor ruxolitinib is used to treat patients with myelofibrosis and despite some improvement in symptoms, it does not eradicate cells expressing JAK2V617F and leads to the paradoxical accumulation of activated JAK2. We have now demonstrated strong activation of autonomous JAK/STAT signalling following ruxolitinib withdrawal in myelofibrosis patient samples alerting us to the possibility that JAK Type I inhibitor-induced accumulation of activated JAK2 may act as a pathogenic signalling node which has to be carefully monitored upon drug withdrawal.

We have been investigating the role of elevated expression of the IL-3 receptor alpha subunit (IL3Rα, CD123) on stem cells from patients with acute myeloid leukaemia (AML). CD123 over-expression is used as a biomarker for AML stem cells but we have found in collaboration with Associate Professor Paul Ekert's laboratory (Murdoch Children's Research Institute (MCRI)) that it also results in reduced levels of an adhesion molecule (called CXCR4) contributing to leukaemic cell egress from the bone marrow. CD123 is also overexpressed in chronic myeloid leukaemia and in collaboration with Professor Hughes we are elucidating how this receptor signals within leukaemic cells.

Key discoveries 2017

In collaboration with Professor Paul Ekert, Dr Gabriela Brumatti (MCRI) and Professor Richard D'Andrea (CCB) we demonstrated that elevated IL3Rα expression is associated with enhanced responsiveness to IL-3 but downregulated CXCR4 expression and reduced chemotaxis. These observations may provide a mechanism to account for the release of leukaemic stem cells from the bone marrow in patients with AML that express elevated CD123 (Wittwer *et al*, *Blood Advances*, 2017).

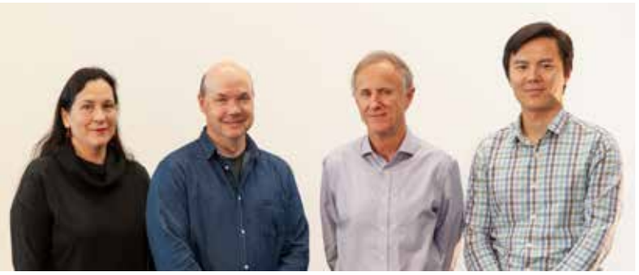
In collaboration with the laboratory of Professor Vinay Tergaonkar we are elucidating the basis of allergic inflammation by studying the fundamental roll of mast cells. By defining their transcriptional programme we are confident of identifying specific regulators of their function that can be targeted for therapeutic purposes (Cildir *et al*, *The Journal of Experimental Medicine*, 2017).

The work on leukaemia is also being advanced through collaboration with Professor Stuart Pitson's laboratory and its cutting-edge expertise on the sphingosine kinase pathway. Targeting of this pathway induces MCL1-dependent death of leukaemic cells. We hope that by harnessing this signalling pathway we can achieve new avenues to halt leukaemia cell growth (Powell *et al*, *Blood*, 2017).

Type I JAK inhibitors promote accumulation of JAK2 activation-loop phosphorylation by preventing the action of phosphatase activity and ubiquitination, resulting in strong STAT activation upon drug withdrawal.

Outcomes for the Community

Using tissue samples from patients suffering from leukaemia and from allergic diseases we are understanding these diseases better and are designing new strategies to control them.



Rosemary Sladic, Andrew Bert, Greg Goodall, Dawei Liu
Absent: Kate Dredge

Katherine Pillman, Emily Hackett-Jones, John Toubia, Pannapa (Bim) Pinweha

Gene Regulation Section

Professor Greg Goodall PhD, FAHMS

Most deaths from cancers are due to the transition of the cancer to the form that can invade through the tissues and then travel through blood and lymph vessels to secondary sites, where they may establish additional tumours, a process called metastasis. Our research investigates the molecular mechanisms that drive a cancer to become invasive and metastatic.

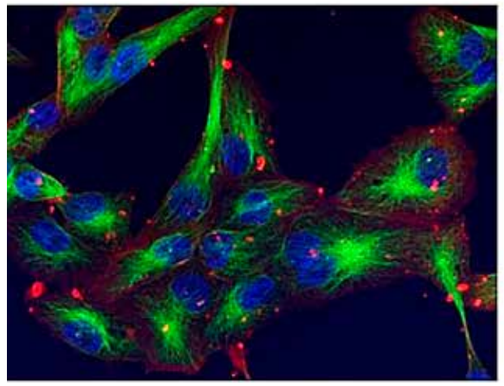
The most common cancers, such as breast, prostate, colorectal and lung cancer, arise from epithelial cells that line the internal surfaces of these organs, and the transition of these cancers to the invasive form is called epithelial to mesenchymal transition (EMT). The term Epithelial-Mesenchymal Plasticity (EMP) is sometimes used in recognition of the ability of epithelial-derived cancer cells to transition partially between cell states that are intermediate between fully epithelial and fully mesenchymal. Our vision is to apply multidisciplinary cutting-edge approaches to make significant discoveries of genes, non-coding RNAs and regulatory networks that determine the malignancy of cancers through their influence on EMT. Because EMT also confers enhanced resistance to chemotherapy on the cells that undergo this transition, the studies on the mechanisms that control epithelial plasticity are at the nexus of investigations on the cause of cancer progression and resistance.

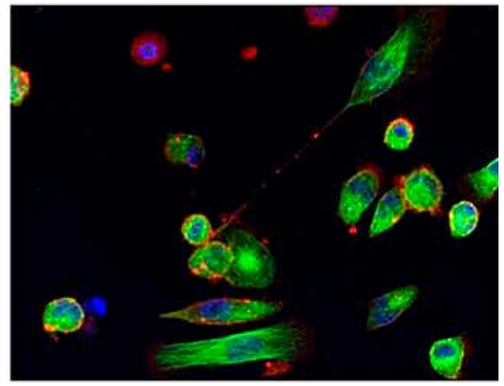
We focus especially on various types of RNA molecules that act as the intermediaries in controlling epithelial plasticity. EMT is driven by coordinated changes in the expression of many RNAs and proteins, and these changes are determined by integrated gene expression networks that themselves involve numerous components. We are contributing to the understanding of this process by determining how microRNAs and circular RNAs play a central role in controlling and coordinating the regulatory networks that underlie EMT in cancer cells. In the past few years the almost ubiquitous involvement of microRNAs in shaping cellular properties has become evident, along with the recognition that longer non-coding RNAs also have a range of regulatory functions, but much remains to be discovered in this burgeoning area. We recently opened a new avenue in this area with our discovery of regulated production of circular RNAs in EMT (*Cell* 2015). Our current work focusses on developing our understanding of how microRNAs, circular RNAs and their targets control EMP, and examining their consequences for cancer progression.

Outcomes
for the **Community**

We have found further molecular events that are involved in the progression of cancers to metastasis. These pathways may eventually be targeted by drugs to reduce metastasis in patients. In 2017 our publications received 1,460 citations.

Key discoveries 2017





Breast epithelial cells into which the short form (left panel) or the long form (right panel) of miR-222 have been introduced

Naturally existing isoforms of miR-222 have distinct functions

Deep sequencing of microRNAs in cancer and normal cells by ourselves and others has revealed that many microRNAs have isomeric forms, mostly due to variability in the cleavage step of their maturation, which results in a range of lengths, and hence sequence, especially at the 3' end of the microRNA. In collaboration with Dr Cameron Bracken's group at the Centre for Cancer Biology we found that the microRNA miR-222 is especially variable in length, and that the different length isoforms have different effects on the cell. The longer form reduces the levels of components of a signalling pathway (the PI3K-AKT pathway) that normally promotes survival of cells, by preventing them from initiating the programmed cell death response (apoptosis). This finding has potential consequences for cancer cells, which would be expected to have more resistance to apoptosis-promoting therapies. It also indicates that specific functions of length isomers should be examined for the many other microRNAs that have abundant alternative forms. (Yu *et al, Nucleic Acids Research* 45: 11371-11385, 2017)

MicroRNAs that promote or inhibit prostate cancer metastasis

Together with the Gregory group at the CCB, we have an ongoing collaboration with Dr Luke Selth and Professor Wayne Tilley at Adelaide University to study the effects of microRNAs in prostate cancers. In an earlier study, we had found that the microRNA, miR-194, was elevated in metastatic tissues, suggesting it could be a driver of disease progression. The pathway through which miR-194 acts in prostate cancer has now been defined. We find the transcription factor, GATA2, regulates miR-194, which in turn reduces the level of suppressor of cytokine signaling 2 (SOCS2) and thereby enhances the STAT3 and ERK signalling pathways. Inhibition of miR-194 activity suppressed the invasive capacity of prostate cancer cell lines in vitro and in vivo, whereas low levels of SOCS2 correlated strongly with disease recurrence and metastasis in clinical specimens. Pharmacologic inhibition of ERK and JAK/STAT pathways reversed miR-194-driven phenotypes in the cell lines. (Das *et al, Cancer Res* 77:1021-1034, 2017)

In contrast, we have found that miR-375 can drive mesenchymal-epithelial transition (MET) in model systems, inhibiting invasion and migration of multiple prostate cancer lines. We found that the pathway through which miR-375 has its effects involves two transcription factors, ZEB1 and YAP1, both of which have been previously associated with EMT. The activity of the miR-375 gene was found to be directly repressed by the EMT transcription factor, ZEB1, while the transcription factor YAP1 was found to be a direct target of miR-375 in prostate cancers. (Selth *et al* Oncogene 36:24-34, 2017)

Caroline Philips, Rachael Lumb, Philip Gregory, Daniel Neumann

Gene Regulation in Cancer Group

Dr Philip Gregory PhD

As solid tumours progress towards more aggressive states they exhibit considerable heterogeneity. These changes are often driven by environmental cues that trigger adaptive changes in tumour cells, commonly referred to as tumour cell plasticity. Epithelial-mesenchymal transition (EMT) is an important form of cell plasticity that enables tumour cells to become more invasive and metastatic, as well as resistant to chemotherapies.

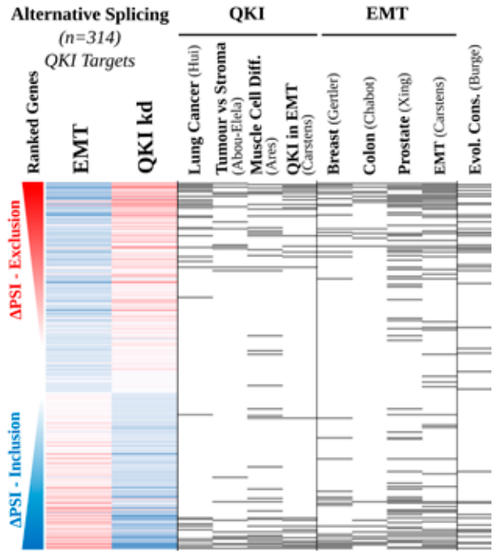
Our laboratory investigates the molecular mechanisms controlling tumour cell plasticity in breast and prostate cancer. We have made important discoveries showing specific microRNAs influence whether tumour cells become more invasive and metastatic in nature. MicroRNAs are small non-coding RNAs that have the ability to control many tumour promoting pathways simultaneously. Because of this, microRNAs represent promising therapeutic targets and can be utilised to identify critical combinations of pathways that drive tumour metastasis. Our laboratory uses *in vitro* and *in vivo* models of breast and prostate cancer, to identify the function of microRNAs and their target genes in cancer cell invasion and metastasis. We also use cutting edge cross-linking immunoprecipitation (CLIP) and sequencing techniques to identify the pathways through which microRNAs exert their effects on tumour progression.

In recent work, we have found two microRNAs (miR-200 and miR-375) that regulate global changes in alternative splicing via targeting a single RNA binding protein called Quaking. Quaking levels are correlated with higher rates of metastasis and poor outcome in breast and prostate cancer. We are investigating the function of Quaking and several important alternatively spliced events during cancer progression. We have also identified a microRNA (miR-342) that is down-regulated in triple-negative breast cancers that are more likely to metastasise. As triple-negative breast cancers have limited therapeutic options we are hoping that by understand miR-342 we can identify new avenues for treating this deadly disease.

Key discoveries 2017

MicroRNA-194 promotes prostate cancer metastasis
In collaboration with Dr Luke Selth and Professor Wayne Tilley at the University of Adelaide, we identified a microRNA which drives prostate cancer metastasis in animal models and is indicative of poor survival rates in humans (Das *et al*, *Cancer Res* 2017). MiR-194 is elevated in the circulation of men who experience biochemical (PSA) relapse and controls prostate cancer cell plasticity and invasion. One of the prominent targets of miR-194 is SOCS2, whose repression leads to activation of ERK and STAT3 signalling. These findings uncovered a novel pathway through driving prostate cancer progression, which we are currently investigating in further detail.

Alternative splicing is critical for tumour cell plasticity
By globally profiling human mammary epithelial cells that have undergone EMT, we identified hundreds of alternative splicing changes that are conserved across multiple cancers. In 2015, we reported that a subset of these changes involve circularisation of the RNA (Conn *et al*, *Cell* 2015). Further investigation of publically available data show that EMT-associated splice events also occur frequently in other contexts of cell differentiation, indicating they have important and conserved functions (Neumann *et al*, *Semin Cell Dev Biol* in press).
As part of our ongoing work, we are investigating the function of key alternative splicing events in cancer progression.



Heat map showing conservation of alternative splicing changes regulated by the RNA binding protein Quaking (QKI) during epithelial-mesenchymal transition (EMT). Produced by John Toubia.

Outcomes for the Community

Tumour metastasis is the major cause of cancer related death in solid tumours such as the breast and prostate. We have identified important microRNAs that control the aggressiveness of tumour cells. By investigating how these microRNAs function, we aim to identify new avenues through which therapeutic targets may be developed to limit the development of metastasis, and ultimately, improve patient outcomes.

Kaitlin Scheer, Cameron Bracken, Sunil Sapkota, Laura Sourdin

Gene Regulation Networks Group

Dr Cameron Bracken PhD

Cancer is a genetic disease, characterised by the dysregulation of genes and genetic networks. One key regulator of gene expression networks that are frequently affected in cancer is microRNAs which are capable of targeting multiple components within a signalling pathway to have profound effects on cell identity and behaviour.

Our laboratory looks at the co-ordinated manner by which multiple microRNAs regulate the genetic switches associated with the differentiation and motility of cancer cells and uses a combination of "wet-bench" experimentation, high-throughput sequencing and bioinformatic investigation to better understand the role of microRNAs in cancer progression.

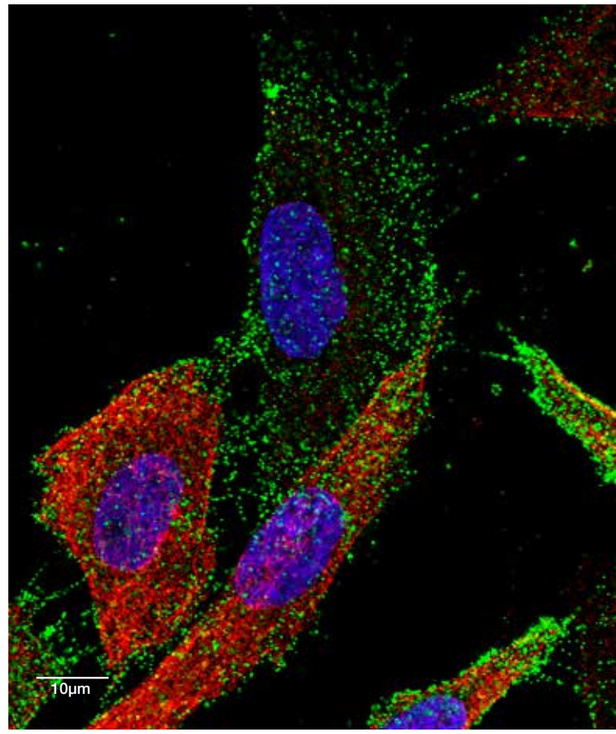
In recent work, we are uncovering important ways in which microRNAs function together to coordinate gene expression, and through work conducted at the CCB and in conjunction with external collaborators, are discovering the importance of these co-ordinated functions. This has potential implications for future therapies, where we find that the traditional approach of single microRNAs expressed at very high levels, may not be as effective as combinations of more modestly expressed microRNAs, which have an additional benefit of also causing less unwanted side-effects.

We are also uncovering a previously unknown layer of complexity, whereby even the same kind of microRNA can be expressed in many subtly different forms. We find not only is this variation extensive, but importantly, that this variation can have very large effects on how microRNAs function that have further implications for the use of microRNAs in both diagnosis and therapy.

Key discoveries 2017

Naturally occurring microRNA variation is of major functional consequence

With the advent of high-throughput sequencing technologies, in recent years it has become apparent that microRNAs are expressed with a great range of subtle sequence variation, but most of this was dismissed as unlikely to be of functional consequence to how microRNAs behave and to the genes that they regulate. In a recent work published in *Nucleic Acids Research*, we provide one of the first proofs that sequence variation (at the 3' end of microRNAs) is extremely important, with subtle sequence variation quite literally being a matter of life and death for cancer cell lines in which they are expressed. While this is very important in better understanding the role of miR-222 on which this study was focused, it has far broader implications as almost all microRNAs show similar 3' variability. It may also help explain a large amount of disagreement in scientific literature, where the same microRNA is often reported as exerting very different effects – observations that may be explained, at least in part, by researchers unwittingly using different variants of the same microRNA (Yu *et al*, *Nucleic Acids Research* 45: 11371-11385, 2017).



The Epidermal Growth Factor Receptor (EGFR) is one of the most heavily targeted molecules in cancer therapy. We have identified a family of microRNAs that directly regulate not only the EGFR, but also many of the genes that act downstream to mediate the signalling events that control cell proliferation and motility. This image shows neuroblastoma cells stained to show the actin cytoskeleton (red), nuclei (blue) and clustered EGFR proteins (green) after EGF treatment.

Outcomes for the Community

MicroRNAs offer tremendous potential to both better understand cancer progression, and to be utilised for diagnostic and therapeutic application. Our work provides fundamental insights into how microRNAs work in cancer, and indicates previously unknown layers of complexity that exist both with the importance of microRNA co-operativity and microRNA sequence variability.

Vinay Tergaonkar

Gokhan Cildir, Nirmal Robinson, Ava Zhou

Inflammation and Human Ailments Laboratory

IMCB Visiting Professor

Professor Vinay Tergaonkar PhD

Inflammation is an underlying cause of chronic human diseases including allergies, obesity and cancer. In our lab, we study the roles of novel inflammatory pathways to better understand the common human disorders with the overall goal of finding novel therapeutic targets.

GREB1 in breast cancer

Inflammation is now well-recognized as one of the hallmarks of cancer. Breast cancer is the most prevalent cancer in women, and there is an urgent need to identify novel therapeutic targets for better disease prognosis and improved response to therapies. Our lab has identified a protein known as GREB1, critically involved in the progression of estrogen receptor alpha (ER^+) breast cancers, comprising nearly 80% of breast cancers in women. Using genetic mouse models and human patient samples, we are investigating a novel, hitherto unknown enzymatic function of GREB1 which could have immense therapeutic potential in the clinic.

Mast cells in allergic inflammation

There is an epidemic of allergies worldwide. It is estimated that 40% of the human population will develop an allergic disease in their lifetime. Mast cells are tissue-resident immune cells playing critical and non-redundant roles in the progression of common allergic diseases. In our lab, using cutting-edge genomics technologies such as CHIP-seq, ATAC-seq and RNA-seq, we are investigating the genome-wide chromatin response and transcriptome dynamics of human and mouse mast cells to better understand their complex activation programme in allergic diseases. We identified several novel regulators of mast cells and are investigating their functions in different disease models.

"Collaboration is the only way we are going to stop people dying from cancer. It's so important that everyone plays their part, and that we come together to solve this global problem. Cancer has too many steps to not have partnerships in place to beat it. The way this research collaboration is unique is that both Singapore and Australian institutes and people leverage on each other's strengths and expertise. This is unique and as far as I know attempted for the first time in the world. This is what makes this collaboration a win-win for many people, not just in Singapore and Australia but for the millions in other parts of the world who will benefit from the accelerated research due to the drive of the two Governments (Australia and Singapore) behind this partnership."

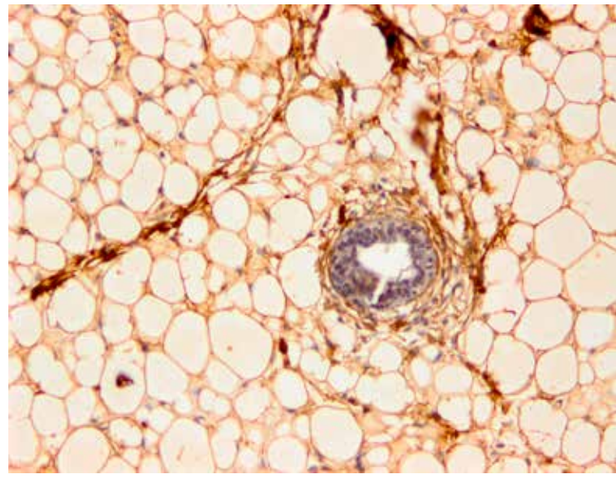
Professor Vinay Tergaonkar PhD

Key discoveries 2017

Although GREB1 is known to be an estrogen-responsive gene, its function is largely unknown. Our *in vitro* experiments had suggested novel enzymatic functions of GREB1 which will be tested with *in vivo* models. To this end, we first generated whole body GREB1 knockout (KO) mice. Importantly, our preliminary results suggested that although GREB1 is not essential for embryonic development, it regulates body weight in a sex-specific manner and GREB1 deficiency leads to significant metabolic abnormalities especially in adipose tissue.

In collaboration with Dr Marina Kochetkova, we are also investigating the novel functions of GREB1 in the context of mammary gland development and breast cancer progression. We have crossed GREB1 KO mice with the MMTV-PyMT mouse model of breast cancer, and we are evaluating the impact of GREB1 deficiency on breast cancer development. Overall, these mouse models will allow us to investigate the roles of GREB1 in metabolic diseases and breast cancer progression.

Furthermore, we have conducted several genome-wide studies to better understand the allergic inflammation commonly observed in diseases such as asthma and eczema. In collaboration with Prof Angel Lopez and clinicians at the Royal Adelaide Hospital (RAH), we are now investigating the functions of novel regulators of mast cells which could have therapeutic implications in clinical settings. We also identified a novel chromatin signature in mast cells which is essential for the regulation of allergic inflammation.



Immunohistochemical staining of GREB1 in mammary fat pad from C57BL/6 mouse

Recent articles

Cildir G, Pant H, Lopez AF, Tergaonkar V. The transcriptional program, functional heterogeneity, and clinical targeting of mast cells. *The Journal of Experimental Medicine* 214(9): 2491–506, 2017. This article is the first literature review outlining the heterogeneity of mast cells from a transcriptional point of view. Furthermore, it provides thought provoking novel inputs which could be experimentally evaluated to understand the pathogenic role of mast cells in inflammatory disorders.

Conn VM, Hugouvieux V, Nayak A, Conos SA, Capovilla G, Cildir G, *et al*. A circRNA from SEPALLATA3 regulates splicing of its cognate mRNA through R-loop formation. *Nat Plants* 3: 17053, 2017. This work is the first demonstration of a circular RNA regulating an organismal-level phenotype.

Outcomes for the Community

The primary focus of our laboratory is to understand the molecular details of inflammation, a process that is critical for the progression of various human diseases including cancer, infectious diseases, metabolic disorders such as obesity and allergies. Taking advantage of the latest genome technologies, we have unravelled the molecular functions of novel proteins and RNAs involved in regulating the core machinery of inflammation. This approach has helped us identify unique biomarkers which could be utilized in diagnosis and for developing new therapies to treat these debilitating human diseases.

Zoe Donaldson, Nur Hezrin Shahrin, Susan Branford, Linda Welden, Naranie Shanmuganathan

Alexandra Yeoman, Jasmina Georgievski, Carol Wadham, Daniel Thomson

Leukaemia Unit, Genetics and Molecular Pathology

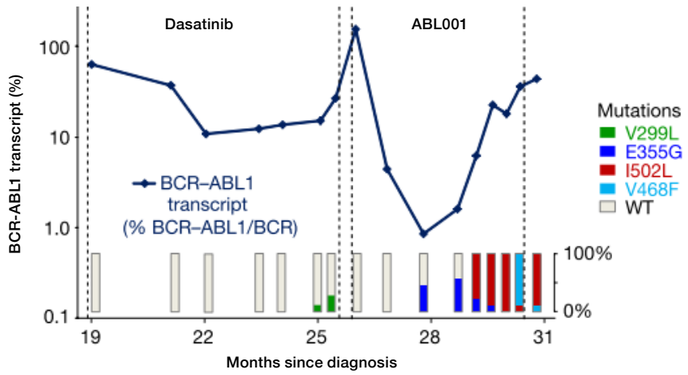
Associate Professor Susan Branford PhD, FFSc (RCPA)

Our laboratory studies patients with chronic myeloid leukaemia (CML). If patients with CML do not receive treatment they will invariably die within three to five years. However, the development of new drugs over the last 20 years has meant that most patients will now have a normal life expectancy. This shift in patient outcome has been one of the greatest triumphs of cancer research. A small percentage of patients can even stop therapy without relapse, thereby relieving drug-related side-effects that impact quality of life.

However, despite improved survival, ~40% of patients will have drug resistance or intolerance and require a change of therapy. More potent drugs can induce higher rates of response and lower rates of transformation to a rapidly fatal acute leukaemia. However, these drugs are associated with higher toxicity and have not shown a survival advantage. Unfortunately, it is currently not possible to identify patients at the time of diagnosis who are destined to fail therapy. Therefore, it is not possible to determine which patients may benefit from more potent drugs despite the increased risk of toxicity.

Our research aims to understand the molecular basis for the difference in treatment outcome between patients and to identify biomarkers at diagnosis that will predict response. We and others established that gene mutations within the BCR-ABL1 gene, which is the genetic abnormality that causes CML, are a major cause of drug resistance. These mutations occur in 50% to 60% of resistant patients. New, advanced technology is now available to perform expanded genomic studies to simultaneously assess all genes to search for other mutations that modify response to therapy. Our initial mutational analysis suggests that additional mutations cooperate with BCR-ABL1 to drive CML progression. In vitro functional validation of the mutations is underway to provide a functional proof-of-principle for cooperation of BCR-ABL1 with individual mutations. A more complete understanding of these mutations should advance drug development and allow personalised therapy. Our aim is to translate our work to the clinic by introducing a comprehensive biomarker testing panel at diagnosis that will more reliably predict treatment response and guide appropriate therapeutic decisions.

Clonal evolution of resistance mutations in a CML patient treated with a new BCR-ABL1 inhibitor ABL001
Plot of BCR-ABL1 transcript values over time in response to therapy. A rise indicates drug resistance. Novel BCR-ABL1 myristoyl-site point mutations emerged that conferred specific resistance to the inhibitor and disease relapse after an initial response. Selection and deselection of the novel mutations indicates clonal competition between resistant clones with varying drug resistance profiles.



Key discoveries 2017

Long-term outcomes of imatinib treatment for chronic myeloid leukemia
This publication was the culmination of a long-term international project dedicated to defining treatment response and mechanisms of drug resistance in the treatment of CML and received global recognition in the leading medical publication *The New England Journal of Medicine* (Hochhaus *et al*, *NEJM* 2017;376:917-927.) The study reported the 10 year follow up of the first study of the new class of drugs that led to unprecedented patient responses by inhibiting the causal genetic abnormality, BCR-ABL1. Subsequent studies revealed other cancers in which the drug was active through a different genetic target. The study was pivotal in establishing the importance of monitoring treatment response at the molecular level and was followed by the global adoption of standardised molecular monitoring for patients with CML.

The allosteric inhibitor ABL001 enables dual targeting of BCR–ABL1
This publication in Nature was the first on ABL001, a new allosteric inhibitor likely to revolutionise CML therapy (Wylie *et al*, *Nature*. 2017; 543:733-737.) The drug binds in a different region of the BCR-ABL1 protein from other drugs used to treat CML. Importantly, pre-clinical studies demonstrated that combination therapy with another BCR-ABL1 inhibitor may be effective in the treatment of the acute phase of CML. This phase is usually refractory to therapy and is associated with high mortality. Combination therapy thereby offers new therapeutic opportunities and is an exceptional example of clinical-translational research that will benefit patients with CML. Nevertheless, drug resistance to ABL001 occurs and our laboratory identified the first clinical case of a resistant mutation in the ABL1 myristate binding pocket. The drug has distinct patterns of resistance mutations.

Germline genetic variants predict response and identify CML patients with the greatest risk of treatment failure
We aimed to identify genomic predictive biomarkers of drug response at the time of diagnosis to aid the selection of first-line therapy (Marum *et al*, *Blood Advances*. 2017;1:1369-1381). Algorithms for scoring risk at diagnosis based on clinical parameters, such as percentage of blast cells, platelet count and spleen size, have been in use for decades, but treatment based on these clinical risk scores is not consistently recommended and these risk scores do not reliably identify the patients at highest risk of transformation to acute leukaemia and death. We used next-generation sequencing to interrogate specific regions of the genome to identify inherited genetic differences and identified two genes where inherited variation in the gene sequence was associated with differences in treatment outcome. When the patient genotype was combined with the clinical score in a classification tree model, predicting response to treatment was improved. These data suggest that inherited genetic variation contributes to the heterogeneity of response to treatment and may contribute to a prognostic risk score that allows early optimisation of therapy.

Outcomes for the Community

Associate Professor Susan Branford, representing the work of our laboratory for the development of molecular diagnostic testing for patients with CML, was awarded the 2017 International Federation of Clinical Chemistry and Laboratory Medicine Distinguished award for significant contributions in molecular diagnostics. This triennial award recognises unique contributions to the promotion and understanding of molecular biology and its applications to benefit patients. The award is designed to highlight exceptional research and to stimulate and encourage other researchers.

Paul Reynolds, Greg Hodge, Hai Tran, Hubertus Jersmann, Sandra Hodge, Miranda Ween, Rebecca Harper, Rhys Hamon, Jonathan Whittall, Eugene Roscioli

Lung Research Laboratory

Professor Paul Reynolds MBBS, MD, PhD, FRACP, F Thor Soc

Lung cancer is the most common cause of cancer death in both men and women, with just 15% of patients surviving five years after diagnosis. The Lung Research Program conducts studies using samples obtained directly from patients to make new discoveries in the understanding of the biological basis of cancer and to develop novel therapies. This link between the clinic and the laboratory provides an ideal environment for the translation of laboratory discoveries into early phase human trials.

Tobacco smoking is the greatest risk factor for developing lung cancer and smoking-induced Chronic Obstructive Pulmonary Disease (COPD) is an independent risk factor for cancer development, even when corrected for the amount smoked. We discovered some years ago that smoking impairs macrophage function, leading to a build-up of apoptotic and necrotic material in the airways and perpetuating the inflammatory response. Importantly, this problem persists in COPD even after stopping smoking and may have relevance to cancer development.

Macrophage dysfunction provides a new therapeutic target that may have a substantial impact in pulmonary disease. We are investigating macrophage modulating therapies including new generation macrolide molecules and mannose binding lectin, with the aim of progressing this work to new clinical therapies. We are also studying the pro-inflammatory effects of electronic cigarettes (vaping) which have grown rapidly in popularity, but are not 'safe' as is being promoted. New cancer-related projects in 2017 include the establishment of new models whereby human tumour samples are directly implanted into mice to assess the response to novel anti-cancer therapies, particularly addressing the 14-3-3 protein pathway. New clinical studies are looking at improved biopsy techniques using cryoprobes which obtain larger samples using a freezing technique during bronchoscopy. These samples enable greater molecular profiling of tumours, thereby facilitating the use of newer, targeted therapies.

Pulmonary disease also has a major impact on the pulmonary vasculature and in this regard we are studying Pulmonary Arterial Hypertension (PAH), a condition caused by abnormal vascular cell proliferation, which has features in common with malignancy, including monoclonal expansions of endothelial cells. We have been investigating a gene and cell therapy approach targeting the bone morphogenetic protein receptor 2 (BMPR2) pathway which we have shown counteracts TGF-b mediated endothelial to mesenchymal transition (EndMT). We have shown that upregulating this pathway in vivo is an effective treatment for the vascular remodelling seen in PAH, using a viral vector based gene therapy approach. To advance this strategy to clinical translation we are now working on using endothelial progenitor cells (EPCs) engineered to overexpress BMPR2, and evaluating both the cells themselves and exosomes derived thereof as therapies. This approach has proven successful in our models and holds great promise for clinical translation.

In addition to these major themes, the Lung Research Program also conducts a range of projects looking at markers of lung transplant graft rejection, new therapies in asthma, and interstitial lung disease.

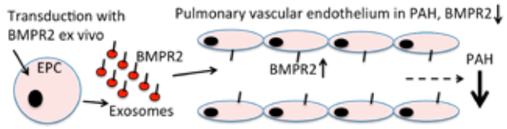
Macrolides in airways inflammation: asthma

As part of a nationwide NHMRC-funded clinical trial we showed that the addition of Azithromycin three times per week on top of usual care reduced asthma exacerbations by more than 40%. This pivotal trial enrolled 420 patients who were treated for 48 weeks. (*Lancet*, 2017 Aug 12; 390 (10095): 659-668).

Further work on macrolides demonstrated that novel agents lacking in antibacterial actions (and thereby reducing the risk of development of resistant organisms) also have significant anti-inflammatory properties. This approach may further broaden the clinical translatability of macrolides. (Hodge S *et al*, *Am J Physiol Lung Cell Mol Physiol* 2017 May 1; 312(5): L678-L687).

Engineered cell therapy for pulmonary hypertension

We have further advanced our EPC therapy program and have demonstrated that EPCs transduced with BMPR2 release exosomes which upregulate BMPR2 in surrounding cells. This may explain the significant therapeutic effects we see with EPC therapy, despite the short retention time of these cells in the lungs. Further, this opens up new therapeutic platform opportunities to use exosomes themselves as the treatment. This work has led to a new NHMRC project grant commencing in 2018.



Transduced EPCs traffic to the lung and release exosomes that can upregulate BMPR2, to treat PAH

Outcomes for the Community

Diseases affecting the lungs are the most common cause of general practitioner consultation and are responsible for huge economic and healthcare costs, morbidity and mortality. Our program is providing new insights into these diseases and new approaches to therapy that will lead to improved health outcomes through addressing currently unmet clinical needs.

Jan Kazenwadel, Natasha Harvey, Drew Sutton, Genevieve Secker, Kelly Betterman

Lymphatic Development Laboratory

Associate Professor Natasha Harvey PhD

Lymphatic vessels are an integral component of the cardiovascular system. These specialised vessels maintain fluid homeostasis, absorb fats from the digestive tract and are an important highway for immune cell transport. Abnormalities in the growth and development of lymphatic vessels underlie human disorders including lymphoedema, vascular malformations, autoimmune diseases and cancer.

Cancer cells exploit the lymphatic vasculature as a route for metastasis and in some cases, promote the growth of new lymphatic vessels in the tumour microenvironment in order to gain entry to this vascular highway and spread throughout the body. The focus of our laboratory is to understand how the lymphatic vascular network is built during development. We are interested in identifying and characterising genes that are important for lymphatic vessel growth, patterning and maturation. Once we understand how lymphatic vessel growth and development is normally controlled, we will gain new insight into how this process "goes wrong" in human disease and moreover, will be afforded the opportunity to rationally design novel therapeutics able to block or promote lymphatic vessel growth and/or function and thereby treat human lymphatic vascular disorders.

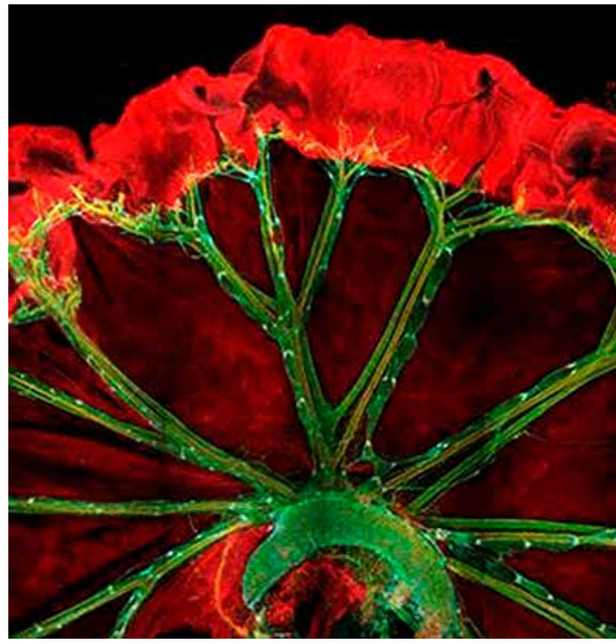
Outcomes for the **Community**

Lymphatic vessels are of major importance to cancer patients. Cancer cells exploit lymphatic vessels as a route for metastasis and can enter pre-existing lymphatic vessels, or promote the growth of new lymphatic vessels in order to gain access to the lymphatic vascular network. Lymphatic vessel damage following cancer surgery results in secondary lymphoedema, a disabling condition for a substantial proportion of cancer patients. There are currently no effective, curative treatments for lymphoedema. By understanding the signals that control the growth and development of lymphatic vessels, we hope to design new therapeutics that either block, or promote lymphatic vessel growth. Blocking agents should prove valuable for reducing cancer metastasis, while growth promoting agents could provide novel therapeutics for the repair of lymphatic vessels and treatment of lymphoedema.

Key discoveries 2017

Understanding how valves are constructed during development

We have had a long-standing interest in understanding how cell identity is programmed during development and in particular, how the identity of the cells that make up our blood vessels and lymphatic vessels is imparted. We have identified a number of molecular switches called transcription factors that are important for this process and in particular, that are important for turning on the identity of the cells that build valves in our vasculature. Valves in our hearts, blood vessels and lymphatic vessels are vital for ensuring that blood and lymph is transported in a unidirectional manner and aberrations in valve development result in human conditions including congenital heart disease, venous disease and lymphoedema. Following our discovery that the transcription factor GATA2 is important for the construction and maintenance of lymphatic vessel valves (Kazenwadel *et al*, *J Clin Invest*, 2015), we have focussed on defining the cellular and molecular mechanisms by which GATA2 orchestrates lymphatic vessel valve development. We have identified several new genes that are regulated by GATA2 and have important roles in valve construction. Ultimately, our goal is to identify new therapeutic targets to which effective therapeutics for the treatment of lymphoedema could be designed.



Blood vessels (green) and lymphatic vessels (green), punctuated by valves, (cyan) that supply and drain the intestine.

Understanding the genetic and developmental basis of human primary lymphoedema syndromes and human lipedema

Primary lymphoedema results from the failure of lymphatic vessels to develop or function properly and results in painful and often disabling fluid accumulation in affected tissues, which is further complicated by inflammation and susceptibility to infection. Lipedema, while sharing features with lymphoedema that include lymphatic vessel dysfunction, tissue swelling and inflammation, is a distinct, yet very poorly understood condition that is characterised by the accumulation of painful adipose tissue. In collaboration with Professor Hamish Scott's research team at the Centre for Cancer Biology and our clinical partners, we are investigating the genetic basis of human primary lymphoedema syndromes and human lipedema by sequencing the genomes of affected patients and their family members. Once the genetic events that cause these diseases are identified, studies to define gene function in lymphatic vessel growth and development are undertaken in order to understand how distinct gene mutations cause disease. Ultimately, we aim to develop novel diagnostic and therapeutic tools that can be employed to aid patient prognosis and treatment.

Anna Brown, Milena Babic, Hamish Scott,
Saba Montazeribarforoushi, Parvathy Venugopal

Chris Hahn, Tristan Hardy, Peer Arts, Peter Brautigan, Alicia Byrne

Molecular Pathology Research Laboratory

Professor Hamish S Scott PhD FFSc (RCPA) FAHMS

Human diseases often have a substantial genetic component giving rise to diversity of presentation, progression and response to treatments. We use state-of-the-art technologies to identify genetic contribution to these disease processes to better understand the pathogenic mechanisms with the aim that targeted treatments that are more efficacious with fewer side-effects can be administered or developed.

We identified the mechanism by which some patients with bone marrow failure disorders such as Diamond Blackfan Anaemia (DBA) spontaneously correct their disease. We identified a *de novo* (ie new–not inherited) causal mutation on the maternal chromosome in a young boy with DBA. Using state-of-the-art genomic technologies, we then showed that partial correction of the disease was due to the mutated maternal chromosome being spontaneously replaced by the normal functioning paternal chromosome which then expanded to over half of the boy's bone marrow cells. Importantly, this provides opportunities/strategies to develop effective cell-therapy approaches in other Diamond-Blackfan Anaemia and bone marrow failure sufferers.

(Venugopal P *et al*, Self-reverting mutations partially correct the blood phenotype in a Diamond Blackfan Anemia patient. *Haematologica* 102: e506-e509, 2017)

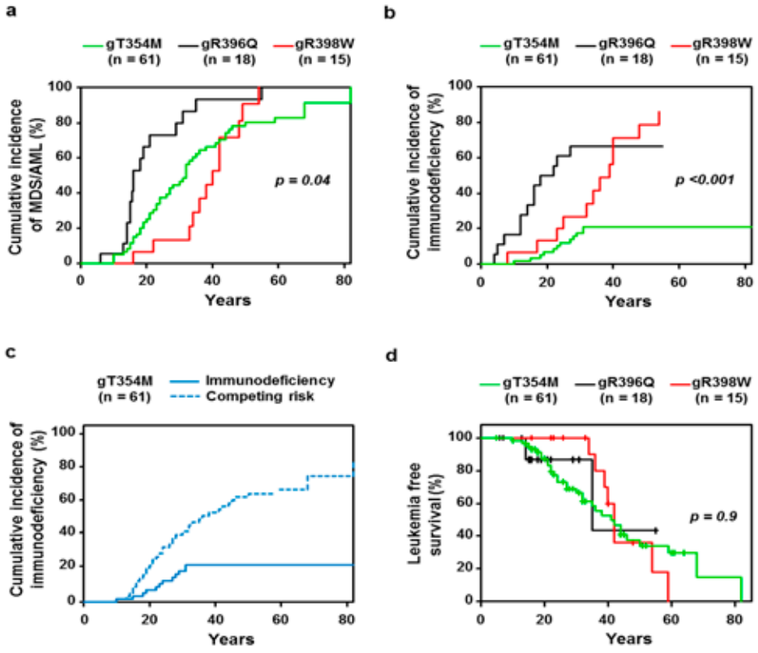
In 2011, we first published that inherited mutations in a gene called GATA2 can predispose to developing acute myeloid leukaemia at a young age. Here we generated mutant versions of GATA2 that relate to known mutations found in human leukaemias, and performed a range of functional analyses. We have shown how these mutations affect normal GATA2 function and revealed a novel mechanism by which several of these mutations might lead to leukaemia.

(Chong C-E *et al*, Differential effects on gene transcription and hematopoietic differentiation correlate with GATA2 mutant disease phenotypes. *Leukemia* 32: 194-202, 2017)

Outcomes for the Community

We continue to identify new leukaemia and lymphoma predisposition genes/mutations in families which can have immediate impact on individuals and families. Similarly, discovery of new perinatal lethal genes/mutations continues to offer hope, practical outcomes and importantly answers for an increasing number of families. Findings from both of these studies have the potential to impact individuals and families locally and world-wide.

Key discoveries 2017



Analyses of clinical outcomes for most common germline GATA2 mutations. Time to event analyses were performed using the cumulative incidence function with adjustment for competing risk. (a) Cumulative incidence of MDS/AML stratified by GATA2 mutations. (b) Cumulative incidence of immunodeficiency for three germline GATA2 mutations. (c) Cumulative incidence of immunodeficiency syndrome in gT354M patients. AML, MDS and death from any cause were considered competing risk events that prevent or mask the development of immunodeficiency. (d) Kaplan–Meier plot of leukemia transformation free survival for GATA2 mutants. An event is either diagnosis of AML or death. All P-values (log-rank test) are for overall global comparisons.

Genetics and pathologic mechanisms of haematological malignancy (HM, leukaemia and lymphoma) predisposition and progression

Exciting work in our laboratory includes disease gene discovery and confirmation utilizing latest genomic technologies. We have accrued samples from over 120 families with predisposition to HM, which are an invaluable resource for the identification of genetic and epigenetic changes leading to these and other cancers. Using a combination of strategies including state-of-the-art whole exome and genome next generation sequencing, we have identified known and novel genes that segregate with diseased individuals in some of these families and/or are mutated in sporadic samples. We continue to hunt for genes/mutations in 'unsolved' families and sporadic samples. Functional studies on potential and identified genes continues *in vitro*, *ex vivo* and *in vivo* in mice to expose mechanisms for predisposition and progression to HM. Opportunities exist for students/researchers to be involved in utilising latest genomic and bioinformatic technologies to identify new disease genes and how mutations cause disease.

'Genetic autopsy' of perinatal death: diagnosis and discovery

This is an exciting project that has already benefitted numerous families and individuals. We use state-of-the-art next generation sequencing and genomic technologies to identify genetic causes of perinatal death (ie childhood death around full term). This can assist in accurate diagnosis, family planning, and discovery of new syndromes. Importantly, in some cases, it can also lead to novel treatments to alleviate symptoms or disease progression.

Mab immunotherapies for myeloid leukemia patients with germline or somatic RUNX1 mutations

Mutation of RUNX1 (germline and somatic) is one of the most widespread, frequent and aggressive drivers of HM, currently without any effective targeted treatments available. We have identified 2 FDA approved potential targeted monoclonal antibody therapies that may prove beneficial against RUNX1-mutated leukaemias. In this study, we aim to perform pre-clinical testing to establish a precedent for mutation-specific cell-surface immunotargets in familial cancer, and to provide rationale for rapid translation to human clinical testing.

Back row: Claire Wilson, Ammara Farooq, Natalie Foot, Dylan De Bellis, Yoon Lim
Front row: Kelly Gembus, Sharad Kumar, Jantina Manning, Loretta Dorstyn

Back row: Andrej Nikolic, Julian Carosi, Tianqi Xu, Sonia Dayan, Ian Nicholson
Front row: Tanya Henshall, Xin Jiang, Donna Denton, Shannon Nicolson

Molecular Regulation Laboratory

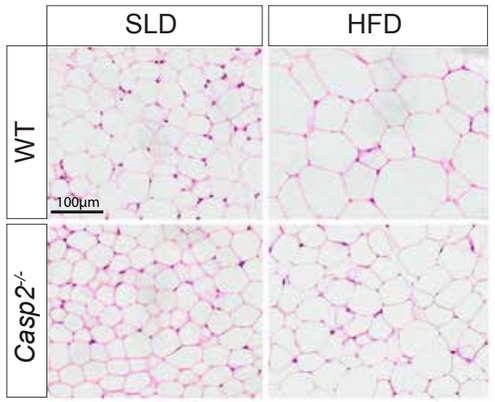
Professor Sharad Kumar AM MSc PhD FAA FAHMS

Our research focuses on the fundamental aspects of two key biological processes: "programmed cell death" and "protein ubiquitination", both of which have direct implications for our understanding of the basis of major human ailments including cancer, cardiovascular and inflammatory diseases. The study of these critical cellular pathways is essential for finding new ways for early detection and better treatments of human disease.

Caspase-2 is important for maintaining energy metabolism and homeostasis

Caspase-2 is a conserved cell death protease that has roles in both apoptosis and non-apoptotic pathways. Our previous studies demonstrated that caspase-2 deficiency (*Casp2*$^{-/-}$) enhances premature ageing-related traits and increases susceptibility to oxidative stress-induced damage and tumour development in mice. We recently identified caspase-2 as a potential regulator of metabolism and glucose homeostasis and demonstrated that caspase-2 loss protects against aged-induced glucose intolerance, independent of insulin sensitivity. Our new findings now suggest that caspase-2 has a role in basal energy metabolism by regulating adipocyte biology and fat expansion (Wilson *et al*, *Cell Death Dis*, 2017). In particular, we found that *Casp2*$^{-/-}$ mice have altered glucose homeostasis as a result of increased carbohydrate utilisation and believe this is due to mild energy stress.

As a consequence, aged *Casp2*$^{-/-}$ mice show altered body composition (reduced fat and muscle mass), smaller white adipocytes, increased fasting-induced lipolysis of white adipose tissue (WAT) and autophagy of skeletal muscle and liver. Importantly, loss of caspase-2 is protective against high-fat-diet (HFD)-induced obesity, insulin resistance and non-alcoholic fatty liver disease (NAFLD). We propose that caspase-2 deficiency alters metabolic pathways resulting in mild energy stress and adaptive remodelling of adipose tissue.



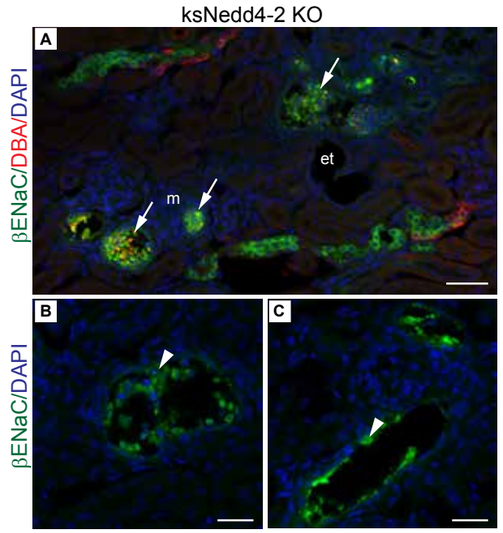
Caspase-2 deficiency prevents HFD-induced obesity
Images of Hematoxylin and Eosin (HandE) stained white adipose tissue showing smaller sized adipocytes in *Casp2*$^{-/-}$ mice compared to wild type (WT) mice, fed a standard laboratory diet (SLD) or high fat diet (HFD).

Key discoveries 2017

Deletion of Nedd4-2 results in progressive kidney disease in mice

Nedd4-2 (NEDD4L) is a ubiquitin ligase of the Nedd4 family and a key regulator of several ion channels and transporters (Foot, Henshall and Kumar, *Physiol Rev*, 2017). The best known target of Nedd4-2 is the amiloride-sensitive epithelial sodium ion (Na+) channel (ENaC), which allows the flow of Na+ from the lumen across the apical cell membrane and into epithelial cells. We previously demonstrated that complete absence of Nedd4-2 results in pulmonary distress and perinatal lethality due to increased cell surface levels of ENaC.

Our new findings now demonstrate that Nedd4-2 deficiency also affects the kidney. In particular, kidney specific deletion of the *Nedd4-2* gene (ksNedd4-2 KO) leads to progressive injury associated with elevated ENaC expression (Henshall *et al*, *Cell Death Diff*, 2017). The observed nephropathy is characterised by fibrosis, tubule epithelial cell apoptosis, dilated/cystic tubules, elevated expression of kidney injury markers and immune cell infiltration: features reminiscent of human chronic kidney disease (CKD). Importantly, we found that the extent of kidney injury can be partially ameliorated therapeutically in mice by blocking ENaC with amiloride. Further, we noted that Nedd4-2 deletion is associated with hypertension and electrolyte imbalances on a normal Na^+ diet. These results suggest that increased Na^+ reabsorption via ENaC can lead to kidney injury and establishes a novel role of Nedd4-2 in preventing Na^+-induced nephropathy.



High ENaC in Nedd4-2 KO mice is associated with kidney injury.
(A) ENaC (green) in collecting duct marked with DBA lectin (red). Kidney damage is associated with mesenchyme accumulation (m), enlarged tubules (et) and cellular debris within tubules (arrows) due to loss of lining epithelium. Higher power images (B, C) showing loss of ENaC-expressing epithelium (arrowheads).

Outcomes for the Community

Our findings provide important insight into (i) metabolic homeostasis associated with ageing and (ii) molecular events related to susceptibility to kidney disease. Aberrations in whole body energy homeostasis contribute to the onset and severity of numerous diseases including obesity, type II diabetes and cancer. We have now identified a new role for caspase-2 in this process and suggest that absence of the caspase-2 gene may be a new biomarker to predict susceptibility to these diseases. In addition, the discovery of Nedd4-2 ligase having an important role in preventing Na^+-induced kidney disease has important implications for the diagnosis, management and treatment of human kidney diseases, which affect up to 10% of the global population. Our work also provides key insight into salt-induced kidney damage. This work has been highlighted in recent articles by The Hospital Research Foundation and The Lead SA.

Maurizio Costabile, Melissa Pitman, Alex Lewis, Stuart Pitson, Jason Powell, Lorena Davies

Melinda Tea, Briony Gliddon, Melissa Bennett, Carl Coolen, Jo Woodcock, Paul Moretti

Molecular Signalling Laboratory

Professor Stuart Pitson PhD

The Molecular Signalling Laboratory examines the regulation of cell signalling pathways by sphingolipids; to both determine how defects in this contribute to cancer, wound healing, fibrosis, and other conditions, and to develop agents to target these pathways to improve human health.

Sphingolipids, including ceramide, sphingosine and sphingosine 1-phosphate regulate a diverse range of cellular processes by acting as intracellular signalling molecules, while sphingosine 1-phosphate also acts as a ligand for a family of cell surface receptors. Sphingolipid metabolism is controlled by a complex network of enzymes that are regulated by subcellular localisation and post-translational modifications. The sphingosine kinases are key enzymes controlling sphingolipid metabolism, and through this action can regulate central processes such as cell survival and proliferation. Two sphingosine kinases exist in humans; sphingosine kinase 1 (SK1) and the little studied sphingosine kinase 2 (SK2). We and others have shown that high levels of sphingosine kinase 1 contribute to many of the hallmarks of cancer, including enhanced cell survival and proliferation, promotion of new blood vessel formation, increased cell invasive properties and deregulating cellular energetics. This indicates an oncogenic role for SK1, which is further supported by findings of elevated SK1 in a variety of human cancer cells, and inhibition of tumour growth *in vivo* by genetic or chemical suppression of sphingosine kinase.

Recent work in the Molecular Signalling Laboratory has concentrated on identifying the mechanisms regulating sphingolipid metabolism, the cellular functions controlled by the enzymes involved in this pathway, and in developing small molecule inhibitors as potential anti-cancer agents. In particular we have made several major breakthroughs in understanding how these enzymes are activated, relocalised in the cell, and deactivated, which have provided novel therapeutic targets to control cancer and other diseases.

Key discoveries 2017

Identification of SK1 as a therapeutic target in acute myeloid leukaemia

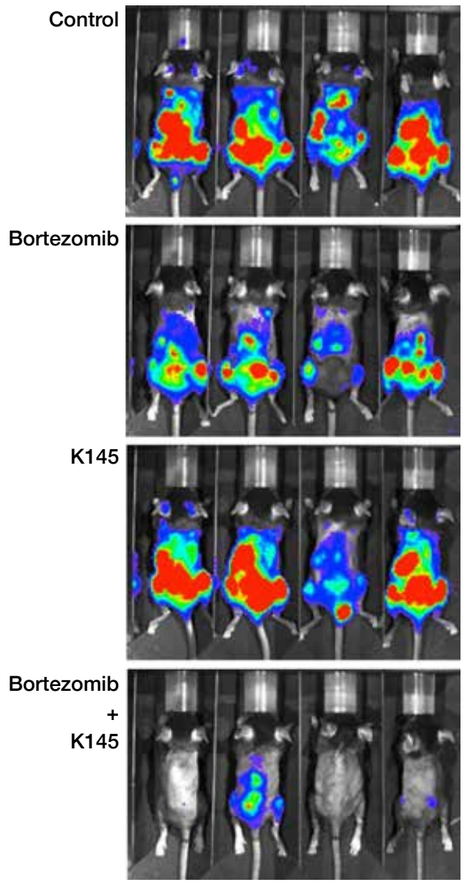
Acute myeloid leukaemia (AML) is an aggressive heterogeneous malignancy with poor clinical outcomes. We and others have shown that SK1 plays an important role in cancer initiation, progression and chemotherapeutic resistance in many solid tumours, but its contribution to AML has not been well defined. In work recently published in Blood (Powell *et al*, *Blood*) we have shown that SK1 is overexpressed and constitutively activated in AML, and that SK1 inhibitors we developed can effectively target AML cells, and reduce tumour load and prolong survival in primary patient derived xenografts of AML in mice. Furthermore, we demonstrated that SK1 inhibition synergised with both chemotherapeutics currently used for AML therapy, as well as with the emerging targeted therapy of BH3 mimetics. Thus, these findings support the notion that SK1 is a bona fide therapeutic target for the treatment of AML.

Defining the CIB2/SK1 axis as a prognostic indicator and chemosensitising target in ovarian cancer

Ovarian cancer has a poor prognosis largely because most patients are diagnosed when at an advanced, metastatic stage of the disease where intrinsic or acquired resistance to chemotherapeutics is common. In studies recently published in Cancer Research (Zhu *et al*, *Cancer Res*), we have recently discovered that the CIB2 protein is a natural negative regulator of the pro-survival SK1, suggesting that CIB2 has a potential tumour suppressor role. We also found that CIB2 expression is significantly down-regulated in ovarian cancer patient tissue, promoting hyperactive SK1 in this cancer, and that re-expression of CIB2 or inhibition of SK1 in ovarian cancer cells reduces tumour growth when xenografted into mice. Greatest loss of CIB2 in ovarian cancer correlates with chemoresistance, suggesting that this protein may be of value as a prognostic indicator for this cancer, while SK1 inhibitors significantly sensitise ovarian cancer cells to chemotherapeutics, providing an exciting avenue to improve ovarian cancer therapy.

Identification of SK2 as a therapeutic target in multiple myeloma

Multiple myeloma is an aggressive, incurable plasma cell malignancy for which novel therapeutic strategies are urgently required. Although patients have greatly benefited from the addition of proteasome inhibitors like Bortezomib to multi-drug regimens, resistance to these drugs inevitably occurs. Proteasome inhibitors are effective in myeloma mainly through enhancing endoplasmic reticulum (ER) stress in myeloma cells, which results in selective death of these malignant cells. In work recently published in Oncotarget (Wallington-Beddoe *et al*, *Oncotarget*) we have shown that altering sphingolipid metabolism through sphingosine kinase 2 inhibition also activates ER stress in myeloma cells. Importantly, targeting sphingosine kinase 2 synergised with proteasome inhibitors to induce myeloma cell death in an aggressive mouse model of the disease, leaves us poised to determine the clinical potential of this approach.



Dual bortezomib and K145 (SK2 inhibitor) therapy shows efficacy in the aggressive C57BL/KaLwRij murine myeloma model
Bioluminescence imaging of myeloma burden in mice after two week treatment with bortezomib alone, the SK2 inhibitor K145 alone, or a combination of bortezomib and K145 demonstrated that the combination therapy had significantly better efficacy that the monotherapies.

Outcomes for the Community

Cancer has a major human and economic impact on the community, with new therapeutic options desperately needed to combat this disease. Our research has not only helped to determine the molecular basis for the progression and chemotherapeutic resistance of some cancers, but also identified new targets and agents for potential use in future cancer treatment.

Zarina Greenberg, Iman Lohraseb, Quenten Schwarz, Ellen Potoczky, Xiangjun Xu
Absent: Sophie Wiszniak

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz PhD

Over 20 children are born with a congenital birth defect within Australia every day. These disorders often require medical intervention at birth and ongoing treatment throughout life. A significant proportion of these disorders arise from abnormal development of the neuronal and vascular systems.

During embryonic development multiple different cell types, such as precursors of neurons and blood vessels, communicate with each other to control organ formation. How and why these cell types talk to each other is a major question that the Neurovascular Research Laboratory is trying to answer. Using in vivo model systems from mouse to zebrafish, our laboratory explores how the precursors of neurons (neural crest cells) coordinate the development of other seemingly unrelated organ systems such as the vasculature, the heart, the craniofacial skeleton and adrenal gland. Our findings identify previously unrecognised co-dependencies between these cell and organ systems and demonstrate that each cell type uses similar molecular pathways to communicate with each other to control their development.

Our current research projects incorporate high-throughput proteomics and genomics approaches with novel animal models to identify the signalling pathways through which: 1) neurons establish appropriate interactions in the brain to form functional circuits that are affected in schizophrenia and autism, 2) neural crest cells sense their environment to position themselves in appropriate locations to form a functional nervous system, 3) neural crest cells differentiate into bone and cartilage to control craniofacial morphogenesis, 4) blood vessels signal to other cell types to modulate their development, and 5) neural crest cells communicate with blood vessels and cardiac precursors to control formation of the heart.

Outcomes
for the **Community**

Our work is providing novel insight to the origins of a large number of common congenital birth defects and childhood cancers, including autism, schizophrenia, craniofacial disorders and cardiac outflow tract defects, neuroblastoma and pheochromocytoma. Aberrant developmental processes sit at the heart of these disorders and our findings offer hope of innovating new diagnostic and prognostic tests, and for the generation of new therapies.

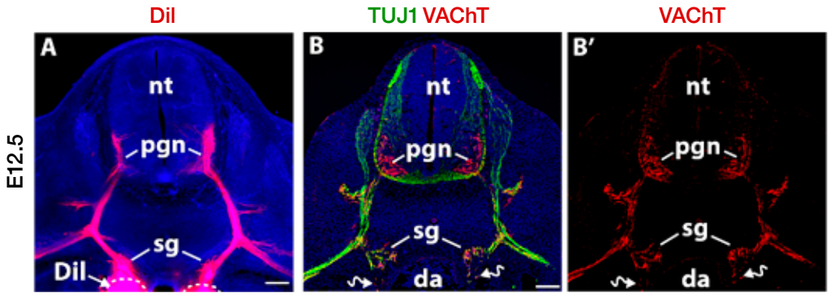
Key discoveries 2017

In 2017 the Neurovascular Research Laboratory had several discoveries that provide novel insight to embryonic development and the origins of childhood cancers.

The origins of craniofacial disorders were traditionally thought to arise from developmental defects in neural crest cell development. Our recent work demonstrates that blood vessels play an important role in promoting craniofacial development and that aberrant blood vessel growth underlies common craniofacial disorders. In the past year we have identified several factors secreted by blood vessels that control craniofacial development. Such factors represent ideal candidates for future therapies to treat craniofacial disorders, but more broadly for the treatment of any defect affecting cartilage such as achondrodysplasia and common sporting injuries. We are currently employing mouse models to address if these factors could be used in a therapeutic setting.

We have recently identified an essential role for the protein 14-3-3ζ in neuronal development and defined a causal relationship between deficiencies of 14-3-3ζ and neurodevelopmental disorders such as schizophrenia and autism. How 14-3-3ζ plays a role in neuronal development and how deficiencies give rise to neuronal pathologies is an ongoing line of investigation in our laboratory. In the past year we have discovered that 14-3-3ζ regulates a well known signalling pathway to control formation of a specialised type of neuron in the brain. By altering this pathway we aim to establish novel paradigms for the treatment of these disorders.

Aberrant development of the peripheral nervous system has significant impact on the body's fight or flight stress response and forms the basis of several childhood cancers, including neuroblastoma and pheochromocytoma. Using mouse models our work has elucidated a novel mechanism by which the building blocks of the peripheral nervous system, neural crest cells, are positioned in correct locations within the body. We have found that neural crest cells follow axons to their destinations and that this mechanism drives connections between the central and peripheral nervous systems to control physiological homeostasis. These findings provide new insight to the origins of common childhood cancers.



(A) DiI crystals placed into the adrenal primordia (dashed lines) of wild type E12.5 embryos identifies the origin of the preganglionic neurons (pgn) which control the fight or flight stress response. (B) Immunolabelling confirms that the preganglionic axons innervating the adrenal primordia (curved arrow) are cholinergic. Blue, DAPI. Scale bars = 100μm.

Guillermo Gomez, Mariana Oksdath Mansilla

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez PhD

Our research aims to understand the biochemical and biomechanical processes that contribute to the establishment of human tissue architecture and organ function. Physical forces are key determinants of tissue architecture and central in controlling different cellular behaviours. In particular, our lab studies the biomechanical processes that contribute to intestine and brain development, and how these are affected in cancer, chronic inflammatory conditions and in different brain disorders.

We are currently using stem cell derived organoids in combination with bioengineering approaches and high-resolution imaging to study:

Malformation of cortical development (MCD)
These neurodevelopmental disorders are associated with psychomotor delays and drug-resistant epilepsy. Its diagnosis and treatment can be very challenging since these alterations of human brain development start during the first weeks of gestation. Using human stem cells and brain organoid models we are currently investigating the role of physical forces in the formation of MCD to understand the biomechanical processes that contribute to the establishment of these types of disorders.

Chronic inflammation and inflammatory bowel disease
Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), have no curative therapies and patients with IBD are also at an increased risk of developing colitis-associated colorectal cancer (CAC). We are using intestinal organoid models to develop a personalised platform to identify the key drivers of IBD in patients and reduce their risk to acquire CAC. By investigating the role of inflammatory signalling and altered epithelial tissue homeostasis in chronic inflammation, we aim to identify key molecular signatures that contribute to the establishment of IBD.

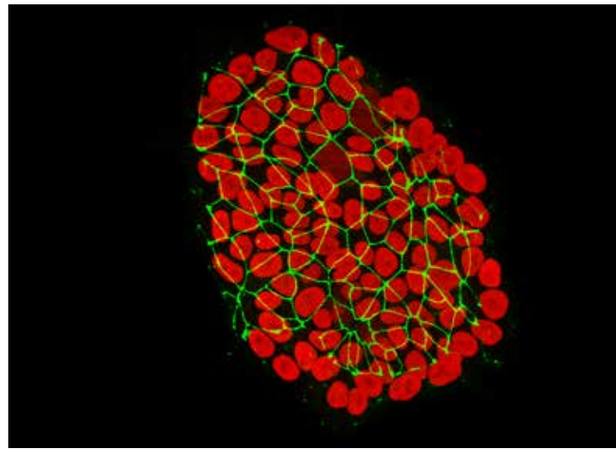
Personalised treatments for glioblastoma
Our principal goal is to develop a personalised platform to enable us to inhibit cancer cell invasion in glioblastoma. By using stem cell derived organoids and patient-derived glioblastoma cells, we are investigating the gene expression signatures associated to the process of cell invasion as well as performing drug screenings to identify drugs that not only stop the process of invasion but also do not affect brain physiology and function.

Outcomes for the Community

Our work aims to generate fundamental knowledge and experimental platforms for drug and genetic screening for different diseases, especially in glioblastoma, malformation of cortical development, and inflammatory bowel diseases to develop personalized therapies for their treatment. Working with human stem cells and organoid models present several advantages, including the fact that these could be obtained directly form the patient and analysed in a clinically relevant time window, so results can be delivered back to the patient in time, as well as being able to be manipulated genetically to develop tools that allow us to better understand the mechanobiology behind tissue architecture and organ function.

Key discoveries 2017

Tyrosine dephosphorylated cortactin downregulates contractility at the epithelial zonula adherens through SRGAP1
Contractile adherent junctions support cell–cell adhesion, epithelial integrity, and morphogenesis. However, how these junctions are regulated is still unknown. In Liang's work (Liang *et al*, 2017 *Nature Communications*), we identified an inhibitory pathway that is mediated by the cytoskeletal scaffold, cortactin. Mutations of cortactin that prevent its tyrosine phosphorylation downregulate RhoA signalling and compromise the ability of epithelial cells to generate a contractile zonula adherents. These findings identify a novel function of cortactin as a regulator of RhoA signalling that can be utilized by morphogenetic regulators for the active downregulation of junctional contractility.



Human immunopluripotent stem cells expressing GFP-ZO1 (Allen Cell Collection, green) and immunostained against Oct4

ROCK1 but not ROCK2 contributes to RhoA signaling and NMIIA-mediated contractility at the epithelial zonula adherens
Rho kinases (ROCK1 and ROCK2) function downstream of the small GTPase RhoA to drive actomyosin cytoskeletal remodelling. In this work, we report differential functional effects for these ROCKs at the epithelial zonula adherens (ZA). We show that ROCK1 depletion disrupted cadherin organization at the ZA, accompanied by loss of F-actin and NMIIA, whereas ROCK2 knockdown had no significant effect. Further, ROCK1, but not ROCK2, was necessary to stabilize GTP-RhoA at the ZA, thereby sustaining junctional tension and inhibiting intraepithelial cell movement. We also found that nonmuscle myosin IIA is a major determinant of ROCK1 cortical stability. Thus, despite sharing the catalytic domain with ROCK2, ROCK1 appears to be the dominant kinase essential for junctional integrity and contractile tension at epithelial ZA.

Role of contact inhibition of locomotion and junctional mechanics in epithelial collective responses to injury
Epithelial tissues are an integrated barrier where the cell is subject to different challenges. In particular, cells collectively respond to injuries by reorganizing their cell–cell junctions and migrating directionally towards the sites of damage. In this work, we show two key properties of epithelial response to injury as: (1) local relaxation of the tissue and (2) collective reorganization involving the extension of cryptic lamellipodia that extend, on average, up to three cell diameters from the site of injury and morphometric changes in the basal regions. Moreover, active responses involving the formation of the actomyosin purse string and softening of cell–cell junctions, are needed to drive morphometric changes that are important for collective cell rearrangements that are required for the removal of dying cells from the epithelium and therefore, to preserve the epithelial barrier function in response to injury.

Wenbo (Stanley) Yu, Lisa Ebert, Michael Brown, Nicole Wittwer, Alex Staudacher

Erica Yeo, Bill Liapis, Paul Reid, Tessa Gargett, Yanrui (Judy) Li, Nga Truong

Translational Oncology Laboratory

Professor Michael P Brown MBBS, PhD, FRACP, FRCPA

The Translational Oncology Laboratory is associated with the Royal Adelaide Hospital Cancer Clinical Trials Unit, which has tumour subspecialty interests in melanoma, lung cancer, brain cancer (glioblastoma) and ovarian cancer.

In the ongoing CARPETS phase 1 clinical trial of autologous, GD2-specific, chimeric antigen receptor (CAR)-T cell therapy, we have collaborated with Miltenyi Biotec to alter the CAR-T cell manufacturing conditions. We found that these modified conditions produced CAR-T cells with an enhanced memory phenotype and lower rates of activation-induced cell death, which we hypothesise will result in greater CAR-T cell expansion and persistence in vivo. We propose to test this hypothesis via an upcoming amendment to the clinical protocol.

In collaboration with the South Australian Health and Medical Research Institute (SAHMRI), we have used lentiviral gene transfer technology to make CAR-T cells specific for the myeloid leukaemia antigen, CD123. An optimised third-generation CD123-targeted lentivector has shown superior anti-leukaemic activity in vitro while sparing normal bone marrow progenitor cells. In our work targeting glioblastoma, we have characterised the expression profile in both freshly obtained and archival normal and malignant brain tissues of our two brain tumour target antigens of interest. Both of these antigens are found in malignant brain tissue but not in normal brain tissue, which suggests that they will be useful for the therapeutic targeting of T cells. In addition to developing CAR-T cells of dual antigen specificity for brain cancer treatment, we have also developed a recombinant tribody protein, which simultaneously targets both brain tumour antigens while engaging endogenous T cells via an anti-CD3 moiety.

Our novel, cancer cell death-specific antibody, APOMAB®, has been coupled to a long-lived positron emitter, Zirconium-89, to enable PET imaging in vivo. We are working with a more human-like version of the APOMAB antibody called chimeric APOMAB, which is suitable for clinical trials. To prepare for a clinical trial, we have been working with scientists in the Metabolic Imaging and Therapy Research Unit at SAHMRI (i) to label chimeric APOMAB® with Zirconium-89 and (ii) to demonstrate post-chemotherapy uptake of Zirconium-89-labelled APOMAB in the tumours of mice, which have previously been engrafted subcutaneously with human lung or ovarian cancer cell lines. We anticipate that positive results will show that we can develop a theranostic imaging agent, which can allow non-invasive detection of chemotherapy-related tumour cell death and thus help to determine the effectiveness of current anti-cancer treatments.

Key discoveries 2017

For the therapeutic targeting of T cells to our brain tumour antigens, we have developed *in vitro* preclinical proof of concept for a ‘split receptor’ approach. In this approach, we use lentivectors to express in the same T cell two CARs, each specific for one of these two brain tumour antigens. One CAR mediates only T-cell co-stimulation whereas the other CAR only mediates T-cell activation. Hence, this CAR-T cell of dual antigen specificity only becomes maximally activated when the brain tumour antigens are both engaged by their respective CARs. This property will be of advantage in minimising the chances that brain tumour cells will ‘escape’ from the CAR-T cells by losing expression of one of the targeted antigens (Ebert LM *et al*, *Biochemical Society Transactions*, in press).

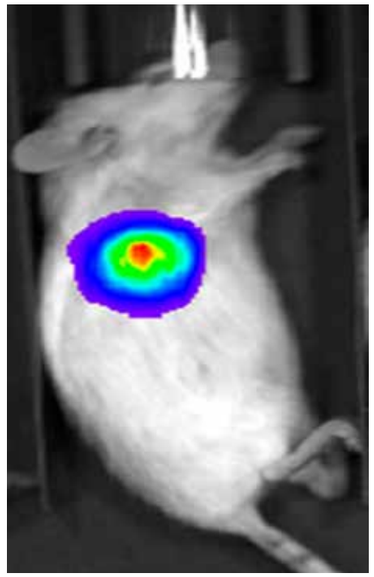


Figure A

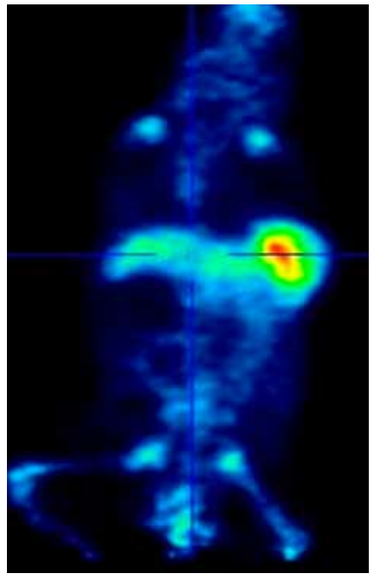


Figure B

An immunodeficient mouse bearing a subcutaneous tumour of a luciferase-tagged human lung cancer cell line, H460, was given a single injection of cisplatin chemotherapy. The next day, the mouse was given an injection of chimeric APOMAB, which had been radiolabelled with Zirconium-89. Figure A shows the IVIS whole body image of the mouse with a luciferase-expressing tumour 5 days after cisplatin treatment. Figure B shows the PET image of the same mouse also 5 days after cisplatin treatment to show uptake of APOMAB by the dying cells in this tumour.

Outcomes for the Community

Our work aims to improve the otherwise poor survival outcomes for patients with melanoma, lung, ovarian and brain cancers, by using new methods to replace those components of the patient’s own immune system that have not been working well enough to fight the cancer. To ultimately improve results in the clinic, we are arming T cells and antibodies with new treatment modalities to do that job.

Sarah Boyle, Michael Samuel, Diana Iarossi
Absent: Jasreen Kular, Natasha Pyne

Zahied Johan, Valentina Poltavets, Natasha Kolesnikoff

Tumour Microenvironment Laboratory

Associate Professor Michael Samuel PhD

Cells of the body exist within a microenvironment consisting of a scaffold of proteins, the extra-cellular matrix (ECM), which determines the way in which the cells and the tissue they make up function. This ECM is set down and regulated by a collection of stromal cells including fibroblasts and cells of the immune system. However, the precise molecular mechanisms that underpin the interplay between the parenchyma and the extra-cellular matrix and its population of stromal cells are not well understood.

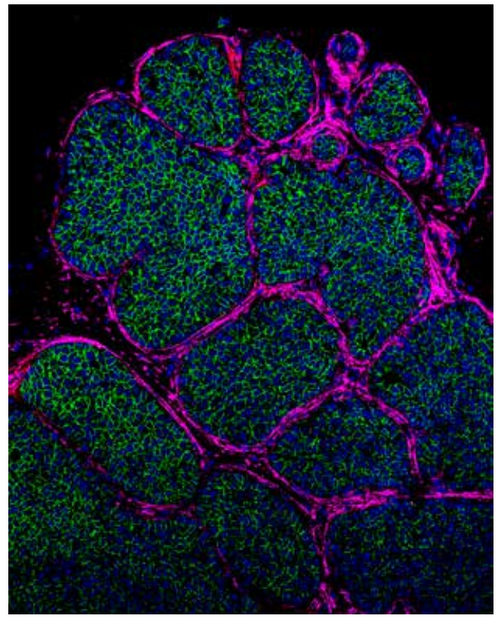
In cancers, the ECM exhibits abnormal characteristics, and there is evidence that this abnormal matrix promotes tumour growth and spread. Our laboratory uses genetic tools and animal models to understand how the ECM is remodelled at both the biophysical and biochemical levels during tumour initiation and progression, with the aim of identifying new targets that could be used to normalise the tumour microenvironment as a novel approach to cancer therapy.

We have previously shown that signalling through Rho kinase (ROCK) promotes epidermal proliferation by increasing ECM production, elevating dermal stiffness and enhancing integrin-mediated signalling. In turn, elevated dermal stiffness further stimulates ROCK activation, initiating a positive feedback loop that promotes skin tumours. We have also demonstrated that changes in different aspects of the microenvironment downstream of ROCK activation promote tumour progression in breast and intestinal cancers. We are working to determine the mechanisms by which ROCK activation regulates these tumour-promoting changes in the microenvironment.

Following on from our discovery that the molecular adaptor protein 14-3-3ζ negatively regulates signal flux through ROCK, we are working to determine whether 14-3-3ζ inhibition may be useful to accelerate healing of diabetic wounds. We are also employing unbiased screening approaches to identify novel negative regulators of ROCK signalling, which may have utility in accelerating the healing of chronic non-healing wounds.

Key discoveries 2017

Compressive stress on normal epithelial tissues enhances proliferation and induces EMT markers
Tumours growing within a restricted space are subjected to increasing levels of compressive stress. The effect of this on tumour biology is relatively understudied. We therefore sought to determine whether compressive stress changed the biology of tissues. To do this, we embedded cells in a 3D collagen matrix and subjected them to compressive stress using the FlexCell FX-5000 compression system (the purchase of which was generously funded by the Health Services Charitable Gifts Board), which permits the exertion of defined pressure upon substrates. The application of 20 kPa of stress significantly and persistently increased the number of cells with GTP-bound, active RHOA by ~9-fold after only 2 minutes of compression, resulting in increased proliferation and the enhanced production of markers of epithelial-mesenchymal transition. Furthermore, the application of compressive stress of 20 kPa upon intestinal, mammary and skin tissues using the FlexCell FX-5000 compression system also caused activation of ROCK signalling, suggesting that this phenomenon has physiological significance. This discovery has significance for cancers growing in a restricted space, which grow and progress rapidly because of the compressive force they are unavoidably subjected to. (Boyle *et al*, Small GTPases)



A perilous landscape: This is an image of a fluorescently stained mouse mammary cancer. This tumour is stained for a protein of the extracellular matrix, periostin (magenta), which can increase as cancer progresses and cancer cells begin to remodel their environment. Cell-cell junctions are labelled using E-Cadherin and cell nuclei are labelled by DAPI. (Sarah Boyle)

Transient ECM priming with a ROCK inhibitor increases sensitivity to chemotherapy in pancreatic cancer
Pancreatic cancer is characterised by copious fibrosis, which interferes with therapy. A multi-centre collaborative project, led by Paul Timpson from the Garvan Institute and including our laboratory, demonstrated that pre-treatment with the selective ROCK inhibitor Fasudil causes rapid structural changes in the fibrotic ECM in a pancreatic cancer model, which reduces mitogenic signalling, dilates blood vessels and renders tumours more susceptible to chemotherapy. This discovery suggests that pancreatic cancer patients whose cancers are otherwise refractory to chemotherapy may benefit from ECM conditioning via transient treatment with ROCK inhibitor. (Vennin *et al, Sci Transl Med*, 2017)

Outcomes for the Community

Abnormal changes in the tissue microenvironment can result in cancer, abnormal wound healing and metabolic diseases. Some of these changes are associated with abnormal production of the scaffold that holds tissues together. We are working to identify the mechanisms underlying this process to discover new approaches to normalise this pathway that could lead to new therapies against cancer and other diseases.

Michaelia Cockshell, Claudine Bonder, Eli Moore, Mark DeNichilo

Kay Khine Myo Min, Lih Tan, Camille Duluc, Danielle King

Vascular Biology and Cell Trafficking Laboratory

Associate Professor Claudine Bonder PhD

Endothelial cells (ECs) form the inner lining of all blood vessels and are thus the gatekeepers intersecting the circulating blood from all tissues and organs throughout the body. Blood vessels are critical in the fight against disease and understanding the fundamental biology of ECs continues to reveal new treatment options for the most deadly and debilitating diseases.

With an overall focus on blood vessels in disease, our laboratory has three main areas of interest. The first, vasculogenic mimicry (VM), is a process whereby cancer cells themselves mimic ECs to form vascular-like structures for increased blood supply to tumours to support growth and metastasis. In fact, tumours with high VM content are associated with poor clinical outcomes and we have identified novel elements in the VM closely associated with breast cancer and melanoma. Second, vascular occlusions are a major contributor to cardiovascular disease (CVD) and are a leading cause of death worldwide. Overcoming these blockages requires insertion of stents or artificial vascular grafts to maintain vessel diameter. We are developing smart surface biomaterials to revolutionise the stents which are deployed into blocked arteries and veins. Finally, in the development of diabetes, there is increasing evidence for a critical and intimate relationship between pancreatic ECs and the insulin producing islet cells. Our focus on the fundamental biology of the pancreatic vasculature may provide new opportunities to treat and possibly even cure this prevalent and debilitating disease.

Key discoveries 2017

Vasculogenic mimicry:
a key contributor to cancer progression

The growth and spread of solid tumours such as breast cancer and melanoma is dependent on an ability to access the blood supply. To meet this growing demand, cancer cells not only promote blood vessel sprouting (angiogenesis) but can also form vessel-like structures themselves, a process known as vasculogenic mimicry (VM). The presence of VM networks in primary tumours is tightly linked to increased metastasis and poor survival, suggesting that targeting VM in the clinic holds enormous therapeutic potential.

In 2017 we published a timely review in the journal *Clinical and Translational Immunology* on the control of immune cell entry through the tumour vasculature, with a particular focus on immunotherapy for melanoma. This built on our previous Oncotarget publication that desmoglein-2 (DSG2, an adhesion molecule belonging to the desmosomal cadherin family) is highly expressed by ~30% of melanoma patients, that it is used by melanoma cells to form VM channels and that it correlates with poor survival. This review questions the potential of VM structures as an alternative route of leukocyte entry into the tumours.

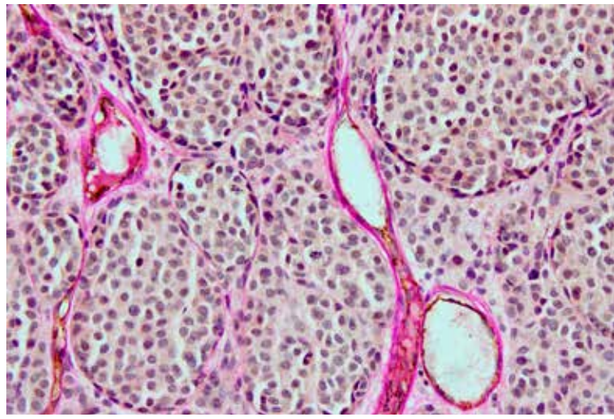
In breast cancer, we have growing evidence that the growth factor interleukin-3 (IL-3) is upregulated in a subset of patients with the most aggressive and invasive ductal carcinoma (IDC) and that it correlates with poor patient outcome. In collaboration with Professor Angel Lopez AO (CCB) we have identified that IL-3 and its receptor (IL-3R) promotes VM by triple-negative breast cancer cells in vitro. In 2017 we published a second timely review in the journal *Cold Spring Harbor: Perspectives in Biology* on the role of the b common family of cytokines (eg IL-3) in health and disease. With inhibition of IL-3R shown to prevent VM formation and tumour growth by breast cancer cells in vitro and in vivo current work now focuses on developing new treatment options for patients with this life-threatening disease.

Revolutionising vascular devices

Vascular occlusions are a major contributor to cardiovascular disease (CVD) and are a leading cause of death worldwide. Overcoming these blockages requires insertion of stents or artificial vascular grafts to maintain vessel diameter and has become a multi-billion dollar industry. Despite recent advances in device technology and post-operative care, clotting and scarring remain a significant health concern which can be life-threatening. Unfortunately, more often than not, anti-clotting medications are required long term and/or more surgical intervention is required. As part of the Cell Therapy Manufacturing Co-operative Research Centre, our team is testing an innovative concept that modified stents (first coated with a patented anti-adhesive surface (patent application PCT/2016/901008) and then topped with our novel peptides to specifically capture EPCs/ECs (patent US13/882806) will provide the rapid revascularisation of implanted devices long sought by surgeons to treat vascular occlusions with minimal intervention and medication. In 2017, we began to publish some of the work supporting this concept in *Biomacromolecules*.

Blood vessels are critical for successful function of the pancreas

Pancreatic islet transplantation is a promising clinical treatment for type 1 diabetes, but success is limited by extensive b-cell death in the immediate post-transplant period and impaired islet function in the longer term. Following transplantation, appropriate vascular remodeling is crucial to ensure the survival and function of engrafted islets. The sphingosine kinase (SK) pathway is an important regulator of vascular beds and in our 2017 *Diabetes* publication we reveal that the sphingosine kinase (SK) pathway controls the migration of intraislet endothelial cells, and thus represents a potential clinical target for improving transplant outcomes.



Blood vessels in cancer: a looping interconnected network supporting tumour growth. (CD31, brown; PAS stain, pink; H&E)

Outcomes for the Community

Our expertise in blood vessels, and the endothelial cells which form their inner lining, allows us to critically interrogate diseases such as cancer, cardiovascular disease and diabetes. Our ultimate aim is to understand the fundamental biology of the vasculature so that new treatment opportunities for the most debilitating and deadly diseases (cancer, heart disease and diabetes) can be generated to save thousands of lives every year, worldwide

David Lawrence, Andreas Schreiber, Paul Wang

John Toubia, Julien Soubrier, Emily Hackett-Jones, Jinghua (Frank) Feng
Absent: Katherine Pillman, Klay Saunders

Nathalie Nataren, Joel Geoghegan, Rosalie Kenyon, Ming Lin
Absent: Wendy Parker

The Australian Cancer Research Foundation Cancer Genomics Facility

Professor Greg Goodall, Co-Director Professor Hamish Scott, Co-Director
Mr Joel Geoghegan BSc, MSc Facility Manager Dr Andreas Schreiber PhD Head of Bioinformatics

The ACRF Cancer Genomics Facility is an integral part of the cutting-edge research occurring within the CCB. With an emphasis on translating innovative research into tangible results for patients, the CCB's partnership with SA Pathology has enabled the efficient application of genomic technologies in a diagnostic setting.

Research and Diagnostics

The ACRF Cancer Genomics Facility continues to support and provide access to cutting edge genomics technology for both the South Australian research community and the diagnostic labs of SA Pathology. In the past year, about 4000 research samples have been processed for next-generation sequencing, SNP arrays, qPCR and other genomics related services. In addition, 3000 samples have been run through NATA accredited services for the Genetics and Molecular Pathology Directorate of SA Pathology. This includes diagnostic tests for familial cancer predisposition, cardiomyopathies, metabolic disorders, blood disorders and neurological conditions.

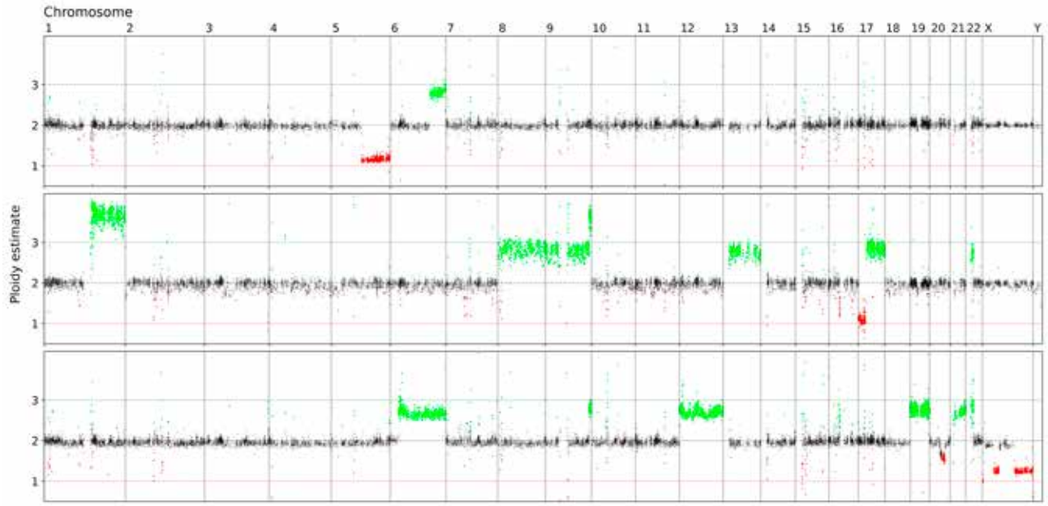
In 2017, the Genomics Facility also acquired a Pacific Biosciences Sequel system to enable long-read sequencing technology. This was made possible by a generous grant awarded to CCB researchers from the Australian Cancer Research Foundation. The advantages of long reads allow for improved detection of structural variants, isoform sequencing to elucidate the splicing patterns of RNA molecules, complete assembly of microbial genomes, improved detection of triplet repeat expansion disorders and more accurate assessment of disease causing mutations in genes with pseudogenes. As we look forward to 2018, we hope to expand the services offered with this third-generation long-read sequencing technology and acquire new technology for improved single cell genomic assays.

Bioinformatics

The bioinformatics group continues to be engaged with numerous CCB research groups on analysis of high throughput data described elsewhere in this report, particularly of sequencing data generated in the Genomics Facility. New algorithms and pipelines have been developed to enable molecular barcoding techniques for sensitive somatic mutation detection, copy number variation analyses and gene fusion detection all from next-generation sequencing data.

In addition, the group is increasingly providing bioinformatics training to researchers from CCB, UniSA and colleagues at SA Pathology. During the course of the year we ran three four-week workshops, covering introduction to the Linux operating system, Bash shell scripting as well as elementary NGS data analysis. The interactive training, which included take-away homework assignments, was designed to provide participants with the tools to tackle essential tasks such as analysis of their NGS mutation and RNA-Seq experiments.

Key discoveries 2017

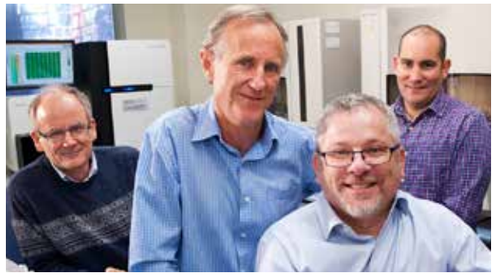


The Bioinformatics team in the Genomics Facility has developed an algorithm to perform copy number variation detection using next-generation sequencing data. Data from three cancer patients is shown with copy number gains (amplifications) coloured in green and copy number loss (deletions) coloured in red.

Outcomes for the Community

Since the inception of the Genomics Facility in 2012, we have grown to hit a critical mass of wetlab and bioinformatics expertise. The close collaboration between the research labs of the Centre for Cancer Biology and SA Pathology encourages rapid adoption of new technologies and new research discoveries to improve patient outcomes. We are increasingly representing South Australia in national genomics medicine initiatives and for oncology we are working to increase the number of clinical trials available to South Australian patients.

Aldgate schoolboy Angus Bond received state-of-the-art genetic DNA sequencing which assisted in the diagnosis of a rare bone marrow disease



ACRF Cancer Genomics Facility leaders: Andreas Schreiber, Greg Goodall, Hamish Scott, Joel Geoghegan

Mr Joel Geoghegan and Dr Karin Kassahn from the Centre for Cancer Biology ACRF Cancer Genomics Facility and the Genetics and Molecular Pathology Directorate of SA Pathology are working to translate research technologies into routine diagnostics advancing patient care.

Outcomes for the Community

In 2015, the Centre for Cancer Biology's ACRF Cancer Genomics Facility became the first laboratory in Australia to offer state-of-the-art DNA sequencing technology for selected South Australian patients in partnership with SA Pathology. The Facility is led by Professors Hamish Scott and Greg Goodall (Co-Directors), Mr Joel Geoghegan (Facility Manager), and Dr Andreas Schreiber (Head of Bioinformatics), and conducts ground-breaking research in genetic mapping.

Case Study

Nine year old Aldgate schoolboy Angus Bond endured years of failed tests to attempt to diagnose his illness. Other world-leading diagnostic and research laboratories could find no definitive cause for Angus' condition, but subsequent analysis by Professor Hamish Scott's team at the ACRF Cancer Genomics Facility was able to pinpoint the genetic mutation as the rare bone marrow disease Diamond-Blackfan Anemia (DBA). The Genomics Facility used new genetic technology and computational analyses to test Angus' complete set of genes in a single sweep, to see the 'spelling mistakes' in DNA. Identifying these 'spelling mistakes' in patients allows a more rapid diagnosis of genetic diseases and cancer and can pinpoint where to target therapies, reducing both time and costs.

Angus' condition prevents bone marrow from producing enough red blood cells to move oxygen around the body, necessitating more than 100 blood transfusions in his short life so far. Professor Scott's laboratory was also able to identify why Angus was transfusion independent for two years – in what is called 'a spontaneous remission.' In some of the cells in Angus' bone marrow, the DNA from one chromosome had spontaneously copied itself to fill in the missing DBA gene. This finding raises the possibility of selecting for these repaired cells in patients or replicating the same changes in other patients using revolutionary gene or cell therapy approaches. South Australia is at the forefront of this biomedical revolution and sequencing technology is changing the way we understand human health and disease.

Professor Hamish Scott FAHMS
Head, Department of Genetics and Molecular Pathology, SA Pathology
Head, Molecular Pathology Research Laboratory
Co-Director, ACRF Cancer Genomics Facility
Centre for Cancer Biology

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Yu F, Pillman KA, Neilsen CT, Toubia J, Lawrence DM, Tsykin A, Gantier MP, Callen DF, Goodall GJ, Bracken CP. Naturally existing isoforms of miR-222 have distinct functions. *Nucleic Acids Research* 45(19): 11371-11385, 2017.

Zhang Y, Chiu S, Liang X, Chai YH, Qin Y, Wang J, Li X, Qiu B, Tergaonkar V, Tse HF, Lian Q. Absence of NUCKS augments paracrine effects of mesenchymal stem cells mediated cardiac protection. *Exp Cell Res* 356(1): 74-84, 2017.

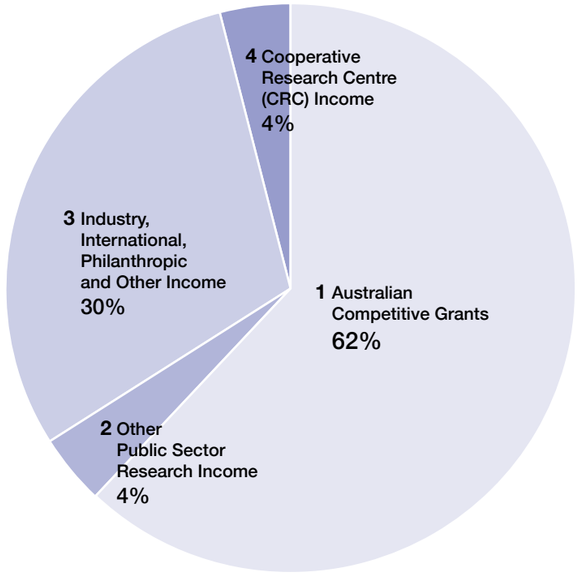
Zhu W, Gliddon BL, Jarman KE, Moretti PAB, Tin T, Parise LV, Woodcock JM, Powell JA, Ruszkiewicz A, Pitman MR, Pitson SM. CIB1 contributes to oncogenic signalling by Ras via modulation of sphingosine kinase 1. *Oncogene* 36: 2619-2627, 2017.

Zhu W, Jarman K, Lokman NA, Neubauer HA, Davies LT, Gliddon BL, Taing H, Moretti PAB, Oehler M, Pitman MR, Pitson SM. CIB2 negatively regulates oncogenic signaling in ovarian cancer via sphingosine kinase 1. *Cancer Research* 77: 4823-4834, 2017.

Financial Highlights

Research Income 2017 Calendar Year

1 Australian Competitive Grants		6,270,708
2 Other Public Sector Research Income		426,983
3 Industry, International, Philanthropic and Other Income		3,088,208
4 Cooperative Research Centre (CRC) Income		418,211
Total	AUD	10,204,110



New Grants and Fellowships

Dr Philip Gregory, head of the Gene Regulation in Cancer Group, and his team are investigating how breast and prostate cells become aggressive and spread throughout the body. Their research aims to identify new targets to limit the deadly spread of these cancers and improve survival outcomes for patients.

New Grants and Fellowships

Investigator	Title	Granting Body
Beattie D, Sizeland K, Krasowska M, Samuel MS	Structural signatures of skin and skin cancers from combined mechanical and x-ray scattering studies	Australian Synchrotron
Bonder CS, Benveniste G, Moore E	Revolutionising vascular devices with a novel non-clotting and pro-healing coating	Heart Foundation (Vanguard Grant)
Branford S	NHMRC Senior Research Fellowship	National Health and Medical Research Council
Brown AL, Scott HS	RUNX1 mutation data aggregation, analysis and sharing proposal	RUNX1 Research Foundation
Brown AL, Scott HS, Hahn CN, Schreiber AW, Lewis ID, Godley LA	Biological characterisation and therapeutic options for high risk, DDX41 mutated, haematological malignancies	Cancer Council South Australia (Beat Cancer Grant)
Brown MP	FLIGHT Protocol: An open label phase 1 study investigating the effects of CDX-301 on the safety, clinical activity, and immune priming of glembatumumab vedotin combined with anti-PD1 therapy in unresectable or metastatic melanoma patients	Celldex Therapeutics, Inc.
Brown MP	Pre-clinical proof of concept study: Augmenting immune priming and tumor-specific T-cell activity using a triple immuno-oncology approach - mesothelin-specific antibody drug conjugate, FLT3 ligand and immune checkpoint blockade	Bristol Myers Squibb
Brown MP, Staudacher AH, Scott CL	Can high-grade serous ovarian cancer be eradicated using a novel antibody drug conjugate?	Health Services Charitable Gifts Board
Byrne A	Research Degree Student International Travel Grant	University of South Australia
Conn S, Tergaonkar V, D'Andrea RJ, Gan H, Moore A	Circular RNAs: Trojan horses of oncogenesis	National Health and Medical Research Council
D'Andrea RJ, Deans AJ, Gonda TJ, Scott HS, Lewis ID	FANC gene mutations in Acute Myeloid Leukaemia biology and treatment	National Health and Medical Research Council
D'Andrea RJ, Gonda T, Moore A	Implication of BRCA1/2 germline variants for childhood AML biology and treatment	Channel 7 Children's Research Foundation
D'Andrea RJ, Kats L, Garrett-Bakelman F, Blancafort P, Lewis ID	Pathogenesis and treatment of AML associated with GADD45A promoter methylation	Cancer Council South Australia (Beat Cancer Project)
De Sousa SMC	AR Clarkson Scholarship	Royal Adelaide Hospital
De Sousa SMC	Travel Grant	Endocrine Society of Australia
De Sousa SMC, Torpy DJ	Whole exome sequencing to identify driver mutations in prolactinomas	RAH Gum Bequest
Dorstyn L, Kumar S	Using mouse models to decipher the function of caspase-2 in limiting aneuploidy tolerance and cancer	National Health and Medical Research Council
Ebert L, Brown MP, Tan LY	Scientific correlates of a new triple immuno-oncology combination therapy in metastatic melanoma patients	Royal Adelaide Hospital
Ebert L, Kavallaris M, Brown MP, Ziegler D, Tsoli M	Discovering targets for immunotherapy of aggressive childhood brain cancers	Neurosurgical Research Foundation
Gargett T, Brown MP	Optimising the manufacture of CAR-T cells for the treatment of solid cancers	Miltenyi Biotec
Gregory PA	New regulators of advanced prostate cancer	The Hospital Research Foundation
Gregory PA, Anderson RL, Goodall GJ	miR-342: A novel suppressor of a pro-metastatic gene network in triple-negative breast cancer	National Breast Cancer Foundation
Hamon R	PhD Scholarship	University of South Australia
Harvey NL	Putting the brakes on lymphatic vessel growth	The Hospital Research Foundation Project Grant
Harvey NL	Understanding how GATA2 controls lymphatic vessel valve development	National Health and Medical Research Council
Harvey NL, Hogan BM	Understanding the role of the atypical cadherin Fat4 in lymphatic vascular development	National Health and Medical Research Council
Harvey NL, Scott HS, Piller N, Haan E	Investigating the genetic and developmental basis of human lipedema	US Lipedema Foundation Project Grant
Harvey NL, Scott HS, Taoudi S	Defining the role of a novel transcriptional enhancer element in regulation of Prox1 expression and endothelial cell identity	National Health and Medical Research Council
Hercus T, Lopez A	Structure-based design of novel IL-3 variants with selective function in cancer therapy	Cancer Council South Australia
Hughes T, Yong A, Branford S, White D, Ross D, Reynolds P	Chronic Myeloid Leukaemia: Changing the treatment paradigm	National Health and Medical Research Council
Khew-Goodall Y	The fight against triple negative breast cancer	The Hospital Research Fund
Khew-Goodall Y, Harvey N	Trafficking mechanisms governing receptor availability for signalling	National Health and Medical Research Council
Kumar S	Cell death by self-eating: Autophagy-dependent tissue removal	Australian Research Council
Kumar S, Denton D, Baehrecke EH	Hormone-dependent autophagy and growth signalling in developmental cell death	National Health and Medical Research Council
Kumar S, Mathivanan S	Exploring the role of Arrcd4 in extracellular vesicle biogenesis and its implications in tissue homeostasis	National Health and Medical Research Council
Lewis AC	Travel Grant to attend the American Society for Hematology Conference	Cancer Council South Australia
Lock R, Haber M, Marchall G, Norris M, Moore A, Ekert P, D'Andrea R, Lopez AF, Arndt G	A personalised medicine approach to the treatment of acute myeloid leukaemia in children	Tour de Cure
Lopez AF, Geoghegan J, Scott HS	Translating health discoveries	Therapeutic Innovation Australia / NCRIS
Moodley Y, Corte T, Knight D, Reynolds PN, Walters EH, Glaspole I, Baltic S, Sohal S, Grainge C	Circulatory biomarkers for Idiopathic Pulmonary Fibrosis: Improving patient outcomes	National Health and Medical Research Council
Moore E	Non-clotting and pro-healing coating for vascular devices	Heart Foundation (ECR Fellowship)
Moore E	Non-fouling antithrombotic polymer coating displaying pro-healing biomarkers for implantable vascular devices	Royal Adelaide Hospital (Mary Overton Fellowship)
Pitson SM, Powell JA	Targeting sphingosine kinase 1 to sensitise acute myeloid leukaemia to BH3 mimetic therapy	National Health and Medical Research Council
Pitson SM, Powell JA, Tea M	Stereotactic system for the generation of orthotopic xenografts of human brain tumours	Neurosurgical Research Foundation
Reynolds PN, Bonder CS, Bourke J, Voelcker N	Engineered cell and exosome therapy for pulmonary vascular disease	National Health and Medical Research Council
Reynolds PN	BMPR2 directed therapy for IPF	Royal Adelaide Hospital
Ross D	Clonal haematopoiesis and secondary neoplasia in chronic myeloid leukaemia: A case-control study	RAH Contributing Haematologists' Committee Research Fund
Samuel MS, Swarbrick A	How does ROCK 'education' of fibroblasts drive neoplastic progression in the breast?	National Health and Medical Research Council
Schwarz Q	Novel mechanisms integrating the central and autonomic nervous system	Australian Research Council
Schwarz Q, Ramshaw HR, Pitson S	Investigating the role of 14-3-3ζ in medulloblastoma	Neurosurgical Research Foundation
Schwarz Q, Wiszniak S	Defining the role of IGF-1 as a novel angiocrine factor in the development and treatment of common craniofacial disorders	National Health and Medical Research Council
Schwarz Q, Wiszniak S	Novel roles for neural crest cells in cardiac morphogenesis	National Health and Medical Research Council
Scott HS	Beat Cancer Principal Research Fellowship, PRF0517	Cancer Council South Australia (Beat Cancer Grant)
Scott HS, Brown AL, Lewis ID, D'Andrea RJ, Powell JA, Ramshaw HS, Godley LA	Mab immunotherapies for myeloid leukemia patients with germline or somatic RUNX1 mutations	National Health and Medical Research Council
Stefanidis C	Honours scholarship	Hallett Cove District Lions Club
Woodcock JM, Lopez AF, Pitson SM	Preclinical evaluation of 14-3-3 protein inhibitors for lung cancer therapy	National Foundation of Medical Research and Innovation
Woodcock JM, Reynolds PN, Pitson SM, Lopez AF	New molecular therapies for lung cancer	Ray and Shirl Norman Cancer Research Trust

Seminar Program

Dr Pirjo Apaja
EMBL Fellow, Lysosomal Diseases Research Unit, SAHMRI
Regulation of ubiquitin-mediated misfolded membrane protein trafficking at the endo-lysosomal 9/2/2017

Dr Dinshaw J. Patel
Abby Rockefeller Mauzé Chair in Experimental Therapeutics, Memorial Sloan-Kettering Cancer Center, New York, USA
Structural biology of RNA-mediated gene regulation and cGAS-STING-mediated immune regulation 20/02/2017

Dr Tim Sargeant
Head of Neurobiology, Lysosomal Diseases Research Unit, SAHMRI
Tipping the balance of proteostasis in Alzheimer's disease 23/2/2017

Professor Frederic Meunier
Queensland Brain Institute, The University of Queensland
Tracking Munc18 in health and disease uncovers unsuspected link with synucleopathies 9/3/2017

Professor Philip Woodman
Professor of Cell Biology, University of Manchester, UK
The role of endocytosis in receptor down-regulation and tumour suppression 21/3/2017

Dr Vi Wickramasinghe
Head, RNA Biology and Cancer Laboratory, Peter MacCallum Cancer Centre
RNA Biology and Cancer 23/3/2017

Professor Robert Richards
Head of the Discipline of Genetics, The University of Adelaide
Non-self mutations and autoinflammatory disease as the common cause of the late-onset neurodegenerative diseases 30/3/2017

Dr Ben Roediger
Head, Skin Inflammation Group, Immune Imaging Program, The Centenary Institute for Cancer Medicine and Cell Biology
Cutaneous mast cells, type 2 inflammation and the atopic march 13/4/2017

Professor Gerhard Christofori
Department of Biomedicine, University of Basel, Switzerland
The regulatory networks of EMT, cell plasticity and metastasis 20/4/2017

Dr Seth Masters
Laboratory Head, Walter and Eliza Hall Institute of Medical Research
New mechanisms of autoinflammatory disease 27/4/2017

Dr Minni Anko
Group Leader, RNA Processing in Health and Disease Laboratory, Monash University
The potency of RNA regulation in self-renewal and cell fate transitions 4/5/2017

Dr Thomas Cox
Group Leader: Matrix and Metastasis, Garvan Institute of Medical Research
Fibrosis, cancer and the pre-metastatic niche: implications for lysyl oxidases in cancer progression and metastasis 11/5/2017

Professor Ricky Johnstone
Associate Director, Laboratory Research; Head, Gene Regulation Laboratory, The Peter MacCallum Cancer Centre
Development and use of genetically engineered mouse models to study oncogene addiction 18/5/2017

Professor Frank Gannon
Director and CEO, QIMR Berghofer Medical Research Institute
Lessons learned from how gene expression is controlled by the estrogen receptor 25/5/2017

Dr Pilar Blancafort
Laboratory Head, School of Anatomy, Physiology and Human Biology, The University of Western Australia
Mirall trencat: The breast cancer landscape, from the break to the glue 1/6/2017

Dr Andrew Moore
Group Leader, Childhood Leukaemia Research Laboratory; Paediatric Oncologist, Lady Cilento Children's Hospital; Director, Queensland Children's Tumour Bank
Childhood acute myeloid leukaemia: small patients, small numbers, big challenges 14/06/2017

Dr Traude Beilharz
Head, RNA Systems Biology Lab, Monash University
Alternative polyadenylation in the regulation and dysregulation of gene expression 15/6/2017

Professor Ramon Varcoe
Director of the Vascular Institute, Prince of Wales Hospital
The conundrum of restenosis after contemporary endovascular revascularisation for peripheral artery disease: methods of prevention and unmet needs 22/6/2017

Dr Andrew Deans
Head, Genome Stability Unit, St Vincent's Institute of Medical Research
Biochemical reconstitution of the Fanconi anaemia DNA damage response 28/6/2017

Professor Thomas Preiss
Leader, RNA Biology Group, ANU College of Medicine, Biology and Environment
RNA-binding proteomes and translation cycle dynamics 29/6/2017

Dr Kelly Smith
Group Leader, Genomics of Development and Disease Division; Investigator, Centre for Rare Diseases Research, The University of Queensland
Understanding the genetic regulation of cardiac form and function 6/7/2017

Dr Rachel Hill
NHMRC Career Development Fellow;
Head, Behavioural Neuroscience Laboratory, Monash University
Utilizing animal models to understand the molecular biology underlying psychiatric illness 13/7/2017

Dr Brett Hollier
Research Fellow, Australian Prostate Cancer Research Centre; Research Fellow and Group Leader, IGF Mechanistic studies, Tissue Repair and Regeneration Program, Institute of Health and Biomedical Innovation, Queensland University of Technology
Targeting the adaptive plasticity response to androgen-targeted therapies in advanced prostate cancer 20/7/2017

Dr Michael Buchert
Senior Postdoctoral Fellow, Olivia Newton-John Cancer Research Institute
Insights into the role of the Tuft cell marker DCLK1 in gastric cancer 27/7/2017

Dr Christine Chaffer
Garvan Institute of Medical Research
Understanding cancer development and metastasis through regulation of cell plasticity 10/8/2017

Professor Rik Thompson
Associate Director, Institute of Health and Biomedical Innovation, Translational Research Institute
Probing the molecular and cellular basis of breast cancer risk associated with mammographic density: A within breast comparative approach 17/8/2017

Dr Peer Arts
Post-doctoral Fellow, Department of Human Genetics, Radboud University Medical Center, Nijmegen, Netherlands
Primary immunodeficiencies: from genetic basis to therapeutic targets 21/8/2017

Associate Professor Gyorgy Hutvagner
ARC Future Fellow, Faculty of Engineering and Information Technology, Centre for Health Technologies, University of Technology
The regulation of the miRNA pathway and small RNAs derived from tRNAs 24/8/2017

Dr Pascal Duijf
Senior Research Fellow, Diamantina Institute, The University of Queensland
Overexpression of the cell cycle regulator Emi1 promotes chromosome instability and tumorigenesis 31/8/2017

Professor Rodney Hicks
Director, Centre for Cancer Imaging; Head, Molecular Imaging and Targeted Therapeutic Laboratory, The Sir Peter MacCallum Department of Oncology
Tumour Heterogeneity as a Challenge and Opportunity in Oncology 7/9/2017

Professor Peter Leedman
Director, Harry Perkins Institute of Medical Research; Head, Perkins Laboratory for Cancer Medicine; Professor of Medicine, Royal Perth Hospital
RNA-based therapeutics for cancer: Are we there yet? 14/9/2017

Dr Nirmal Robinson
Principal Investigator, Cluster for Excellence in Aging Associated Diseases (CECAD), University of Cologne, Germany
Metabolism at the crossroads of inflammation and immunity: Lessons from Salmonella 28/9/2017

Associate Professor Nathan Pavlos
Head, Cellular Orthopaedic Laboratory, School of Surgery, University of Western Australia
Sorting-out the Skeleton: The role of intracellular trafficking in bone homeostasis and disease 9/10/2017

Professor Tony Cunningham AO
Executive Director, The Westmead Institute for Medical Research and the Institute's Centre for Virus Research; AAMRI President
How does HIV obtain a 'toehold' in the genital tract? 12/10/2017

Professor Mubeccel Akdis
Head of Immunodermatology, Swiss Institute of Allergy and Asthma Research (SIAF), Switzerland
Mechanisms of immune tolerance to allergens: T and B regulatory cells 19/10/2017

Professor Cezmi Akdis
Director, Swiss Institute of Allergy and Asthma Research (SIAF), Switzerland
Epithelial barrier in allergic disease: implications for prevention and treatment 19/10/2017

Associate Professor Michelle Hill
Group Leader, QIMR Berghofer Medical Research Institute; Principal Research Fellow, Diamantina Institute, The University of Queensland
RNA motif-guided exosomal microRNA export regulated by caveolin-1 20/10/2017

Professor Rajiv Kumar
Division of Molecular Genetic Epidemiology, German Cancer Research Center (DKFZ), Germany
Telomere length, TERT promoter mutations and melanoma risk 23/10/2017

Associate Professor Joseph (Sefi) Rosenbluh
Biomedicine Discovery Institute, Department of Biochemistry and Molecular Biology, Monash University; Director of Functional Genomics, The Hudson Institute
Pooled genome wide CRISPR screens identify biological mechanisms and targets for cancer drug development 26/10/2017

Dr Nicholas Huntington
Laboratory Head, Molecular Immunology, Walter and Eliza Hall Institute of Medical Research
NK cell checkpoints in cancer 2/11/2017

Dr Esther Camp-Dotlic
Mesenchymal Stem Cell Laboratory, Faculty of Health and Medical Sciences, Adelaide Medical School, University of Adelaide; SAHMRI
Role of TWIST-1 and the c-ros oncogene 1 in regulating cranial bone formation in health and disease 9/11/2017

Dr Shigeki Sugii
Group Leader, Fat Metabolism and Stem Cell Group, Singapore Bioimaging Consortium, A*STAR; Assistant Professor, Cardiovascular and Metabolic Disorder Program, Duke-NUS Medical School, Singapore
Adipose-derived stem cells: potential for metabolic reprogramming 7/12/2017

Professor Matthew Cook
Professor of Medicine, Australian National University; Director of Immunology, The Canberra Hospital
A whole genome approach to primary antibody deficiency 14/12/2017

Professor Jin-kun Wen
Department of Biochemistry and Molecular Biology, Hebei Medical University, Shijiazhuang, China
NRG-1/circACTA2/miR-548f-5p axis regulates smooth muscle α-actin expression 20/12/2017

Invited Presentations

Acute Leukaemia Laboratory

Professor Richard D'Andrea

Session Chair

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Dr David Ross

Invited speaker

MPN Advocacy and Education International Patient and Physician seminar. Melbourne, Australia, April

Dr Saumya Samaraweera

Invited Speaker

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

ACRF Genomics Facility

Dr Katherine Pillman

Invited Speaker

miR-200 and the Quaking RNA binding protein control a large alternative splicing network and cell plasticity in epithelial cells, Genome Biology Symposium. Queenstown, NZ, September

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall

Invited Speaker

EMBO Endocytosis Conference. Warsaw, Poland, September

ComBio 2017. Adelaide, Australia, October

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

The International EMT Conference. Houston, TX, USA, December

Session co-chair

Hunter Systems and Cell Biology. Pokolbin, Australia, April

ComBio 2017. Adelaide, Australia, October

Dr Ana Lonic

Invited speaker

ComBio 2017. Adelaide, Australia, October

Cytokine Receptor Laboratory

Professor Angel Lopez AO

Invited Speaker

2nd Aegean International Conference on Cytokine Signaling in Cancer. Greece, May-June

Institute Molecular Celullar Biology (IMCB). Singapore, August

Murdoch Children's Research Institute (MCRI). Melbourne, Australia, October

Cytokine Conference. Kanazawa, Japan, October-November

The University of Tokyo. Japan, November

Dr Winnie Kan

Invited Speaker

7th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting. Adelaide, Australia, November

8th Barossa Meeting: Cell Signalling in Cancer Medicine Barossa Valley. Australia, November

Gene Regulation Section

Professor Greg Goodall

Invited Speaker

Keystone Symposium Noncoding RNAs, disease to therapeutics. Banff, Canada, February

2nd Australian Translational Breast Cancer Symposium. Sydney, Australia, February

2nd International Conference on the Long and the Short of Non-Coding RNAs. Heraklion, Crete, June

Epigenetics 2017. Brisbane, Australia, October

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Gene Regulation in Cancer Group

Dr Philip Gregory

Invited Speaker

Queensland Institute of Medical Research departmental seminar. Brisbane, Australia, May

Queensland University of Technology departmental seminar. Brisbane, Australia, May

The International Epithelial-Mesenchymal Transition Association (TEMTIA) 2017 Meeting. Houston, TX, USA, November

Gene Regulation Networks Group

Dr Cameron Bracken

Invited Speaker

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Invited Presentation

Walter and Eliza Hall Institute. Melbourne, Australia, August

Inflammation and Ailments Laboratory

Professor Vinay Tergaonkar

Invited Speaker

Samsung Medical Centre, Tumor Heterogeneity conference. Seoul, Korea, January

National Institute of Immunology. New Delhi, India, February

Toho University, Dept of Biochemistry. Japan, September

76th Annual Meeting of the Japanese Cancer Association (JCA). Tokyo, Japan, September

Research Institute for Microbial Diseases, Osaka University. Japan, October

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Organiser of Major Conferences

8th TNF Superfamily Meeting. Singapore, April

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Leukaemia Laboratory

Associate Professor Susan Branford

Chair

Haematology of Australia and New Zealand Conference 2017: Satellite Molecular Haematology Meeting. Sydney, Australia, October

Invited Speaker

Molecular Monitoring Optimisation Workshop, Sunshine Coast University Hospital. Sunshine Coast, Australia, May

European Hematology Association Satellite Symposium. Madrid, Spain, June

The University Hospital Geelong Molecular Monitoring Meeting. Geelong, Australia, August

Genomic Medicine in SA, MS McLeod Research Seminar. Adelaide, Australia, August

Canberra Hospital Research Meeting. Canberra, Australia, August

ComBio 2017: Cancer Genomics Symposium. Adelaide, Australia, October

Emerging Global Market Molecular Monitoring Meeting. Dubai, UAE, November

Inaugural Pathology Colloquium 2017 at SA Pathology. Adelaide, Australia, November

Research presentation and Webinar at Cepheid Corporation. San Francisco, USA, December

International Chronic Myeloid Leukaemia Foundation Forum at the American Society of Hematology Meeting. Atlanta, USA, December

Lung Research Laboratory

Professor Paul Reynolds

Session Chair

Advances in Interstitial Lung Disease. Asian Pacific Society of Respirology. Sydney, Australia, November

Dr Rebecca Harper

Chair

Poster Discussion, Asia Pacific Society of Respirology 2017. ASM, Sydney, November

Thematic Poster Discussion, ATS Annual Scientific Meeting. Washington DC, USA, May

Invited talks

PAH Symposium, Asia Pacific Society of Respirology 2017. ASM, Sydney, Australia, November

Invited Presentation

Novel Therapies in Pulmonary Arterial Hypertension, Asian Pacific Society of Respirology. Sydney, Australia, November

Lymphatic Development Laboratory

Associate Professor Natasha Harvey

Invited Speaker

Combined Biological Sciences Meeting 2017. Perth, Australia, August

Australia Vascular Biology Meeting. Mooloolaba, Australia, September

Lymphatics Symposium 2017. Melbourne, Australia, October

North American Vascular Biology Meeting. Asilomar, USA, October

6th Australian Network of Cardiac and Vascular Developmental Biologists Meeting. Brisbane, Australia, NovemberAsia-Australia Vascular Biology Meeting. Osaka, Japan, December

Invited Seminars

SAHMRI Heart Health Seminar Series. SAHMRI. Adelaide, Australia, May

Wihuri Research Institute, Biomedicum Helsinki. Helsinki, Finland, May

Monash Institute of Pharmaceutical Sciences. Melbourne, Australia, August

National Cerebral and Cardiovascular Centre. Osaka, Japan, December

Kitasato University. Tokyo, Japan, December

Organising Committee and Session Chair

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Program Chair

ComBio 2017. Adelaide, Australia, October

Co-convenor and Session Chair

The Hunter Cell and Developmental Biology Meeting. Hunter Valley, Australia, April

Molecular Pathology Research Laboratory

Professor Hamish Scott

Steering Committee, Invited Speaker and Discussion Panel Member

Third Annual Australian Clinical Genomics Symposium. Melbourne, Australia, November

Organising and Program Committee, Session Chair and Invited Speaker

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Workshop Organiser, Chair

Australian Genomics Cancer Functional Genomics Workshop. Adelaide, Australia, November

Invited Speaker

Symposium in honour of Stylianos Antonarakis. Geneva, Switzerland, September

Discussion Panel Member

HGSA SA Branch Symposium. Adelaide, Australia, September

Korean Hematology Society. Seoul, Korea, May

Australian and New Zealand Children's Haematology/Oncology Group (ANZCHOG) Annual Scientific Meeting. Adelaide, Australia, June

11th National Conference for Clinical Research (NCCR 2017) held in conjunction with the 5th Regional Asian Clinical Trial Association (REACTA) Forum. Putrajaya, Malaysia, September

Conference Committee, Session Chair and Invited Speaker

Royal College of Pathologists of Australasia (RCPA): Pathology Update 2017. Melbourne, Australia, February

Workshop scientific organiser and Co-chair

Friday Scientific Workshop on Hematopoietic Malignancies, 59th American Society of Hematology Annual Meeting. Atlanta, USA, December

Dr Anna Brown

Invited speaker

Keynote address, HSANZ: SA State Branch, 20th Scientific Weekend Meeting. Barossa Valley, Australia, August

International Meeting on Childhood Myelodysplastic Syndromes and Severe Aplastic Anemia in Childhood (European Working Group). Rome, Italy, September

Novartis Molecular Haematology Meeting. Sydney, Australia, October

The 21st International RUNX Meeting. Philadelphia, USA, November

59th American Society of Hematology Annual Meeting. Atlanta, USA, December

Dr Christopher Hahn

Invited Speaker

Friday Scientific Workshop on Hematopoietic Malignancies, 59th American Society of Hematology Annual Meeting. Atlanta, USA, December

Dr Lucia Gagliardi

Member and Program Organising Committee

Endocrine Society of Australia Seminar. Melbourne, Australia, May

Dr Sarah King-Smith

Conference and Workshop Organiser

Human Genetics Society of Australasia: SA Annual Branch Meeting. Adelaide, Australia, July

SA Genomics Health Alliance: Launch. Adelaide, Australia, August

Australian Genomics Health Alliance, Cancer Functional Genomics Workshop. Adelaide, Australia, November

Dr Sunita De Sousa

Speaker

Endocrine Society of Australia Seminar. Melbourne, Australia, May

Endocrine Society of Australia Annual Scientific Meeting. Perth, Australia, August

CASCADE: An Educational And Clinical Meeting in Pituitary Endocrinology. Adelaide, Australia, September

Ms Alicia Byrne

Invited Speaker

inBio: Cold Spring Harbor Innovation Showcase. Cold Spring Harbor, New York, USA, May

Speaker

Perinatal Society of Australia and New Zealand 2017 Congress. Canberra, Australia, April

The Biology of Genomes 2017 Meeting. Cold Spring Harbor, New York, USA, May

Human Genetics and Genomics, Gordon Research Seminar and Conference. Stowe, USA, July

Co-Convenor

Human Genetics Society of Australasia, SA Branch Annual One Day Symposium. Adelaide, Australia, July

Molecular Regulation Laboratory

Professor Sharad Kumar AM

Chair

EMBO Keynote Session, 17th Hunter Meeting. Hunter Valley, Australia, April

Invited Speaker

UQCCR Seminar Series, Centre for Clinical Research, University of Queensland. Herston, Brisbane, Australia, May

The 8th International Symposium on Autophagy. Nara, Japan, May-June

Indian Society for Developmental Biologists Biennial Meeting 2017 (InSDB2017). Pune, India, June

Tata Institute for Fundamental Research. Mumbai, India, June

The 3rd International Insect Hormone (21st Ecdysone) Workshop. Nasu Highland, Japan, July

Seminar, Hudson Institute of Medical Research. Clayton, Australia, August

Focus Group Speaker, Membrane and Ion Transport, Department of Physiology, University of Otago. Dunedin, New Zealand, August

Seminar, Department of Biochemistry, University of Otago. Dunedin, New Zealand, August

Seminar, University of Rome Tor Vergata. Rome, Italy, September

EMBO Meeting, Autophagy: From Molecular Principles to Human Diseases. Cavtat-Dubrovnik, Croatia, September

Inaugural Symposium of the Japan Society for Promotion of Science Australian Alumni Association (JSPSAAA). Australian Academy of Science, Canberra, Australia, October

Dr Donna Denton

Invited Speaker

17th Hunter Meeting. Hunter Valley, Australia, April

4th Asia Pacific Drosophila Research Conference. Osaka, Japan, May

Model Organisms in Human Health Australia (MOHHA) Meeting. Yarra Valley, Australia, June

Dr Loretta Dorstyn

Co-Chair

ComBio 2017, Cell Death Symposium (Cell Biology Stream). Adelaide, Australia, October

Invited Speaker

17th Hunter Meeting. Hunter Valley, Australia, April

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

3rd Proteostasis and Disease Symposium. Wollongong, Australia, November

Dr Natalie Foot

Session Chair and Judge

Australian Society for Medical Research (ASMR) Scientific Meeting. Adelaide, Australia, June

Selected Speaker

7th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting. Adelaide, Australia, November

Dr Tanya Henshall

Co-Chair

7th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting. Adelaide, Australia, November

Dr Jantina Manning

Chair

Special Symposium, 7th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting. Adelaide, Australia, November

Dr Claire Wilson

Session Chair

Australian Society for Medical Research (ASMR) Scientific Meeting. Adelaide, Australia, June

Selected Speaker

Keystone Symposia, Ageing and Mechanisms of Ageing-Related Disease. Yokohama, Japan, May

Combio 2017, Obesity and insulin resistance Symposium (Cell Signalling and Metabolism Stream). Adelaide, Australia, October

7th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting. Adelaide, Australia, November

Invited Presentations continued

Molecular Signalling Laboratory

Professor Stuart Pitson

Invited Speaker

Lightsview Ride Like Crazy Presentation Event. Adelaide, Australia, April

Cell Signalling and its Therapeutic Implications (CSTI) Meeting. Mornington Peninsula, Australia, May

Chris Adams Ball, Adelaide, Australia, May

ASMR Dinner with a Scientist. Adelaide, Australia, June

South Australian Health and Medical Research Institute Seminar Series. Adelaide, Australia, July

FASEB Science Research Conference on Lysophospholipids and Related Mediators: From Bench to Clinic. New Orleans, USA, August

Neurosurgical Research Foundation Annual General Meeting. Adelaide, Australia, September

Flinders Medical Centre Brain Tumour Update Symposium. Adelaide, Australia, October

Australasian Wound and Tissue Repair Society Symposium. Adelaide, Australia, October

Chair

Cell Signalling Session: Hunter Cell Biology Meeting. Hunter Valley, Australia, April

Stream Coordinator for Cell Signalling and Metabolism Stream: ComBio2017. Adelaide, Australia, September

New Technologies for Wounds and Burns Injuries Session: Wound Healing Symposium. Adelaide, Australia, October

Convenor

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Dr Maurizio Costabile

Chair

Education Symposium: ComBio2017. Adelaide, Australia, September

Dr Jason Powell

Invited speaker

Hallett Cove District Lions Club. Adelaide, Australia, June

Chair

Signalling stream, ASMR SA Annual Scientific Meeting. Adelaide, Australia, June

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz

Co-Chair

ASMR South Australia State Meeting, Ross Wishart Presentations. Adelaide, Australia, June

ComBio 2017, Neurodevelopment session. Adelaide, Australia, October

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Invited Speaker

Hunter Cell Biology 2017. Hunter Valley, Australia, April

Heart Foundation SA Research Showcase. Adelaide, Australia, September

Connectome 2017. Adelaide, Australia, November

Australian Society of Cardiovascular Developmental Biology 2017. Brisbane, Australia, November

Dr Sophie Wiszniak

Invited Speaker

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Ms Zarina Greenberg

Invited Speaker

ComBio 2017. Adelaide, Australia, October

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez

Co-Chair

ComBio 2017. Adelaide, Australia, October

Invited Speaker

Mechanical Forces in Biology, EMBO/EMBL. Heidelberg, Germany, July

SA Cell and Developmental Biology Meeting. Adelaide, Australia, November

Translational Oncology Laboratory

Professor Michael P Brown

Co-Chair

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Invited Speaker

Royal Australasian College of Surgeons Annual Scientific Congress. Adelaide, Australia, May

Immunotherapy@Brisbane. Brisbane, Australia, May

Cancer Nurses Society of Australia Annual Meeting. Adelaide, Australia, June

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Brisbane Cancer Conference. Brisbane, Australia, November

New Strategies in Treatment and Prevention of Autoimmune Side Effects of Immune Checkpoint, Centenary Institute. Sydney, Australia, November

Dr Vasilios Liapis

Invited Speaker

22nd World Congress on Advances in Oncology and 20th International Symposium on Molecular Medicine. Athens, Greece, October

Tumour Microenvironment Laboratory

Associate Professor Michael Samuel

Co-Chair

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Invited Speaker

3rd International Symposium on Mechanobiology. Singapore, December

Singapore Bioimaging Consortium Seminar series. Singapore, December

Peter MacCallum Cancer Institute Research Seminar series. Melbourne, Australia, May

Translational Research Institute Seminar Series. Brisbane, Australia, June

Inaugural Victorian Comprehensive Cancer Centre Conference. Melbourne, Australia, September

Dr Sarah Boyle

Invited Speaker

ComBio 2017. Adelaide, Australia, October

Co-Convener

Australia and New Zealand Society for Cell and Developmental Biology 7th Adelaide Meeting. Adelaide, November

Vascular Biology and Cell Trafficking Laboratory

Associate Professor Claudine Bonder

Invited Speaker

Olivia Newton-John Cancer Research Institute. Melbourne, Australia, April

South Australian Health and Medical Research Institute: Heart Health. Adelaide, Australia, April

Sansom Institute, University of South Australia. Adelaide, Australia, May

Future Industries Institute, University of South Australia. Adelaide, Australia, July

Federation of American Societies for Experimental Biology (FASEB) Lysophospholipid and Related Mediators: From Bench to Clinic. New Orleans, USA, August

Thomas Jefferson University. Philadelphia, USA, August

Australian and New Zealand Microcirculation Society. Mooloolaba, Australia, September

ComBio 2017. Adelaide, Australia, October

8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia, November

Session/Symposium Chair

ComBio 2017. Adelaide, Australia, October

Australasian Society for Immunology. Brisbane, Australia, November

Dr Eli Moore

Invited Speaker

Australasian Society for Biomaterials and Tissue Engineering (ASBTE). Canberra, Australia, April

Centre for Cancer Biology 2017 Awards

Ms Zarina Greenberg received the Adelaide Protein Group Student Award for the Most Outstanding Oral Presentation

Awards

Cytokine Receptor Laboratory

Professor Angel Lopez AO

Officer to the Order of Australia (AO), June

Dr Winnie Kan

Runner-up, Outstanding Postdoctoral Oral Presentation Prize: 7th ANZSCDB Meeting. Adelaide, Australia

Leukaemia Laboratory

Associate Professor Susan Branford

International Federation of Clinical Chemistry and Laboratory Medicine Distinguished Award for Significant Contribution to Molecular Diagnostics

Joint Winner, Best Primary Research Publications from CCB Researchers Award

Lung Research Laboratory

Dr Rebecca Harper

Doctoral Research Medal, University of Adelaide

PhD Thesis Excellence Award, Centre for Cancer Biology

Best Oral Presentation, Thoracic Society of Australia and New Zealand, ASM, Canberra

Best Poster Presentation Stem Cells, Cell Therapies and Bioengineering in Lung, Burlington, USA

Dr Eugene Roscioli

Winner Japanese Respiratory Society Travel Award

Finalist, Thoracic Society of Australia

Finalist, New Zealand Young Investigator Award

Lymphatic Development Laboratory:

Dr Kelly Betterman

Runner-Up Carl Zeiss Image Prize, 7th Adelaide Cell and Developmental Biology Meeting, Adelaide

Dr Genevieve Secker

Winner, Outstanding Postdoctoral Oral Presentation Award, 7th ANZSCDB Meeting. Adelaide, Australia

Ms Jan Kazenwadel

Winner, Outstanding Postdoctoral Poster Presentation Award, 7th ANZSCDB Meeting. Adelaide, Australia

Molecular Pathology Research Laboratory

Professor Hamish Scott

Joint Winner, Best Primary Research Publications from CCB Researchers Award

Dr Parvathy Venugopal

Early Career Researcher Poster Presentation Award, Australian Society for Medical Research, SA Annual Scientific Meeting, Adelaide, June

Ms Alicia Byrne

Australian Genomics Health Alliance PhD Top-Up Award

The Biology of Genomes 2017 Meeting Stipend Award

Perinatal Society of Australia and New Zealand Early Career Researcher Travel Award

Molecular Regulation Laboratory

Dr Natalie Foot

Winner, Carl Zeiss Image Competition Award, 7th ANZSCDB Meeting. Adelaide, Australia

Poster Award, Australasian Extracellular Vesicles Conference, Lorne, Australia

Dr Tanya Henshall

Joint Runner-up, Best Post-Graduate Poster Award: 7th ANZSCDB Meeting. Adelaide, Australia

Dr Jantina Manning

Joint Runner up, Best Post-Graduate Poster Award, 7th ANZSCDB Meeting, Adelaide, Australia

Ms Swati Dawar

Centre for Cancer Biology Best Student Research Publication

PhD (University of South Australia)

Ms Tianqi (Cindy) Xu

PhD (University of South Australia)

Molecular Signalling Laboratory

Dr Maurizio Costabile

Finalist, Tertiary Teaching STEM Awards. Adelaide, Australia

Dr Melinda Tea

Best Poster Prize, 8th Barossa Meeting: Cell Signalling in Cancer Medicine. Barossa Valley, Australia

Mr Alexander Lewis

Best PhD Oral Presentation, ASMR SA Annual Scientific Meeting. Adelaide, Australia

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz

Promoted to Associate Professor, The University of South Australia

Ms Ellen Potoczky

Winner, Outstanding Student Poster Presentation Award, 7th ANZSCDB Meeting. Adelaide, Australia

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez

Physical Biology, Outstanding Reviewer Award, IOP Publishing, Bristol, UK

Vascular Biology and Cell Trafficking Laboratory

Ms Kay Khine Myo Min

Best Oral Presentation by an Early Career Researcher/Research Assistant, Adelaide Immunology Retreat, 13th Annual Meeting of the ASI SA/NT Branch, Australasian Society for Immunology, September

Ms Emma Thompson

Poster Prize Winner, NSW Translational Breast Cancer Research Symposium, April

Professor Michelle Haber presents the CCB Early Career Researcher Award to Dr David Yeung

Sponsored by the Australian Society for Biochemistry and Molecular Biology (ASBMB)

Dr Loretta Dorstyn accepts the award for Best Student Primary Research Publication on behalf of Dr Swati Dawar

Sponsored by Millennium Science

Dr Rebecca Harper and Dr David Yeung receive PhD Thesis Research Excellence Awards

Sponsored by the Australian Society for Immunology (ASI)

Joint winners, Associate Professor Susan Branford and Professor Hamish Scott, receive awards for Best Primary Research Publications from CCB Researchers Award

Sponsored by Miltenyi Biotec

Dr Sophie Wiszniak presents Dr Jan Kazenwadel with the ANZSCDB award for Outstanding Postdoctoral Poster Presentation

Dr Sophie Wiszniak presents Dr Genevieve Secker with the ANZSCDB award for Outstanding Postdoctoral Oral Presentation

Dr Sophie Wiszniak presents Ms Ellen Potoczky with the ANZSCDB award for Outstanding Student Poster Presentation

Zeiss representative, Benjamin Ung, presents Dr Natalie Foot with the ANZSCDB award for the Carl Zeiss Image Competition

Service to the Community

Acute Leukaemia Laboratory

Professor Richard D'Andrea

South Australia Cancer Research Biobank (SACRB) Executive Committee

Australian Familial Hematological Cancer Study Executive Committee

Mentoring Committee, Centre for Cancer Biology

New Directions in Leukaemia Research Organising Committee

Adelaide BioMed City Platforms and Technologies Working Group

Project Control Group, Health Innovation Building, University of South Australia

Interview for UniSA Alumni News, November

Dr David Ross

Associate Editor, Leukemia Research

Elected member, The Australasian Leukaemia and Lymphoma Group (ALLG) Specialist Advisory Committee

Examiner, Royal College of Pathologists of Australasia

ACRF Genomics Facility

Dr Andreas Schreiber

Organizing committee, ABACBS, Adelaide, Australia, November

Dr Katherine Pillman

Organizing committee, ABACBS, Adelaide, Australia, November

Mr Klay Saunders

Convenor, COMBINE symposium, Adelaide, Australia, November

Organizing committee, ABACBS, Adelaide, Australia, November

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall

NHMRC Grant Review Panel

RAH Research Fellowships Review Panel

5AA Radio Breast Cancer Awareness Month, Interview with Rilka Warbanoff

The Hospital Research Fund Luncheon Panellist

Dr Leila Belle

Presentation to YWCA Encore

Cytokine Receptor Laboratory

Professor Angel Lopez AO

Australian Academy of Science Selection Committee 8, Canberra, Australia, February

ACRF Grant Interview Panel, Sydney, Australia, September

Cure Brain Cancer Foundation Grant Interview Panel, Sydney, Australia, October

Viertel Fellowship Association of Australia Interview Panel, Brisbane, Australia, October

South Australian Selection Committee Chairperson of the Australian Academy of Health and Medical Sciences, Adelaide, Australia, January-July

Gene Regulation Section

Professor Greg Goodall

NHMRC Assigners Academy

Associate Editor, Oncogene

Associate Editor, Oncogenesis

Gene Regulation in Cancer Group

Dr Philip Gregory

MC for Oliphant Science Awards, South Australian Science Teachers Association Student Awards

Secretary for The International Epithelial-Mesenchymal Transition Association (TEMTIA)

Prostate cancer presentation to the West Beach Lions Club

Panel speaker at The Basil Hetzel Society Luncheon

Gene Regulation Networks Group

Dr Cameron Bracken

Grant Review Panel, National Health and Medical Research Council

Grant Review Panel, National Breast Cancer Foundation

Inflammation and Ailments Laboratory

Professor Vinay Tergaonkar

Ad hoc reviewer for Nature and Cell Press journals

Adhoc reviewer for Science, Genes and Development, Cell Death and Differentiation, Cancer Research, International Journal of Cancer, JBC, EMBO reports and Apoptosis

Expert Review Panel for National Medical Research Council, Singapore

Grant Review Panel, A*STAR-India DST

Reviewer for Wellcome Trust, NHMRC (Australia), ANR (French), Israel Science Foundation, Department of Biotechnology India and Austrian research grants

Panel member, Duke-NUS and Duke-Durham collaborative grants

Leukaemia Laboratory

Associate Professor Susan Branford

NHMRC Postgraduate Scholarship scheme panel

Board Member, Blood Research

QIAGEN's European Scientific Advisory Board for Hematology/Oncology

Novartis International Molecular Steering Committee

International Chronic Myeloid Leukemia Foundation (iCMLf) Scientific Advisory Committee

Molecular Diagnostics RCPA Quality Assurance Program (QAP) executive

Deputy Facilitator of the Genomics, Genetics and Druggable Targets pillar, South Australian Comprehensive Cancer Consortium

John Goldman Conference on Chronic Myeloid Leukemia Advisory Committee

Lung Research Laboratory

Professor Paul Reynolds

Grant Review Panel, Centres of Research Excellence, NHMRC

Lymphatic Development Laboratory

Associate Professor Natasha Harvey

NHMRC Assigners' Academy

Australian Academy of Science National Committee for Cell and Developmental Biology

Chair, Royal Adelaide Hospital Research Committee Scholarships and Fellowships Committee

5AA Radio interview with Rilka Warbanoff

Molecular Pathology Research Laboratory

Professor Hamish Scott

Associate Editor, PLoS Genetics

Communicating Editor, Human Mutation

Australian Genomics (Health Alliance), National Steering Committee, SA State Coordination Representative, Co-leader of Program 1: A national diagnostic and translational research network

Chair, Clinical Variant Reclassification Working Group

Facilitator of the Genomics, Genetics and Drugable Targets pillar, South Australian Comprehensive Cancer Consortium

GPA Andrew Ursini Charitable Fund presentation

Dr Anna Brown

Charter Member, ClinGen committee (new) for familial haematological malignancies

International RUNX1 Research Foundation Sequencing Project Steering Committee

Dr Chris Hahn

Institute Biosafety Committee, SA Pathology

Dr Sarah King-Smith

Secretariat, Joint Committee on Digital Health and Genomics

Australian Genomics (Health Alliance), Member, Clinical Variant Reclassification Working Group

Ms Alicia Byrne

Committee Member and Secretary of the Human Genetics Society of Australasia, SA Branch

Molecular Regulation Laboratory

Professor Sharad Kumar AM

Beat Cancer Project Research Strategy Group

Convenor, 17th Hunter Meeting, Hunter Valley, Australia, April

Editorial Board and Triage Editor, Cell Death and Differentiation

Editorial Board, Frontiers in Cancer Molecular Targets and Therapeutics

Editorial Board, ScienceOPEN

Editorial Board, Oncotarget (Cell Death and Autophagy Section)

Editorial Board, Molecular and Cellular Oncology

Member, Faculty of 1000

Member, NHMRC Assigners Academy

Member, AAS National Committee for Biomedical Sciences

Member, AAS Fellowship Sectional Committee

President, Australia and New Zealand Society for Cell and Developmental Biology

UniSA Research Leadership Committee

Dr Donna Denton

Adhoc member, Organising Committee for 17th Hunter Meeting, Hunter Valley, Australia, April

Associate Member, Faculty of 1000

Dr Loretta Dorstyn

Associate Member, Faculty of 1000

Dr Yoon Lim

Representative for Centre for Cancer Biology at the South Australian Health and Medical Research Institute (SAHMRI) HDR Recruitment Event

Administrator of The South Australian Forum for Cell Biology and Biochemistry, Facebook group

Poster Judge, ComBio 2017, Adelaide, Australia

SA State Representative, Australia and New Zealand Society for Cell and Developmental Biology

Molecular Signalling Laboratory

Professor Stuart Pitson

NHMRC Assigners Academy

Victorian Cancer Agency Mid-Career Research Fellowship Selection Committee

Editorial Board member, Cellular Signalling

Editorial Board member, Prostaglandins and Other Lipid Mediators

Editorial Board member, Journal of Bioenergetics and Biomembranes

Australian representative for the Lipid Division of the American Society for Biochemistry and Molecular Biology

Judge for ASMR SA Ross Wishart Medal

National Association of Research Fellows of the NHMRC Postdoctoral Award Selection Committee

Chair of the Centre for Cancer Biology Mentoring Committee

Interview for Channel 9 News, Adelaide, Australia, October

Interview for Adelaide Advertiser, Adelaide, Australia, November

Dr Maurizio Costabile

Live interview ABC Radio 639, September

Dr Melinda Tea

Live interview ABC Radio Canberra, November

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz

NHMRC Assigners Academy

Editor for Scientific Reports

5AA Radio interview

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez

JOBEX Jobs in Emerging Industries, Government of South Australia

Member of the Editorial Board Bio-protocol (Cancer and Mechanobiology)

Member of the Editorial Board Cogent Biology

Topic Editor of the Research Topic 'Mechanobiology: Tools and Methods' at Frontiers Bioengineering and Biotechnology

Translational Oncology Laboratory

Professor Michael P Brown

NHMRC Fellowships Panel

Medical Research Advisory Committee, Australian Cancer Research Foundation

Research Committee, Cure Cancer Australia

Royal Adelaide Hospital Research Committee

South Australian Comprehensive Cancer Consortium

Scientific Advisory Board, Cartherics Pty Ltd

Dr Lisa Ebert

Participation as a Partner Scientist in the CSIRO's Scientists in Schools Program

Organising Committee, Australasian Society for Immunology (ASI) Annual Scientific Meeting, Adelaide, December 2019

Organising Committee, Australasian Cytometry Society (ACS) 41st Annual Meeting, Adelaide, October 2018

Tumour Microenvironment Laboratory

Associate Professor Michael Samuel

Grant Review Panel, NMHRC

Secretary, Australia and New Zealand Society for Cell and Developmental Biology

Presentation to Donors, National Breast Cancer Foundation

Dr Sarah Boyle

SA State Representative, Australia and New Zealand Society for Cell and Developmental Biology

Invited mentor, Government of South Australia Office for Women's 'Women in STEM Speed Mentoring Event', Adelaide, March

Poster Teaser Organiser and Session Chair, ComBio 2017, Adelaide, September

Vascular Biology and Cell Trafficking Laboratory

Associate Professor Claudine Bonder

Grant Review Panel, NMHRC

External Assessor for NHMRC Program Grants

Editorial Board Microcirculation

Executive Committee, Australian Vascular Biology Society

Chair, Centre for Cancer Biology Consumer Advocacy Group

SA Tall Poppy Selection Committee

UniSA Division of Research Management Committee

Leadership Group of University of South Australia, Cancer Theme

National Breast Cancer Foundation, VIP donor tour

Leaders' Edge Lunch, as 'Tomorrow's SA Icons', Australian Institute of Company Directors

Advertiser article, Tomorrow's SA Icons

Enterprise Magazine, UniSA, feature on Evolutionary Innovation

Inspire Magazine, Research Australia, feature on Medical Research

Women in Innovation, Awards Launch Panel

Advertiser article, NBCF feature article

Ten Eyewitness National News, headline article on breast cancer research

Radio Canberra 2CC, invited expert to comment on breast cancer research

Cancer Council 'Girl's Night In', invited expert to comment on breast cancer research

Research Staff and Students

Acute Leukaemia Laboratory
Professor Richard D'Andrea
Dr David Ross
Dr Debora Casolari
Dr Saumya Samaraweera
Dr Deepak Singhal
Dr Tatjana Geukens
Mrs Diana Iarossi
Ms Tran Nguyen
Students
Mr Ka-Leung Li (PhD)
Mr Kyaw Zeya Maung (PhD)
Student degrees completed in 2017
Mr Mahmoud Bassal (PhD)

Cell Signalling Laboratory
Associate Professor Yeesim Khew-Goodall
Dr Leila Belle
Dr Xiaochun Li
Dr Ana Lonic
Ms Freya Gehling

Cytokine Receptor Laboratory
Professor Angel Lopez
Dr Tim Hercus
Dr Winnie Kan
Dr Duncan McKenzie
Dr Hayley Ramshaw
Dr Frank Stomski
Dr Daniel Thomas
Dr Denis Tvorogov
Dr Dave Yip
Ms Emma Barry
Mr Cameron Bastow
Ms Mara Dottore
Ms Ceilidh Marchant
Ms Melanie Pudney
Mrs Anna Sapa
Mrs Rebecca Wright

Gene Regulation Section
Professor Greg Goodall
Dr Kate Dredge
Dr Dawei Liu
Mr Andrew Bert

Gene Regulation in Cancer Group
Dr Philip Gregory
Ms Rachael Lumb
Ms Caroline Phillips
Students
Ms Victoria Arnet (PhD)
Mr Daniel Neumann (PhD)

Gene Regulatory Networks Group
Dr Cameron Bracken
Ms Kaitlin Scheer
Students
Mr Klay Saunders (PhD)
Ms Laura Sourdin (PhD)
Student degrees completed in 2017
Dr Feng Yu (PhD)

Inflammation and Human Ailments Laboratory
Professor Vinay Tergaonkar
Dr Gokhan Cildir
Ms Ava Zhou

Leukaemia Unit, Genetics and Molecular Pathology
Associate Professor Susan Branford
Dr Nur Hezrin Shahrin
Dr Daniel Thompson
Dr Carol Wadham
Ms Zoe Donaldson
Ms Jasmina Georgievski
Ms Nathalie Nataren
Mr Adrian Purins

Lung Research Laboratory
Professor Paul Reynolds
Professor Sandra Hodge
Professor Mark Holmes
Professor Hubertus Jersmann
Associate Professor Greg Hodge
Dr Rebecca Harper
Dr Chien-Li Holmes-Liew
Dr Phan Nguyen
Dr Eugene Roscioli
Dr Hai Tran
Dr Miranda Ween
Dr Jonathan Whittall
Mr Rhys Hamon
Ms Suzanne Maiolo
Students
Dr Emily Hopkins (Masters)
Dr Vanessa Tee (Masters)
Dr Michelle Wong (Masters)
Ms Debra Sandford (PhD)

Lymphatic Development Laboratory
Associate Professor Natasha Harvey
Dr Kelly Betterman
Dr Genevieve Secker
Dr Drew Sutton
Ms Jan Kazenwadel

Molecular Pathology Research Laboratory
Professor Hamish Scott
Dr Christopher Hahn
Dr Anna Brown
Dr Chan-Eng Chong
Dr Parvathy Venugopal
Dr Peer Arts
Dr Lucia Gagliardi
Dr Sarah King-Smith
Ms Milena Babic
Mr Peter Brautigan
Ms Saba Montazaribarforoushi
Students
Dr Sunita De Sousa (PhD)
Ms Alicia Byrne (PhD)
Mr Jesse Cheah (PhD)

Molecular Regulation Laboratory
Professor Sharad Kumar
Dr Donna Denton
Dr Loretta Dorstyn
Dr Natalie Foot
Dr Tanya Henshall
Dr Yoon Lim
Dr Jantina Manning
Dr Ian Nicholson
Dr Claire Wilson
Dr Tianqi (Cindy) Xu
Ms Sonia Dayan
Mr Dylan De Bellis
Ms Kelly Gembus
Mr Andrej Nikolic
Students
Mr Julian Carosi (PhD)
Mrs Ammara Usman Farooq (PhD)
Ms Shannon Nicolson (PhD)
Student degrees completed in 2017
Ms Swati Dawar (PhD)
Ms Tianqi (Cindy) Xu (PhD)

Molecular Signalling Laboratory
Professor Stuart Pitson
Dr Maurizio Costabile
Dr Briony Gliddon
Dr Melissa Pitman
Dr Jason Powell
Dr Melinda Tea
Dr Craig Wallington-Beddoe
Dr Jo Woodcock
Mr Carl Coolen
Ms Lorena Davies
Mr Paul Moretti
Students
Ms Melissa Bennett (PhD)
Mr Alexander Lewis (PhD)
Ms Wenying (Layla) Zhu (PhD)
Student degrees completed in 2017
Ms Heidi Neubauer (PhD)
Ms Cassandra Stefanidis (Hons)

Neurovascular Research Laboratory
Associate Professor Quenten Schwarz
Dr Sophie Wiszniak
Ms Zarina Greenberg
Ms Rachael Lumb
Mr Iman Lohresab
Mr Xinagjun Xu
Student degrees completed in 2017
Ms Zarina Greenberg (PhD)
Ms Ellen Potoczky (Honours)

Research Support Staff Angela Ziaei, Selin Cildir, Ian Nicholson, Cathy Lagnado, Natasha Pyne, Andrew Bert, David Tregear, Russell D'Costa

Tissue Architecture and Organ Function Laboratory
Dr Guillermo Gomez
Dr Mariana Oksdath Mansilla

Translational Oncology Laboratory
Professor Michael P Brown
Dr Yann Chan
Dr Lisa Ebert
Dr Tessa Gargett
Dr Yanrui (Judy) Li
Dr Vasilios (Bill) Liapis
Dr Alexander Staudacher
Dr Wenbo (Stanley) Yu
Students
Ms Nga Truong (Masters)

Tumour Microenvironment Laboratory
Associate Professor Michael Samuel
Dr Sarah Boyle
Dr Zahied Johan
Dr Natasha Kolesnikoff
Dr Jasreen Kular
Ms Diana Iarossi
Ms Natasha Pyne
Students
Ms Valentina Poltavets (PhD)
Mr Brock Le Cerf (Masters)

Vascular Biology and Cell Trafficking Laboratory
Associate Professor Claudine Bonder
Dr Mark DeNichilo
Dr Camille Duluc
Dr Eli Moore
Ms Michaelia Cockshell
Mr Brenton Ebert
Ms Samantha Escarbe
Ms Kay Khine Myo Min
Students
Dr Carmela Martino (PhD)
Ms Lih Tan (PhD)
Ms Emma Thompson (PhD)
Mr Jake Treloar (PhD)
Ms Danielle King (Honours)
Student degrees completed in 2017
Dr Carmela Martino (PhD)
Ms Danielle King (Honours)

ACRF Cancer Genomics Facility
Professor Greg Goodall
Professor Hamish Scott
Facility Manager: Mr Joel Geoghegan
Bioinformatics: Dr Andreas Schreiber
Dr Jinghua (Frank) Feng
Dr Marie-Emilie (Maely) Gauthier
Dr Emily Hackett-Jones
Dr Thuc Le
Dr Wendy Parker
Dr Katherine Pillman
Dr Julien Soubrier
Dr Paul Wang
Ms Rosalie Kenyon
Ms Nathalie Nataren
Mr David Lawrence
Ms Ming Lin
Mr John Toubia
Students
Mr Klay Saunders (PhD)

Research Support Staff
Mrs Selin Cildir
Mr Russell D'Costa
Mrs Carmen Holliday
Ms Cathy Lagnado
Ms Marianne Oosterwegel
Ms Geraldine Penco
Ms Natasha Pyne
Mr David Tregear
Ms Angela Ziaei

Animal Care Facility Staff
Ms Kelly Wicks
Ms Melissa Bell
Ms Dominique Broad
Mr Chris Brown
Ms Carly Hancock
Ms Brigitt Hines
Ms Jacqueline Holmes
Ms Nichola Smith
Ms Erin Teasdale
Ms Sylvia Tichborne
Ms Amy Woud

Our Supporters

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SA Pathology

University of South Australia

Donors and Supporters

Robert and Joan Thompson

Robert Kenrick

Government of South Australia, SA Health

Australian Government, National Health and Medical Research Council, NHMRC

Australian Cancer Research Foundation

the hospital research foundation, finding cures improving care

Cancer Council SA

Therapeutic Innovation Australia

Cell Therapy Manufacturing

Fay Fuller Foundation

aamri

Leukaemia Foundation, Vision to Cure, Mission to Care

The University of Adelaide

Royal Adelaide Hospital Research Fund

Royal Adelaide Hospital

Medvet.Science

National Breast Cancer Foundation

Bellberry Limited

hscgb, Health Services Charitable Gifts Board

Captain Courageous Foundation

BioSA

ERSA

Research Australia

The Kids Cancer Project

worldwide cancer research, formerly known as AICR

Australian Government, Cancer Australia

Australian Government, Australian Research Council

NCRIS, National Research Infrastructure for Australia, An Australian Government Initiative

The Hospital Research Foundation Team raises funds for the Centre for Cancer Biology

Supporting Our World Class Research

The Centre for Cancer Biology (CCB) incorporates the Hanson Centre for Cancer Research legacy and works with South Australian-based philanthropic organisations to raise funds to support our vision to find causes and cures for cancer. A key benefit of this collaborative approach is that we can reduce administration costs. We are extremely proud to work with the following organisations to deliver the best value to donors resulting in greater investment in breakthrough cancer research:

The Hospital Research Foundation
The Hospital Research Foundation (THRF) supports and advocates for world-leading medical research that translates into the prevention of disease, the relief of suffering, improved patient care and the restoration of health and wellness for all in our community. THRF is proud to support leadership and innovation in research that translates into the provision of outstanding medical and nursing care in our hospitals and improved health and wellbeing in the community. THRF provides Grants for research projects, programs and research personnel across a number of leading research facilities within South Australia including the CCB.

Royal Adelaide Hospital (RAH) Research Fund
Established in 1981, the Royal Adelaide Hospital (RAH) Research Fund believes everyone deserves access to the best possible treatment and patient care. The RAH Research Fund strives to make this possible by raising funds for medical equipment, lifesaving medical and clinical research and enhanced patient services. The Research Fund works with its community supporters, to raise funds for vital medical research. Most of the funds raised are through the generosity of everyday South Australians who support the Research Fund with kind donations or by leaving a gift in their Will. With the support of our donors, the RAH Research Fund makes a positive impact by funding research into the diseases that affect the people in our local community. All donations made to the RAH Research Fund are vested with The Health Services Charitable Gifts Board (HSCGB).

The University of South Australia Advancement Services
The University of South Australia Advancement Services team facilitates mutually beneficial relationships between the University and its benefactors, alumni and friends. Advancement Services is responsible for the alumni network of over 174,000 graduates, and managing programs aimed to foster life-long partnerships with graduates and benefactors. The University's alumni network spans every industry and profession, and spreads all over the world.

What will my donation support?
Your donation will be used to fund breakthrough research on the fundamental causes of cancer and to translate these discoveries into cures, with global impact. In addition to general donations to the CCB, you may wish to consider the following donation options:

Make a donation in memoriam and in honour
Make a gift to the Centre for Cancer Biology in lieu of flowers to honour a loved one who has passed away from cancer, or to mark special occasions such as birthdays, weddings and anniversaries.

Purchase state of the art research equipment
The CCB relies heavily on donations to enable us to purchase the equipment we require to undertake our research. Please contact us or one of our philanthropic partners above to discuss options. A personalised plaque may be affixed to any equipment bought.

Fellowships
These can be from one to five years and can be named after a family, a family member, or a company.

Build a corporate partnership
The Centre for Cancer Biology welcomes the support of the business community. Please contact us to discuss how we might partner with your organisation.

Sponsorship
Companies or individuals may wish to sponsor a research project or individual.

You can make a donation at any time online:
centreforcancerbiology.org.au,
or contact us directly:
Email info@centreforcancerbiology.org.au
Telephone: +61 8 8302 7916

Thank you

Notes