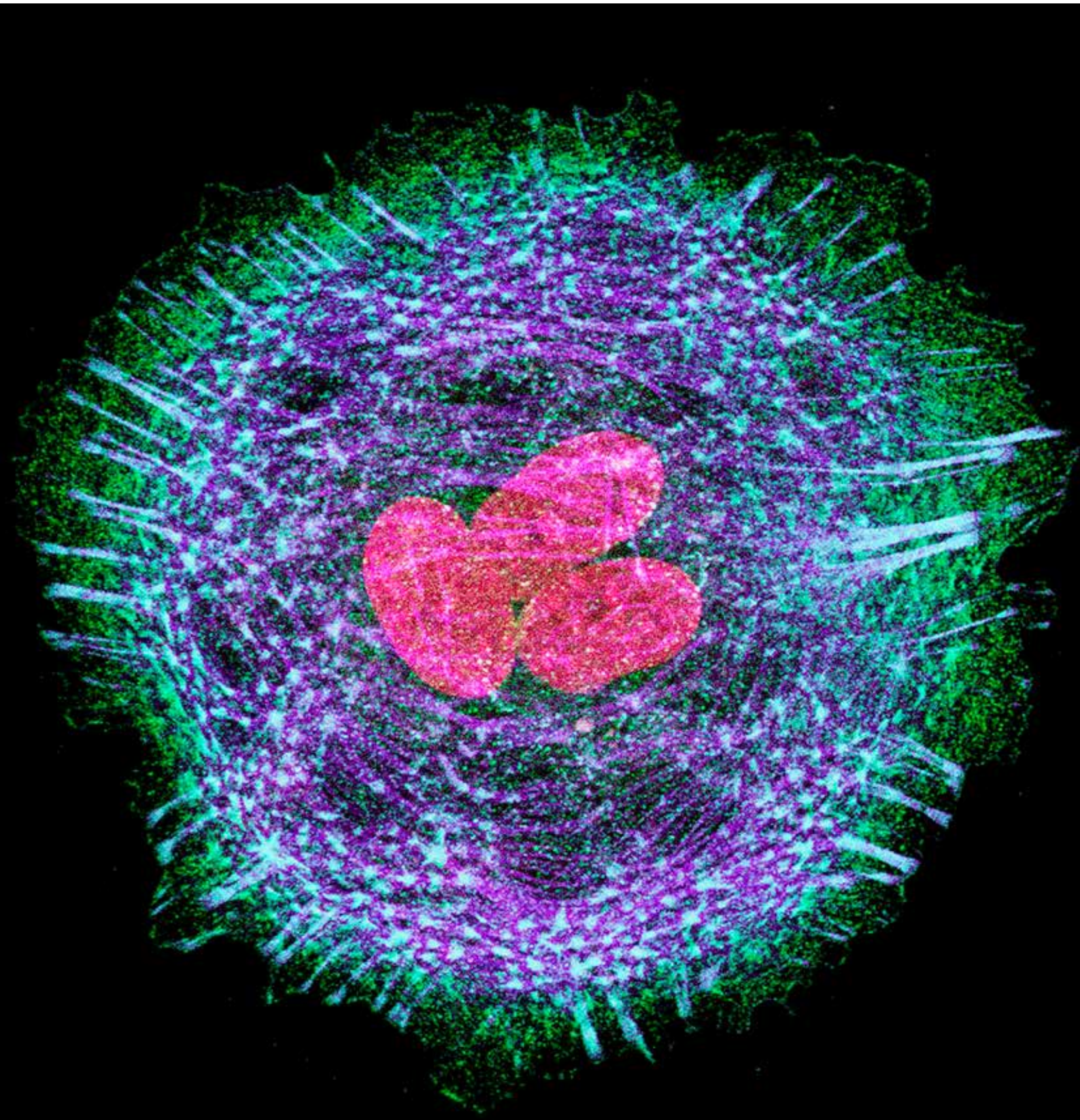
2018
Annual Report

Centre for Cancer Biology



Centre for Cancer Biology Members

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

Associate Members
Professor Leanne Dibbens
Professor Timothy Hughes
Professor Shudong Wang
Professor Andrew Zannettino
Associate Professor Michael R Beard
Associate Professor Michele Grimbaldeston
Associate Professor Andrew Ruszkiewicz
Dr Cameron Bracken
Dr Anna Brown
Dr Loretta Dorstyn
Dr Guillermo Gomez
Dr Philip Gregory
Dr Christopher N Hahn
Dr Jason Powell
Dr Nirmal Robinson
Dr Damon Tumes
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

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cover image Breast Nest: a cluster of fluorescently labelled mammary cancer cells. The cells are stained for a protein (green) that localises to the edges of the cell where it can then be released from the cell and act upon its supporting environment to help cancer to grow. The actin cytoskeletons are labelled using phalloidin (purple) and cell nuclei are labelled with DAPI (pink). Image captured by Dr Sarah Boyle

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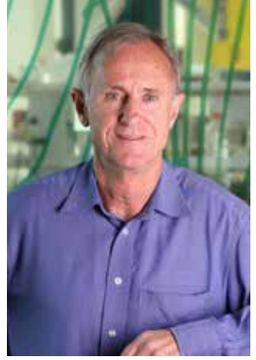
Organisation

Professors Sharad Kumar AM and Angel Lopez AO

Claudine Bonder, promoted to Professor

Natasha Harvey, promoted to Professor



Professor Greg Goodall, elected to the Australian Academy of Science

Dr Damon Tumes, Head, Allergy and Cancer Immunology Laboratory

Some of our NHMRC and Beat Cancer grant recipients: Stuart Pitson, Tessa Gargett, Claudine Bonder, Sharad Kumar, Chris Hahn, Loretta Dorstyn, Phil Gregory

Directors' Report

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

It is ten years since the Centre for Cancer Biology (CCB) was established, initially as a centre of excellence within SA Pathology. As we contemplate the past we plan a future towards achieving breakthrough discoveries and clinical interventions that save the lives of patients with cancer. We reflect on a proud ten-year history of collaboration with colleagues in the old Precinct on Frome Road and North Terrace and now in the new developing Precinct, Adelaide BioMed City.

In March 2018, most of the CCB moved to the top four floors of a new UniSA building right in the heart of the Adelaide BioMed City. After directly contributing to the layout and design we were delighted to see how the CCB floors came together in a cohesive environment where offices and open plan laboratory spaces are flooded with natural light and beautiful views. The lecture theatre, with flexible and expandable space for seminars and meetings, opens up into an area for morning coffee and afternoon tea. Architectural firm Swanbury Penglase were recently recognised in the 2019 SA Architecture Awards for the striking architecture and interior design. Whilst we are enjoying our new venue, we don't forget that the CCB is its people. We were aware of the risks that come with larger spaces and we wanted to maintain close personal interactions through seminars and coffee breaks as a way to promote ideas and collaborations. This new location will continue to facilitate our interaction with other cancer and medical research groups in the Precinct and facilitate the use of shared infrastructure. Furthermore, preparations for the new SAHMRI 2 building, which will house the Australian Bragg Centre for Proton Therapy, holds promise for future synergies. Unfortunately, our colleagues at Genetics and Molecular Pathology and the ACRF Cancer Genomics Facility (CCB East) are not located with us yet and we are committed to finding a way to have all of the CCB co-located again to fast track research into treatments for patients.

The ACRF Cancer Genomics Facility, wonderfully led by Professors Hamish Scott and Greg Goodall, works closely with clinical diagnostic associates at SA Pathology resulting in new clinical trials and diagnostic tests (e.g. the first accredited laboratory in Australia for diagnostic whole exome sequencing, received the SA Health Award for Excellence in 2015; the second accredited laboratory in Australia for paired WES for cancer; the first in Australia accredited for copy number variation analyses and RNAseq for splice site mutation detection and fusion transcript detection in 2018).

A major benefit over these last ten years was due to the CCB being embedded in the Health system through the Royal Adelaide Hospital (RAH), SA Pathology and the Central Adelaide Local Health Network (CALHN) overall. Access to patient samples and clinical data has paved the way for us to understand disease better, make practical discoveries and plan clinical trials. This connection with SA Health has occurred at other levels too, such as with the mentoring of medical students, young doctors and specialists who want to understand the 'whys' and 'hows' of cancer. Their involvement and contribution has been wonderful and encouraged us to recognise them through the formation of a Clinical Affiliate membership category of the CCB.

As we look back, we can see the CCB evolving from a centre of excellence launched by Professor Ian Frazer AC in April 2009 into a fully accredited medical research institute with a focus on cancer discovery, diagnosis and treatment. By being a member of the Australian Association of Medical Research Institutes (AAMRI) family we feel privileged to be part of the medical research institute environment that allows us to participate in cutting-edge ideas, technology platforms and Australia-wide initiatives to improve patient health.

Our long-standing CCB Thursday seminars, which bring the best interstate scientists, pathologists and clinicians to Adelaide, has developed into a city-wide seminar firmly in the Adelaide BioMed City's calendar. This has been complemented by our biennial Barossa Cancer Medicine and Signalling Meetings, which now enter their ninth edition. This has helped the CCB link up with colleagues and like-minded scientists both interstate and overseas. We are pleased to be recognised as hosting a major international cancer meeting and delighted to see the strong support we receive from our colleagues. With the award of the Clifford Prize for Cancer Research at these meetings, which is always accompanied by a special celebratory dinner catered by the Beer family, we have been able to bring international attention to the best science and culinary delights South Australia can offer.

We are pleased to report that, as in previous years, in 2018 we obtained several competitive NHMRC grants (eight), among a total of over $12 million of new research funding to the CCB. The CCB published 99 scientific papers in highly regarded international journals such as Science Advances, Nature Communications and Leukemia. In 2018 we congratulated Natasha Harvey and Claudine Bonder for their promotion to Professor. Professor Sharad Kumar received an Order of Australia and the 2018 South Australian Indian Medical Association President's Award, and Professor Greg Goodall was elected to the Australian Academy of Science and was also awarded the prestigious Julian Wells Medal at the Lorne Genome Conference. Some of our younger and up-and-coming researchers were also recognised, including Dr Sarah Boyle who was awarded the ANZSCDB Toshiya Yamada Prize.

We are proud to continue to witness the wonderful spirit of collegiality by the CCB membership, amongst ourselves and also with colleagues in Adelaide. Three examples are worth highlighting because of the spread of the collaboration and the depth of the problem being tackled. In the area of brain cancer Dr Guillermo Gomez, who is pioneering the development of brain organoids, leads a multidisciplinary team of experts in cell signalling and drug discovery (Professor Stuart Pitson, CCB), stem cell biology and neurosciences (Dr Cedric Bardy, SAHMRI), artificial intelligence (Professor Chunhua Shen, University of Adelaide), and material sciences (Dr Dario Arrua, UniSA) to deliver personalised information regarding the drugs that best inhibit brain tumour invasion in a matter of weeks after a patient's surgery. In the area of lung cancer, Dr Jo Woodcock is leading a team that includes Professor Paul Reynolds (RAH and University of Adelaide), Professors Pitson and Lopez (CCB) and Clive Prestidge (UniSA) seeking to provide long-lasting therapies to this deadly disease. The CCB has several national and international leaders exploring the identification of germline mutations in families and patients that predispose them to blood cancers and somatic mutations to monitor their disease, often in collaboration with international institutes such as the University of Washington, Seattle, St Judes, Memphis and the University of Chicago. This includes myeloid leukaemia, where the CCB works closely with SAHMRI (Professors Tim Hughes and Deborah White), the RAH (Dr David Ross), the Walter and Eliza Hall Institute of Medical Research (Dr Jeff Babon), and Stanford University (Dr Dan Thomas) in finding their causes and in developing treatments.

Beyond Adelaide BioMed City, we were pleased to see that over the last ten years the CCB has embedded itself in the national and international effort to fight cancer. We are founders of the SA Genomics Health Alliance, SA leaders of Australian Genomics (an NHMRC funded national Health Alliance), and members of the Global Alliance for Genomics and Health (GA4GH), all of whom seek to apply Genomics in mainstream healthcare in an agile and rapid way to the betterment of the Australian and international community.

We are enjoying our participation in the Zero Childhood Cancer Initiative led by the Children's Cancer Institute in New South Wales that aims to provide faster and more precise therapeutic opportunities for children with cancer. In this regard, the imminent building of SAHMRI 2, which will accommodate the Proton Beam Therapy Facility, has important implications for the research and treatment of children's cancers in the future. We recognise that cancer is a global problem, therefore these networks with other Australian medical research institutes are critically important for the CCB to maximise the impact of its research and also open up opportunities with other institutions internationally. As we recognise the value of the pharmaceutical industry in this fight, we are pleased to continue our valued interactions with CSL Limited, Novartis, Bristol-Myers Squibb, and AusHealth Research (formerly MedVet Science) over the last ten years. And recently we have become part of a new commercial entity with a project led by Professor Stuart Pitson, which has now morphed into Cincera Therapeutics Pty Ltd supported by a $7 million investment by the Medical Research Commercialisation Fund, its first in South Australia.

In continuing our tradition of supporting young, promising researchers we welcomed in 2018 Dr Damon Tumes, as the new Head of the Allergy and Cancer Immunology Laboratory, who has joined the CCB to study allergic inflammation and its impact on head and neck cancers. Strongly supported by Dr Dave Yip, Ms Jessica Chao, and our new clinical affiliate and ENT specialist Associate Professor Harshita Pant, this laboratory aims to dissect the immunological basis of allergic inflammation with emphasis on upper and lower respiratory airways. In 2018 we also recruited Dr Nirmal Robinson from Cologne, Germany to help Professor Vinay Tergaonkar drive his Inflammation and Human Ailments Laboratory and to develop his own line of research on antibiotic resistance.

As in previous years, we held our CCB annual meeting at which Professor Peter Leedman (Director, Harry Perkins Institute of Medical Research) gave a keynote address, and we released

Professors Angel Lopez AO and Sharad Kumar AM at the Centre for Cancer Biology opening ceremony, April 2009

Unveiling of the Centre for Cancer Biology dedication plaque: Sharad Kumar, Angel Lopez, Ian Frazer, John Hill, Ruth Salom and Tony Sherbon

The Centre for Cancer Biology team, ten years on

10 Years of the Centre for Cancer Biology

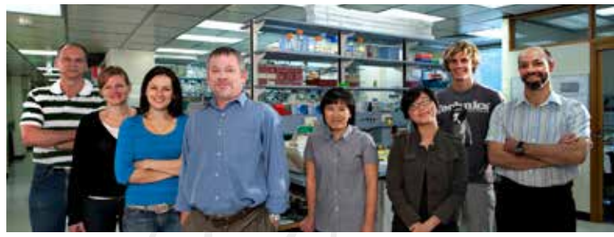
our 2017 Annual Report. This occasion was beautifully rounded out by several messages from our earlier students who, upon finishing their studies at the CCB, went on to work in other cancer institutes interstate and overseas. We were delighted to hear from Dr Heidi Neubauer at the University of Veterinary Medicine in Vienna, Dr Wenying (Layla) Zhu at the Peter MacCallum Cancer Centre in Melbourne, Dr Kate Parham at The University of Western Ontario in Canada and Dr Wai (Kiwi) Sun at Hong Kong University. We were pleased to see our alumni haven't forgotten us and to hear of their wonderful progress.

In 2018 we saw a strong and continuing participation in the life of the CCB by the Consumer Advocacy Group established by Professor Claudine Bonder and Ms Paula Nagel AM. This Consumer Group of ten dedicated supporters have all experienced at least one form of cancer and are critically important to keep the CCB cancer research firmly grounded in what is most relevant for cancer patients and their families. A clear example of their participation in the everyday life of the CCB could be seen in their attendance at 'The Future of Cancer Research in Australia' event, a focal point for the National Science Week that took place in August. This function, at which several CCB Lab Heads spoke, was chaired by the CEO of The Hospital Research Foundation, Mr Paul Flynn. It was a clear reminder to all of the long-term tangible aims of the CCB for the South Australian community.

A major appreciation of support over the last ten years goes to our distinguished Scientific Advisory Board, chaired by Professor Ian Frazer AC (University of Queensland), and including also Professors Brendan Crabb AC (ED, Burnet Institute), Michelle Haber AM (ED, Children's Cancer Institute), Christina Mitchell (Dean of Medicine, Monash University) and Joseph Trapani (ED, Peter MacCallum Cancer Centre). Their wisdom, foresight and wonderful advice has been a source of resilience and direction, which has inspired the creation of a long-term vision for the CCB crystallised in our Strategic Plan.

Finally, we'd like to recognise the philanthropic groups that constantly and tirelessly support the CCB. Nationally, we are indebted to the Australian Cancer Research Foundation (ACRF) which has supported us through two major infrastructure grants to set up the ACRF Cancer Genomics Facility in 2009 and the ACRF Cancer Discovery Accelerator Facility in 2015. We are also grateful to the Cure Brain Cancer Foundation, the Leukaemia Foundation of Australia and the National Breast Cancer Foundation. At the state level we are very grateful for the support of the South Australian Cancer Council through the Beat Cancer Project, the Royal Adelaide Hospital Research Fund and in particular the Health Services Charitable Gifts Board (HSCGB) and The Hospital Research Foundation for the generous support of projects and fellowships over the years. We gratefully acknowledge the various contributions of our wonderful faculty and early and mid-career researchers in helping us manage the CCB, participating in mentoring and many community activities that help raise funds for cancer research, as well as bring the end users of our research close to us.

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



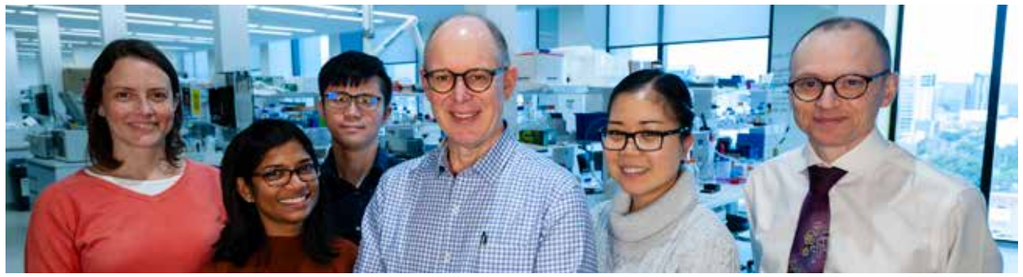
Centre for Cancer Biology
Making News …

In 2018, the CCB continued to be featured on the radio and 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
2018 Laboratory Reports

Professor Sharad Kumar and Dr Jantina Manning are exploring a new molecular pathway involved in kidney damage and the death of epithelial cells.

Image courtesy of The Hospital Research Foundation



Debora Casolari, Saumya Samaraweera, Ka Leung Li, Richard D'Andrea, Tran Nguyen, David Ross

Acute Leukaemia Laboratory

Professor Richard D'Andrea PhD
Clinical Affiliate 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, with the highest risk in AML.

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 improving outcomes for some subtypes and for older patients. We are using new approaches and technologies to better understand the regulatory pathways that are disrupted and lead to disease initiation and progression.

Key discoveries 2018

Rare DNA repair gene variants in AML

In a recent study published in *Blood Cancer Journal*, we have reported that heterozygous mutations affecting FANC genes, which encode DNA repair proteins, confer an approximately 3-fold increased risk of developing AML as an adult. We hypothesize these heterozygous mutations may confer a subtle DNA repair defect that is associated with accumulation of mutations in blood stem cells over time, and increased risk of AML in adulthood. Of the 22 known FANC genes, we observed an increased frequency of occurrence of damaging *FANCL* mutations in AML. Therefore, we have engineered a cell line to carry either heterozygous or homozygous deletions of *FANCL*. Sensitive assays of DNA repair revealed that the heterozygous cells had reduced capacity to repair DNA damage compared to wild type, while being more effective at repairing the damage than the cells with double deletion. Taken together, these findings suggest that decreased function of the FANC mediated DNA repair pathway, in haematopoietic stem cells, due to heterozygous FANC gene mutations may result in a reduced capacity to maintain genome integrity, which may in turn contribute to increased risk of AML.

CDK9 and BET co-inhibition in MLL-r leukaemias

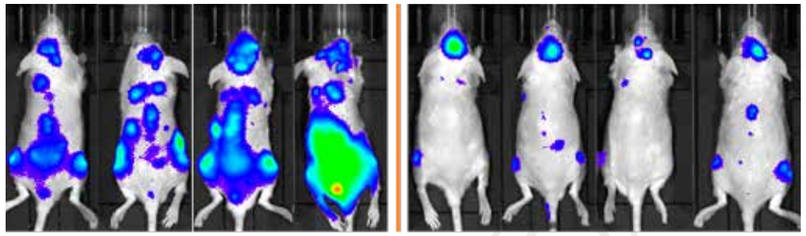
MLL gene rearrangements (MLL-r) result in fusion of the MLL protein with multiple different partners which aberrantly recruit the positive transcription elongation factor b (pTEFb) to MLL target genes resulting in transcription up-regulation. pTEFb has the cyclin dependent kinase 9 (CDK9) as its catalytic subunit. We have shown that a new CDK9 inhibitor (CDKI-73) inhibits growth of a panel of AML cell lines, with the most sensitive lines being those carrying MLL-r. Treatment with CDKI-73 decreases MCL1 protein expression and induces apoptosis in both MLL-r AML cell lines and primary patient samples. We tested CDKI-73 *in vivo* using a xenograft mouse model transplanted with a human MLL-r AML cell line. Drug treatment slows the growth and propagation of the leukaemia in this model. Next we investigated the synergistic efficacy of combining CDKI-73 with bromodomain and extra terminal domain (BET) inhibitors, which also target the activity of MLL fusion proteins. The combination treatment was more effective than single treatments in inhibiting AML cell growth *in vitro*. In AML patient derived xenografts (PDX) the combination treatment significantly decreased leukaemic burden, compared to single treatments, and also resulted in improved survival. These data provide strong evidence for the strategy of combining CDK9 and BET inhibitors, both of which are already in advanced stages of clinical development, as a treatment for MLL-r leukaemias.

10 Year Highlights

AML genetics A key focus of our group has been the genetics of AML. Our studies include international collaborative efforts in this area to define aberrant RNA expression in AML (Beck *et al*, *Leukemia*, 2018), driver events associated with acute erythroleukemia (Iacobucci *et al*, *Nat Genet*, 2019) and therapy-related MDS/AML (Singhal *et al*, *Leukemia*, 2019), and novel germline mutations in families with haematological malignancies (Shahrin *et al*, *Blood*, 2016; Hahn *et al*, *Nature Genetics*, 2011). Our own whole exome sequencing on a large panel of clinically annotated samples from consented AML patients (145 adult and 26 paediatric patients), has been important for our studies defining rare germline variants affecting critical pathways and impacting on development of adult and paediatric AML (eg Maung *et al*, *Blood Cancer J*, 2018).

AML epigenetics Our group has also investigated the role of aberrant epigenetic events in AML. We have demonstrated that DNA hypermethylation of the Kruppel-like factor 5 (*KLF5*) gene is associated with reduced expression and poor overall survival in AML (Diakiw *et al*, *Br J Haematol*, 2013). Likewise, we reported that the *Growth Arrest and DNA Damage inducible 45A (GADD45A)* gene is hypermethylated in a large proportion of AML patients (42%), and this correlates with poor overall survival (Perugini *et al*, *Leukemia*, 2013). A collaboration with Professor Ari Melnick's group at Weill Cornell Medicine (New York, USA), showed that distinct genetic and epigenetic patterns affect the biological and clinical features of AML, and contribute differentially to relapse (Li *et al*, *Nat Med*, 2016).

AML and myeloid neoplasia biology and translational research Our 2016 publication in *Blood* showed that the transcription factor KLF5, which has been reported to be a direct target of C/EBPα, possesses dual functions in regulating hematopoietic stem and progenitor proliferation, and lineage choice of more committed progenitors promoting increased neutrophil output at the expense of eosinophil production (Shahrin *et al*, *Blood*, 2016).
We published several papers on myeloproliferative neoplasms including a recent paper that reported and characterised an Epidermal Growth Factor Receptor (EGFR) mutant identified in a Polycythaemia Vera (PV) patient, which has transforming activity and promotes erythroid lineage choice, consistent with a role of EGF signalling in determining the characteristics of PV. (Casolari *et al*, *Sci Rep*, 2017). Translational studies to develop novel agents for therapy are ongoing in our laboratory and are supported by a number of grants from the pharmaceutical industry.



Drug treatment with CDKI-73 inhibits leukaemia progression in mice transplanted with AML

Outcomes for the Community

Our studies increase fundamental knowledge of pathogenesis of blood cancers, and have important implications for diagnosis and treatment. We continue our laboratory and pre-clinical modelling of these diseases to validate novel mutations and potential therapeutic targets, with ongoing collaborations with other research groups around Australia and overseas. These studies are tightly linked with efforts to translate our laboratory research findings into the clinic through our collaborative links with SA Pathology, major South Australian hospitals, and the pharmaceutical industry.

Jessica Chao, Damon Tumes, Harshita Pant, Dave Yip
Absent: Angus Sarah

Allergy and Cancer Immunology Laboratory

Dr Damon Tumes PhD
Clinical Affiliate Associate Professor Harshita Pant BMBS FRACS PhD

Our laboratory is focussed on defining the mechanisms that drive allergic immune responses at the interface between our bodies and the environment. Airway mucosal tissue is a specialised barrier capable of protecting against infection while facilitating respiration. The skin is the largest barrier tissue in our body and provides both physical and immunological protection from disease.

Our research aims to define the immunological pathways that drive inflammation in human airway and skin tissue. We are using cutting edge techniques, including single cell RNA-Sequencing and a human airway tissue xenograft model, to accomplish this goal. T cells in the airway and skin can specifically recognise pathogens and provide protection from reinfection via immunological memory. When T cells recognise common environmental antigens, they can also drive chronic inflammation and tissue pathology. Several proinflammatory cytokines are produced by T cells that are capable of promoting or suppressing allergic disease. We are using technologies such as chromatin immunoprecipitation followed by next generation sequencing (ChIP-Seq) to provide a global view of gene regulation in T cells. This information is being used to determine how T cell differentiation and plasticity is regulated and to define new ways to control T cell function in diseases such as allergy and cancer. Mast cells are another cell type central to the development of allergic diseases. Mast cells are activated via antigen-mediated cross-linking of IgE bound to their surface. We are defining novel signalling pathways that regulate IgE-driven mast cell activity and testing new topically applied drugs to inhibit allergic skin diseases.

Key discoveries 2018

Early-life antibiotic-driven dysbiosis in mice leads to impaired antibody responses and enhanced T cell cytokine recall responses to vaccination In Australia, around 40% of babies are exposed to antibiotics, either directly or via their mothers before birth. We found that exposure of pregnant mice to antibiotics altered their immune system development and impaired their responses to commonly used vaccines. This effect was found to be dependent on dysbiosis in the offspring of the antibiotics treated animals. This study has strong implications for the use of antibiotics during pregnancy. In collaboration with Professor David Lynn at the South Australian Health and Medical Research Institute and Professor Helen Marshall at the Women's and Children's Hospital, we are now investigating whether antibiotics use during pregnancy impairs vaccine responses in human babies (Lynn, Tumes *et al*, *Cell Host Microbe*, 2018).

DUSP10 constrains innate IL-33-mediated cytokine production in ST2^{hi}_ memory-type pathogenic Th2 cells Innate lymphoid cells (ILC) can produce cytokines in direct response to signals from tissue damage and infection. In contrast, adaptive T cells need to recognise a specific antigen to allow effector function and cytokine production. We were involved in a study that identified the molecule responsible for the difference in function between adaptive T cells and ILC. DUSP10 is expressed in adaptive lymphocytes and stops them from behaving like ILC (Yamamoto *et al*, *Nature Communications*, 2018).

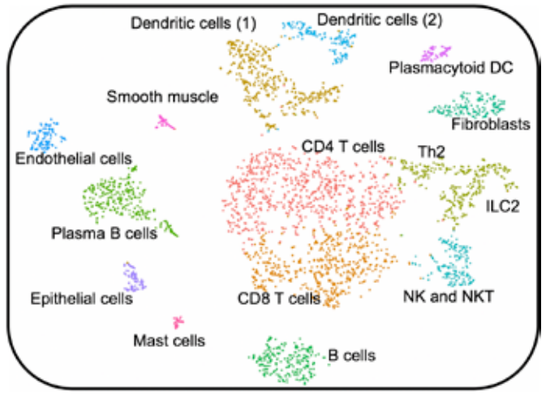
10 Year Highlights

Our laboratory was established in May 2018 and we are very proud to be members of this vibrant Adelaide medical research institute. Highlights from our laboratory members over the last 10 years include:

Epigenetic regulation of T cell development and function
We published a landmark paper in 2013 showing that differentiation and functional plasticity of T cells is dependent on the epigenetic regulator Ezh2 (Tumes *et al*, *Immunity*, 2013). This work used modern technologies such as chromatin immunoprecipitation followed by next generation sequencing (ChIP-Seq) to provide a global view of gene regulation in T cells. We are now using this information to determine how T cell differentiation and plasticity is regulated and to define new ways to control T cell function in diseases such as allergy and cancer.

Development of a novel anti-allergy therapeutic antibody
We have been actively involved in the pre-clinical development of a therapeutic antibody generated by the pharmaceutical company CSL Limited. We have established multiple allergic disease models to explore the therapeutic use of the antibody, and we are proud of the part we are playing in advancing the development of this therapeutic antibody toward the clinic.

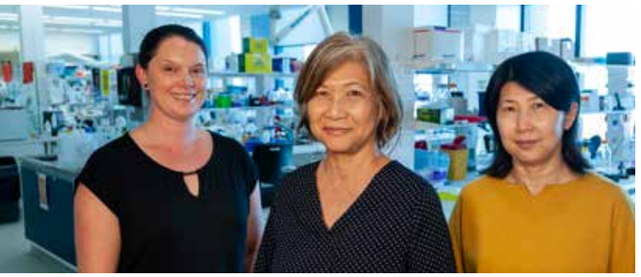
Identification of novel regulators of IgE-dependent mast cell activation
We demonstrated that topical application of vitamin D3 negatively regulates mast cell-mediated cutaneous anaphylaxis and inflammation (Yip and Kolesnikoff *et al*, *JACI*, 2014) and discovered that the ubiquitin ligase Nedd4-2 restrains IgE-induced mast cell activation and associated skin inflammation (Yip *et al*, *Nat Comms*, 2016).



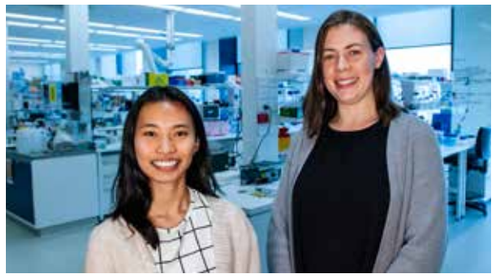
Single cell RNA-Sequencing of 2,300 cells from human airway tissue from three chronic rhinosinusitis patients defines cell types and gene expression profiles in human airway disease. Single cell RNA-Sequencing was done in the Centre for Cancer Biology Genomics Facility and quality control and cell clustering was done in our lab using Seurat.

Outcomes for the Community

Our research has the potential to redefine our understanding of human allergic disease. Detailed analysis of the immunological pathways that drive disease in individual patients will allow us to prescribe targeted treatments for the specific types of inflammation occurring in each person.



Leila Belle, Yeesim Khew-Goodall, Xiaochun Li
Absent: Ana Lonic



Winona Onglao, Freya Gehling

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 death is metastasis.

The 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 and how its dysregulation impacts on cancer progression.

The role of mir-200 in neuroblastoma (collaboration with 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. We are currently investigating their potential as therapeutic targets for neuroblastoma.

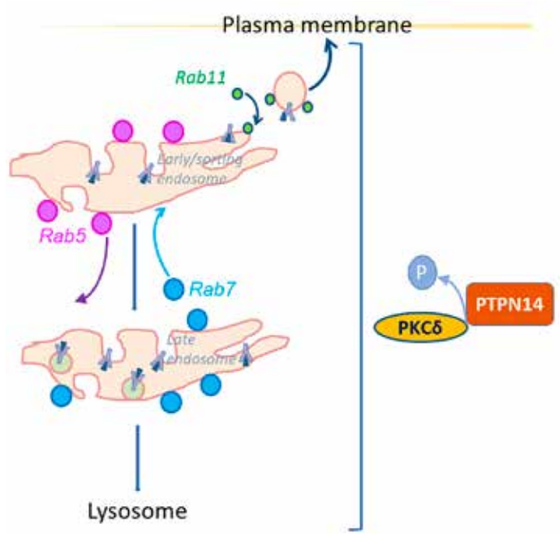
Key discoveries 2018

We have identified biomarkers for stratifying triple negative breast cancer and a potential therapeutic target for treating this cohort of patients, who likely have cancers that are more aggressive and harder to treat. We have also identified novel drivers of metastasis in neuroblastoma.

10 Year Highlights

Over the last ten years, the Cell Signalling Laboratory has discovered new signalling pathways that impact on cancer progression, particularly metastasis, which is the main cause of death for patients with solid cancers. In this time, we have pursued two lines of investigation that stem from our initial discovery that the tyrosine phosphatase PTPN14 can trigger epithelial-mesenchymal transition (EMT) through induction of TGFβ (Wyatt *et al*, *J Cell Biol*, 2007).

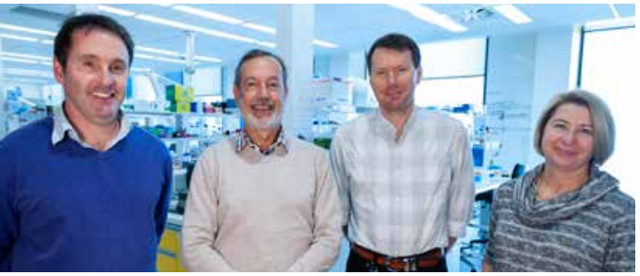
- Using this EMT model initially, and subsequently using breast cancer models of EMT, we (together with the Goodall Lab) discovered that the miR-200 family of microRNAs act as custodians of the epithelial phenotype in 2008 (Gregory *et al*, *Nat Cell Biol*, 2008), which led to a flurry of exciting new discoveries in the last 10 years, including its role in limiting cancer metastasis (Gregory *et al*, *Mol Biol Cell*, 2011; Paterson *et al*, *Neoplasia*, 2013; Lim *et al*, *J Cell Sci*, 2013; Li *et al*, *Oncogene*, 2014; Bracken *et al*, *EMBO J*, 2014).
- We identified novel functions for PTPN14 — a phosphatase that is mutated in multiple cancers but had no known function — which included its role in controlling how proteins are delivered to the cell's surface or exported out of the cell with consequences for breast cancer metastasis (Belle *et al*, *Sci Signalling*, 2015) and rheumatoid arthritis (Bottini *et al*, *Ann Rheum Dis*, 2019). These discoveries led to new hypotheses on how mutations of PTPN14 in cancers can lead to cancer progression.



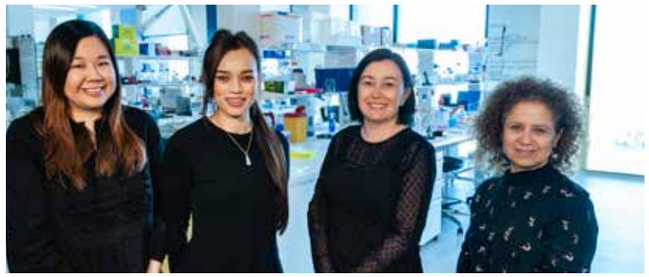
PTPN14 and its substrate PKCδ regulate the balance between degradation and recycling of receptor tyrosine kinases

Outcomes for the Community

Solid tumours constitute the majority of human cancers and 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 have identified novel pathways contributing to the aggressiveness of some triple negative breast cancers and novel pathways that contribute to metastasis in neuroblastoma, will increase our understanding of these diseases and open up avenues for new therapeutics to be developed.



Tim Hercus, Angel Lopez, Denis Tvorogov, Anna Sapa
Absent: Frank Stomski, Cameron Bastow



Winnie Kan, Natasha Hoang, Emma Barry, Mara Dottore

Cytokine Receptor Laboratory

Professor Angel Lopez AO MBBS PhD FRCPA FAA FAHMS
Clinical Affiliate Dr David Ross MBBS PhD FRACP FRCPA

Cytokines are protein hormones that regulate blood cell production and function, immune responses and inflammatory processes. Our laboratory is focussed on the βc family of cytokines that includes GM-CSF, IL-3 and IL-5. Our research seeks to determine how these cytokines engage receptors on the cell surface, in order to decipher the mechanisms underlying receptor signalling.

We will use this knowledge to develop new drugs for use in leukaemia and allergic diseases where abnormal expression and signalling by βc cytokine receptors play a major role in cancer and inflammation.

In collaboration with Professor Michael Parker (Bio21), we have now determined the 3D structure of human IL-3 bound to its receptor complex that reveals a new mechanism of assembly. This provides a molecular explanation for cytokine receptor pleiotropy (or multiplicity of functions) and a road map to select those cytokine functions that are desirable over those involved in disease.

Key discoveries 2018

In collaboration with Professor Michael Parker's group (Bio21), we solved the structure of human IL-3 bound to its receptor and identified an unexpected role for the IL3Rα N-terminal domain in dynamically regulating IL-3 signalling (Broughton *et al*, *Nature Communications*, 2018). Since several cytokine receptors share a mobile N terminal domain-like structure, this is likely to exemplify a general mechanism of signalling used by the cytokine receptor family. In parallel experiments in collaboration with Professor Andrew Perkins and colleagues (Monash University) we found that EPO does not seem to promote interactions between βc and the EPO receptor (Cheung Tung Shing *et al*, *Scientific Reports*, 2018). A comprehensive picture is emerging on the dynamics of receptor assembly and signalling that is amenable to external intervention (Hercus *et al*, *Cold Spring Harb Persp*, 2018).

In collaboration with Professor Michael Parker's group (Bio21), we solved the structure of human GM-CSF bound to an autoimmune antibody and identified a steric clash with the GM-CSF receptor as the mechanism of action for this blocking antibody (Dhagat *et al*, *MAbs*, 2018). The utility of monoclonal antibodies against cytokine receptors in cancer therapy was demonstrated in collaborative work with Prof Jeff Leyton's group (University of Sherbrooke) in which conjugation of our anti-IL-5 receptor antibody A15 with different toxins led to anti-bladder cancer effects.

In collaboration with Professor Jeff Babon (WEHI) and Dr Daniel Thomas (Stanford University) we have uncovered the molecular mechanism of Ruxolitinib withdrawal syndrome. Additionally, we have proposed Type II JAK2 inhibitors as a way to significantly improve therapy for patients with myeloproliferative diseases. This approach may not only lead to symptomatic improvements over Ruxolitinib but also reduce the burden of disease by targeting mutant cells (Tvorogov *et al*, *Science Advances*, 2018).

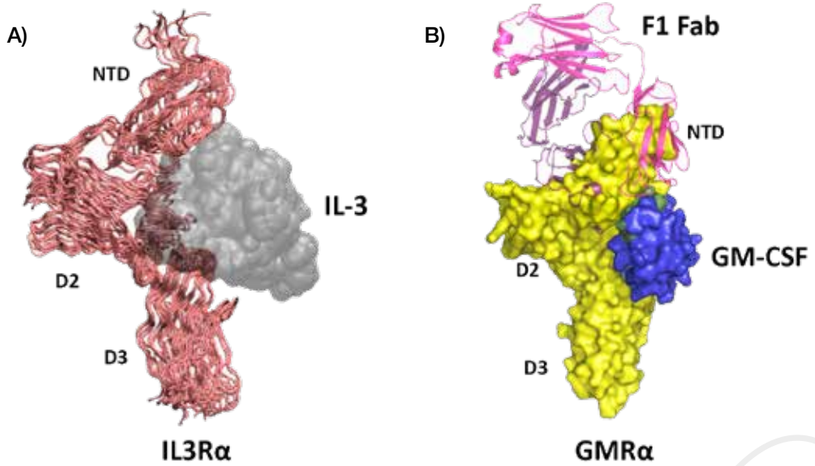
10 Year Highlights

Over the last ten years our laboratory made significant progress in three major areas of blood cell physiology:

Defined the 3D structure and the function of blood cell receptors for the βc family of growth factors/cytokines In collaboration with Professor Michael Parker (Bio21) we solved several atomic structures of the βc receptors which revealed how these receptors normally assemble on the cell surface and signal cellular functions (Hercus *et al*, *Blood*, 2009; Lopez *et al*, *IUBMB Life*, 2010; Broughton *et al*, *Immunol Reviews*, 2012; Hercus *et al*, *Cytokine*, 2014; Broughton *et al*, *Structure*, 2016; Hercus *et al*, *CSH Perspectives*, 2018; Paquette *et al*, *Bioconjugate Chemistry*, 2018).

Identified key abnormal signalling events in cells from leukaemic patients These insights suggest new avenues for clinical intervention in some patients with leukaemia (Powell *et al*, *Blood*, 2009; Sandow *et al*, *Cell Death and Diff*, 2012; Thomas *et al*, *Blood*, 2013; Thomas *et al*, *PLoS Bio*, 2013; Paquette *et al*, *OncoImm*, 2017; Cildir *et al*, *The Journal of Exp Med*, 2017; Cheung Tung Shing *et al*, *Scientific Reports*, 2018; Tvorogov *et al*, *Science Advances*, 2018).

Developed new potential antibody-based therapies for the treatment of leukaemic patients and of patients with chronic allergic conditions This is a fruitful area of collaboration with CSL Limited and with other international groups (Jin *et al*, *Cell Stem Cell*, 2009; Hiwase *et al*, *Leukemia*, 2010; Wang *et al*, *Proc Natl Acad Sci USA*, 2013; Broughton *et al*, *Cell Reports*, 2014; Nievergall *et al*, *Blood*, 2014; Busfield *et al*, *Leukaemia*, 2014; He *et al*, *Leukemia & Lymphoma*, 2015; Panousis *et al*, *MAbs*, 2016; Gargett *et al*, *Clinical & Translational Immunology*, 2016; Powell *et al*, *Blood*, 2017; Broughton *et al*, *Nature Communications*, 2018).

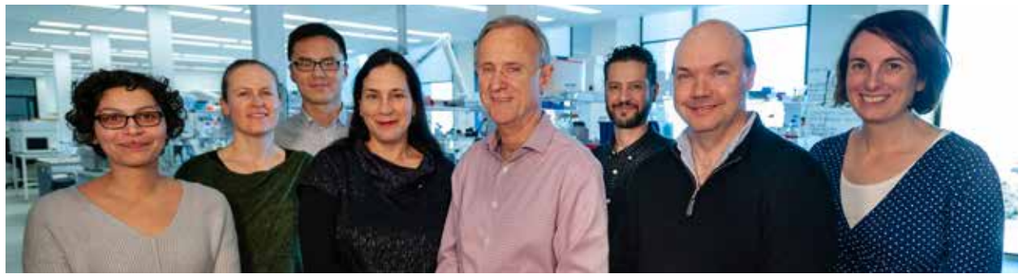


A) Crystal structure of the IL-3:IL3Rα complex showing molecular dynamics snapshots of IL3Rα (salmon) and IL-3 (grey).

B) Crystal structure of a human autoantibody F1 (purple/pink) bound to human GM-CSF (blue) and superimposed on the crystal structure of GM-CSF bound to the GM-CSF receptor alpha subunit (GMRα, yellow).

Outcomes for the **Community**

We are studying the fundamental mechanisms behind how growth factors work in patients suffering from leukaemia and other blood cancers or from allergic conditions in order to understand what goes wrong in these diseases with the long-term aim of developing more effective therapies and with less side-effects.



Mélodie Migault, Kate Dredge, Dawei Liu, Rosemary Sladic, Greg Goodall, John Toubia, Andrew Bert, Emily Hackett-Jones
Absent: Pannapa Pinweha

Gene Regulation Section

Professor Greg Goodall PhD FAA FAHMS

The most prevalent cancers, such as lung, breast, prostate and colorectal cancers, arise from epithelial cells, which are the cells that line the inner surfaces of the alveoli, ducts or lumen of these tissues. These cancers become dangerous if they progress to an invasive form that can spread to other tissues. Epithelial-derived cancers can switch to an invasive form by undergoing the process of epithelial to mesenchymal transition (EMT).

The EMT normally occurs only during early development in the embryo, and in wound healing, but sometimes cancers can initiate the process, leading to tissue invasion and metastasis. We and other researchers in recent years have been identifying the molecular control mechanisms that normally prevent this conversion to the invasive type, and we identified several years ago a molecular regulator, a microRNA called miR-200, that has an important role in preventing this transition. In our recent work we have been investigating how the microRNAs prevent cancers from transitioning to the invasive form, leading us to discover that they participate in regulatory networks that have broad effects on the properties of cells. The identification of these networks, and the individual components within the networks, is revealing new potential approaches for the design of treatment strategies to reduce or block cancer metastasis.

Key discoveries 2018

miR-200/375 control epithelial plasticity-associated alternative splicing by repressing the RNA-binding protein Quaking Since our discovery that miR-200 is a major regulator of EMT, we have been mapping the pathways through which it acts. We had found that miR-200 acts on the regulatory network that controls cell shape, and the ability of cells to migrate. In recent work we have found that one of its important targets is a regulator of alternative splicing, and that this expands the ways in which the miR-200 influences the actin cytoskeleton. We found that miR-200 exerts a widespread influence on alternative splicing during EMT, through its strong regulation of the splicing factor Quaking (QKI) (Pillman *et al*, *EMBO J*, 2018).

Combinatorial targeting by microRNAs coordinates post-transcriptional control of EMT In collaboration with Dr Cameron Bracken (Gene Regulation Networks Group) and Drs Joe Cursons and Melissa Davis and colleagues at the Walter and Eliza Hall Institute of Medical Research we have continued to explore the concept that microRNAs act to a large extent as network regulators of cellular processes. We propose that co-expressed miRNAs can jointly target multiple genes in a common pathway and thereby enhance their common function (Cursons *et al*, *Cell Systems*, 2018).

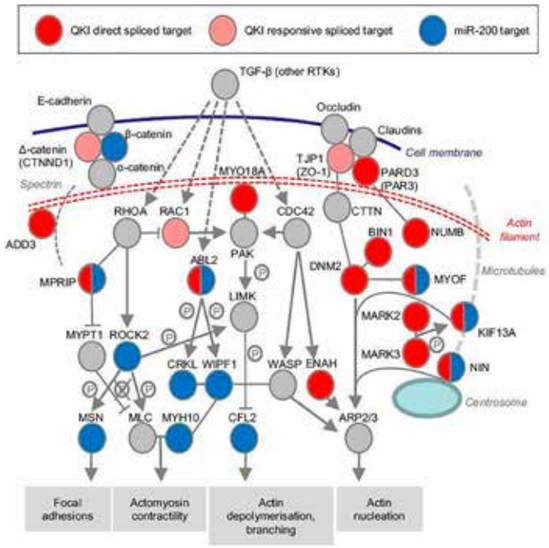
Clinical utility of a STAT3-Regulated miRNA-200 family signature with prognostic potential in early gastric cancer The molecular events that promote gastric cancer initiation are ill-defined. In collaboration with Brendan Jenkins, Centre for Innate Immunity and Infectious Diseases, Hudson Institute of Medical Research, we have identified a gene signature that is regulated by the miR-200 family of microRNAs and that integrates multiple key current indicators of early-stage gastric cancer (EGC), namely tumour invasion depth, differentiation, histology, and stage (Yu *et al*, *Clinical Cancer Research*, 2018).

10 Year Highlights

Over the last ten years we have pioneered major advances in RNA biology and its impact in cancer as demonstrated by:

- Our discovery of the complex involvement of the RNA-binding protein Quaking in multiple aspects of EMT, regulating both circular RNA production (Conn *et al*, *Cell* 2015, PMID: 25768908) and conventional alternative splicing (Pillman *et al*, *EMBO J,* 2018, PMID: 29871889).
- Our demonstration that miR-200 is downregulated at the invasive front of colorectal cancers with degraded basement membrane, providing evidence in human cancers that EMT is involved in cancer progression (Paterson *et al*, *Neoplasia*, 2013, PMID: 23441132).
- Our survey of experimental strategies for microRNA target identification, which has served as a guide for many researchers (Thomsone *et al*, *Nucleic Acids Res*, 2011, PMID 21652644).

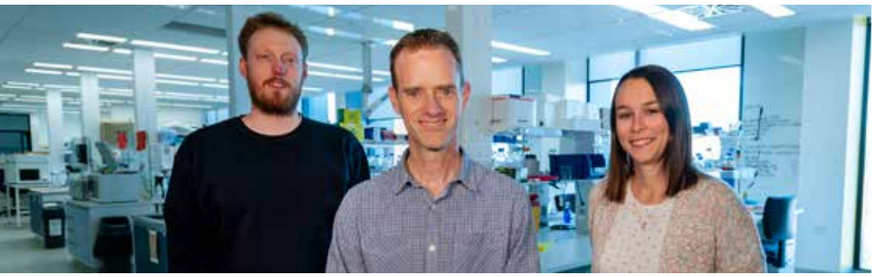
Each of these was designated 'Highly Cited Paper' by *Web of Science* (Thomson Reuters), meaning each received enough citations to place it in the top 1% of the academic field based on the publication year.



Schematic of actin cytoskeletal pathway adapted from Bracken et al (2014) with miR-200 direct targets highlighted in blue, QKI direct targets in red and QKI-responsive targets in pink. Major outputs on actin dynamics are indicated.

Outcomes for the Community

We have found further molecular events that are involved in progression of cancers to metastasis. These pathways may eventually be targeted by drugs to reduce metastasis in patients. In 2018 our publications received 1,342 citations.



Daniel Neumann, Philip Gregory, Caroline Philips

Gene Regulation in Cancer Group

Dr Philip Gregory PhD

Cancers that derive from epithelia of organs, such as the breast and prostate, account for over 80% of cancers. While confined, these tumours are generally amenable to localised or systemic treatments, however their progression to metastases complicates treatment options and accounts for >90% of cancer related deaths. Epithelial-mesenchymal transition (EMT) and its reverse process MET are major facilitators of cancer cell invasion, tumour metastasis and therapy resistance.

Our laboratory investigates the molecular mechanisms controlling tumour cell plasticity in breast and prostate cancer, with a specific focus on the role of microRNAs and alternative splicing in this process. In recent work, we have been defining the landscape of RNA splicing changes that occur as cancer cells undergo EMT. Although most human genes undergo alternative splicing to produce multiple protein isoforms, the functions of the vast majority of these variant proteins are unknown. A better understanding of these isoform changes will allow more rational development of therapeutics to treat metastatic disease. We are using cutting edge cross-linking immunoprecipitation (CLIP) and sequencing techniques to identify splicing pathways and their influence on tumour progression. With this information we are utilising *in vitro* and *in vivo* models of breast and prostate cancer, in collaboration with Dr Luke Selth (University of Adelaide) and Dr Brett Hollier (Queensland University of Technology) to identify the function of spliced variants in cancer cell invasion and metastasis.

Key discoveries 2018

The splicing factor Quaking is a major driver of cancer cell plasticity

In collaboration with Professor Greg Goodall and the ACRF Cancer Genomics Facility, we have identified an RNA binding protein called Quaking which is strongly induced during EMT. We found that Quaking plays a major role in regulating cancer cell plasticity and invasion, but intriguingly does so without influencing gene expression. Instead, using a combination of Quaking-CLIP and high-depth sequencing, we showed that Quaking binds to hundreds of target mRNAs and regulates a global switch in alternative splicing. Furthermore, we found that the expression of Quaking is strongly controlled by two microRNAs (miR-200c and miR-375). Our findings demonstrate the existence of a miR-200c/miR-375/Quaking axis that impacts cancer-associated epithelial cell plasticity through widespread control of alternative splicing.

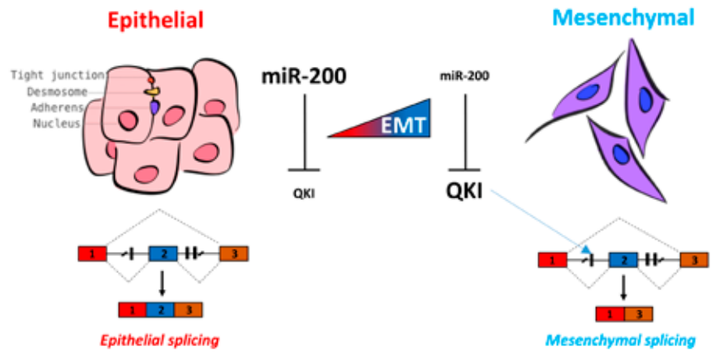
A key microRNA influencing metastasis of triple-negative breast cancer

With funding from the National Breast Cancer Foundation, we used an integrated approach to identify miRNAs that influence breast cancer metastasis as well as indicate patient outcomes. Through this we identified miR-342 which we found is: (1) strongly downregulated in mouse and human triple-negative breast cancer cell lines that are prone to metastasise, (2) sufficient to repress breast cancer metastasis in immune competent and xenograft mouse models, and (3) an independent prognostic marker of patient outcome in large patient cohorts. Using genome-wide Argonaute-CLIP analysis we identified 120 direct target genes of miR-342, including a high representation of E2F1-driven and actin dynamics pathways. We propose these pathways may represent new targets for treatment of metastatic triple-negative breast cancer, and are actively investigating these pathways in metastatic mouse models.

10 Year Highlights

A major highlight in the last 10 years was our discovery of the first microRNAs that regulate epithelial-mesenchymal transition, in collaboration with Professor Greg Goodall and Associate Professor Yeesim Khew-Goodall (Gregory *et al*, *Nature Cell Biology*, 2008). At this time, the notion of EMT contributing to cancer progression was not widely considered, however our mechanistic insights have fuelled research in this area.

- This is evidenced by our *Nature Cell Biology* paper accruing the 14th most citations of any cancer paper in three years (*Nature Med* 17(3): 280, 2011), and now currently being the 10th most cited of >73,000 miRNA papers since 2008 (>3000 citations).
- Following this landmark discovery, we identified a critical feedback loop involving miR-200 and ZEB transcription factors, and later its control by TGFbeta signalling: the major physiological effector of EMT in cancer. The papers reporting these findings (Bracken, Gregory, Kolesnikoff *et al*, *Cancer Research*, 2008 and Gregory, Bracken *et al*, *Molecular Biology of the Cell*, 2011) are among the highest cited papers in the field (>1400 citations). These findings have had a direct impact on many disciplines where the miR-200-ZEB loop has been shown to play critical roles in induced pluripotent stem cells, checkpoint inhibitor therapy, and development biology.
- A recent highlight has been identification of the RNA binding protein Quaking as the major regulator of mesenchymal alternative splicing (Pillman, Goodall, Gregory, *EMBO J*, 2018) following our initial seminal discovery that it could induce circular RNA formation (Conn *et al*, *Cell* 2015). Prior to these findings, the concept of regulated circular RNA production and the role of Quaking as a splicing factor were not widely recognised. These reports have been taken up rapidly by the research community (>500 citations in three years) and have accelerated research into the importance of splicing during cancer progression.



A molecular switch involving miR-200 and Quaking (QKI) regulates widespread alternative splicing changes during epithelial-mesenchymal transition (Credit: PhD student Laura Sourdin for cell designs)

Outcomes for the Community

Tumour metastasis is the major cause of cancer related death in solid tumours such as the breast and prostate. Our laboratory has made important strides forward in identifying key alternative splicing pathways and microRNAs that control cancer cell plasticity and invasion. Our ultimate aim is to uncover new avenues that may be targeted to provide more effective therapies and better outcome for breast and prostate cancer patients.

Klay Saunders, Cameron Bracken, Ayla Orang, Sunil Sapotka
Absent: Laura Sourdin

Gene Regulation Networks Group

Dr Cameron Bracken PhD

MicroRNAs are important regulators of gene expression and play key roles in virtually all biological processes, both in the normal functioning of cells and in pathologies such as cancer. One of the reasons they are so important is that any one microRNA can regulate the expression of dozens, or even hundreds of target genes. Our research seeks to understand how microRNAs select which genes to target and to establish how these genes interact with each other during the growth and spread of cancer.

More specifically, our research investigates several aspects of microRNAs which are poorly understood, but which we believe are central to how microRNAs work. These 'new' areas include studying:

1) how different microRNAs functionally co-operate to control cancer progression

2) the capacity of microRNAs to interact with DNA to directly regulate genes

3) the importance of naturally occurring variations in microRNA sequence

Achieving a better understanding of how microRNAs work is not just important to increase our knowledge of how cancers develop, but microRNAs themselves may be useful as future therapies, directly administering them to patients to target genes whose expression has gone awry in disease. The research we undertake is ultimately geared toward this outcome.

Key discoveries 2018

MicroRNAs co-operate to more effectively and specifically regulate gene regulatory networks
In collaboration with researchers at the Walter and Eliza Hall Institute (Melbourne), we have discovered that microRNAs which have co-evolved together, co-operate to achieve a greater degree of control of desired genes, whilst minimising unwanted 'off-target' effects on bystander genes. This is of direct relevance to future therapy, where our research suggests dramatically lower levels of complementary microRNAs could be administered (compared to the current doses of single microRNAs), which should be both easier to achieve in patients and safer than existing treatment regimens. We have established this looking at a process known as Epithelial-Mesenchymal Transition (EMT), a process with which we have an extensive track record of discovery, which is of particular interest as it underlies both the spread of cancer (metastasis) and resistance to therapy (chemoresistance) (Cursons *et al*, *Cell Systems*).

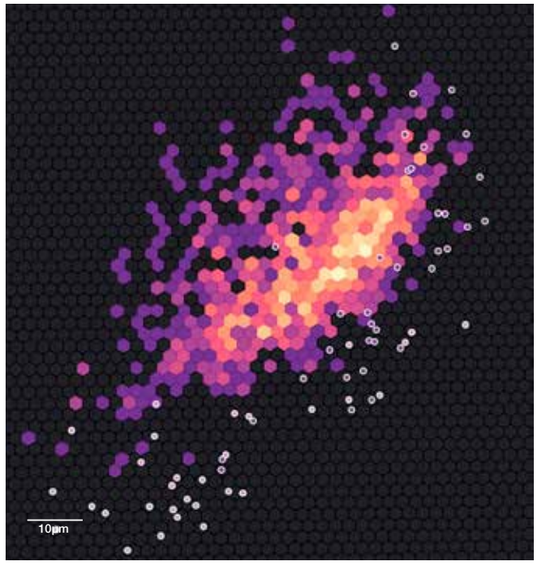
The importance of microRNA length variation
Building on a previous publication from our laboratory (Yu *et al*, *Nucleic Acids Research*, 2017), we continue to investigate the phenomenon of microRNA length variation in cells. Typically this has been dismissed by researchers, however we present evidence that length variation can dramatically alter the function of microRNAs. Work here demonstrates that due to methodological issues, length variation has been widely under-estimated in the field which questions much of the published literature for microRNAs where length variability is especially prominent (Nejad *et al*, *RNA*; Pillman *et al*, RNA).

10 Year Highlights

A major highlight in the last 10 years was our discovery of the first microRNAs that regulate epithelial-mesenchymal transition, in collaboration with Professor Greg Goodall and Associate Professor Yeesim Khew-Goodall (Gregory *et al*, *Nature Cell Biology*, 2008). At this time, the notion of EMT contributing to cancer progression was not widely considered, however our mechanistic insights have fuelled research in this area. Over the last 10 years we molecularly characterised the role of microRNA in normal cell regulation and cancer progression.

Establishing how the miR-200 family of microRNAs control Epithelial-Mesenchymal Transition (EMT) EMT is an important process that underlies the spread of cancer and the resistance of cancer cells to therapy. Work over multiple papers establishes how a critically important family of microRNAs (miR-200) control EMT via a regulatory feedback loop involving a family of genes called the ZEB transcription factors. Not only has this informed our understanding of EMT, but this has also served as a paradigm to understand how microRNAs control genes more widely.

Identifying microRNA target genes on a genome-wide scale As microRNAs regulate hundreds of genes, in order to understand how they work one must identify the genes that they target. Utilising new sequencing technologies, we were the first to identify direct targets of the miR-200 family of microRNAs on a genome-wide scale, then use this information to establish how these microRNAs control the motility of cancer cells (Bracken *et al*, *EMBO-J*, 2014).

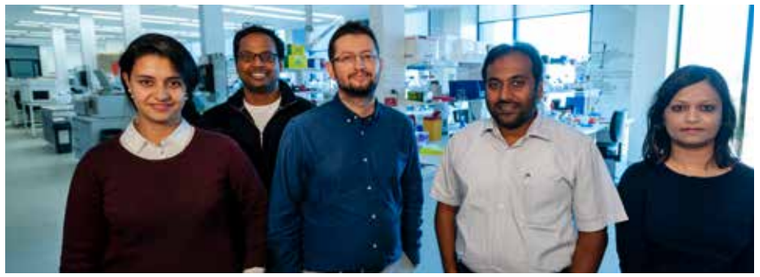


Breast cancer patients (hexagons) and breast cancer cell lines (circles) are represented on an axis of epithelial (y axis) and mesenchymal (x axis) gene expression. This shows the variability in the E/M status between patients and cells which is largely regulated by the miR-200 family of microRNAs.
The figure is adapted from the front cover of the *Cell* family journal, *Cell Systems*, where this work was published.

Outcomes for the Community

MicroRNAs offer great potential as future therapies. Our research suggests that by combining select microRNAs at low concentrations, future therapies may be both more effective and safer than current approaches that require very high doses of single microRNAs. Continuing work aims to identify the best possible microRNA combinations, then to test them in pre-clinical cancer models to establish their effectiveness.

Vinay Tergaonkar



Zahra Esmaeili, Raja Ganesan, Gokhan Cildir, Nirmal Robinson, Shanzana Khan

Inflammation and Human Ailments Laboratory

IMCB Visiting Professor

Professor Vinay Tergaonkar PhD
Dr Nirmal Robinson PhD

Inflammation is a vital immune response to infection and injury, but uncontrolled excessive inflammation can be detrimental. Also, chronic inflammation is an underlying cause of human diseases including allergies, diabetes, obesity and cancer.

In our lab, we investigate the mechanisms that regulate inflammation associated with human diseases with an overall goal of finding novel therapeutic targets. We have found that inflammatory outcomes in immune cells are modulated by metabolism and are epigenetically regulated.

Epigenetic regulation of 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.

Metabolic regulation of Inflammation and Immunity Immune cells perform various activities such as engulfing the pathogen (phagocytosis), producing anti-microbials and other proteins to attract other immune cells (cytokines and chemokines), disintegrating the pathogen, migrating to sites of injury, differentiation and triggering immune responses in other cells etc. These activities greatly rely on metabolism as they consume a lot of energy. Therefore, immune cells rapidly adapt their metabolic pathways to meet the demand. Using metabolomics and transcriptomics, we have unravelled the metabolic pathways that are alternatively regulated in macrophages during infection. We have also discovered the role of proteins such as Sirtuins, AMPK and mTOR which sense changes in metabolism in regulating cell-autonomous defence against bacterial pathogens. Moreover, we have also deciphered the role of metabolic hormones in modulating immune responses.

Key discoveries 2018

Xu X, Li Y, Bharath SR, Ozturk MB, Bowler MW, Loo BZL, Tergaonkar V*, Song H*. Structural basis for reactivating the mutant TERT promoter by cooperative binding of p52 and ETS1. *Nature Communications*, 9 (1): 3183, 2018. *Equal senior author
This publication describes the structure of a ternary p52/ETS1-mutantTERT promoter complex in cancer cells.

Tiku V, Kew C, Mehrotra P, Ganesan R, Robinson N*, Antebi A*. Fibrillarin is an evolutionarily conserved central regulator of pathogen resistance. *Nature Communications*, 9 (1): 3607, 2018. *Equal senior author
This work establishes the role of ribosomal stress and nucleolus in innate immune defence against pathogens.

Tan CSH, Go KD, Bisteau X, Dai L, Yong CH, Prabhu N, Ozturk MB, Lim YT, Sreekumar L, Lengqvist J, Tergaonkar V, Kaldis P, Sobota RM, Nordlund P. Thermal proximity coaggregation for system-wide profiling of protein complex dynamics in cells. *Science*, 359 (6380): 1170-1177, 2018.
This work describes the application of thermal proximity coaggregation (TPCA) for high-throughput intracellular monitoring the dynamics of protein complexes.

10 Year Highlights

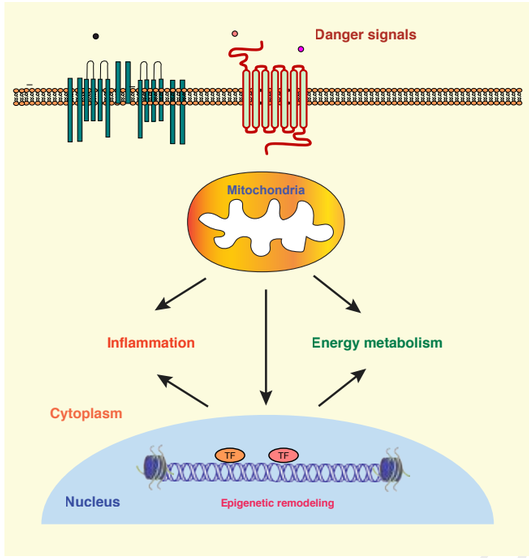
Over the past few years, since the Inflammation and Human Ailments Laboratory was established through the Department of State Development, South Australia Premier's Fellowship awarded to Professor Vinay Tergaonkar, we have made some seminal discoveries.

Transcriptional reactivation of telomerase reverse transcriptase (TERT) reconstitutes telomerase activity in the majority of human cancers leading to increased cell proliferation. We have made key discoveries in understanding the mechanism by which mutated TERT is activated in cancers (Khattar E *et al*, *Journal of Clinical Investigation*, 2016; Akincilar SC *et al*, *Cancer Discovery*, 2016; Li Y *et al*, *Proceedings of National Academy of Science USA*, 2016).

Mast cells play an important role in inflammation associated with allergies (Cildir *et al*, *Journal of Experimental Medicine*, 2017), and for the first time we have mapped the chromatin landscape of mast cells during allergic activation.

We have discovered that during bacterial infection, cells shrink their nucleolus to enhance their ability to defend against invading pathogens and this can be modulated by a nucleolar protein Fibrillarin (Tiku V *et al*, *Nature Communications*, 2018).

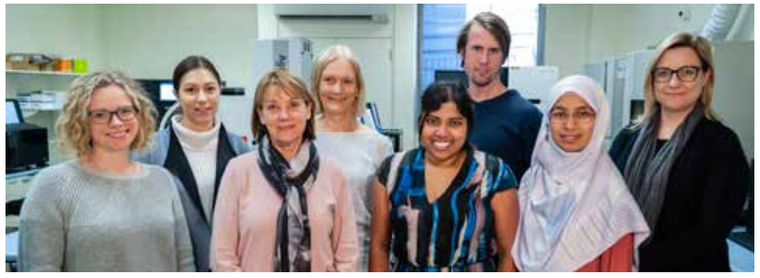
Our recent work has also demonstrated the role of metabolism and proteins linked to metabolism in modulating immune defence (Ganesan R *et al*, *PLoS Pathogens*, 2017). More recently we have reported that leptin-signalling is detrimental for the macrophage-defence against Gram-negative pathogens (Fischer J *et al*, *Proceedings of National Academy of Science USA*, 2019).



Integration of metabolic and inflammatory signals modulate epigenetic responses

Outcomes for the Community

Our findings not only help us better understand the process of inflammation, but also pave the way for therapeutic breakthroughs in treating inflammation associated with the majority of illnesses.



Bronte Jamison, Alexandra Yeoman, Susan Branford, Carol Wadham, Naranie Shanmuganathan, Daniel Thomson, Nur Hezrin Shahrin, Jasmina Georgievski

Leukaemia Unit, Genetics and Molecular Pathology

Associate Professor Susan Branford PhD FFSc (RCPA)

Our research is focussed on the development and clinical evaluation of novel molecular approaches to monitor treatment response and to understand and predict drug resistance for patients with chronic myeloid leukaemia. The disease is invariably fatal within a few years if untreated. However, targeting the primary genetic cause of the disease using daily drug therapy has changed this once fatal disease into one where most patients can now achieve long-term survival.

This form of leukaemia is caused by a genetic defect where two genes break in half and fuse together to form a new, cancer causing gene. The dramatic change in patient outcome due to drug therapy that targets the gene fusion has been one of the greatest triumphs of cancer research. A minority of patients may even be able to stop taking the drug after a number of years and remain in treatment-free remission.

Despite the significant advances in treatment response for patients with CML, about 30% fail therapy. Newer, more potent drugs are continually being developed to treat or limit drug resistance. However, these drugs are associated with higher cardiovascular toxicity and have not shown a survival advantage. 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 could benefit from more potent drugs despite the increased risk.

Key discoveries 2018

Cancer-associated mutations are present at diagnosis of chronic myeloid leukaemia and are associated with poor treatment outcome In 2018 we published our genomic study of patients with various treatment responses to therapy, which was the culmination of many years of research (Branford *et al*, *Blood*, 132: 948-961, 2018). It is believed that progression of chronic myeloid leukaemia from the chronic phase, that is now very well managed, to a rapidly fatal acute leukaemia is due to the accumulation of mutations in critical genes. We hypothesized that patients who had a poor response to treatment would already have additional mutations in cancer-associated genes at the time of their leukaemia diagnosis.

Long-term treatment-free remission of chronic myeloid leukaemia with falling levels of residual leukemic cells We are among the pioneers who conducted clinical trials to determine whether it is possible for some patients to successfully stop taking drug therapy without their leukaemia returning. The patients who enrolled into the trial had maintained undetectable levels of leukaemia for at least two years. We developed sensitive molecular tests to detect residual disease and to select patients for the trial of stopping therapy. About half of the patients who stopped drug therapy maintained treatment-free remission and the other half relapsed. Most of the relapses occurred within six months of stopping therapy. These patients recommenced therapy, while the other patients have maintained undetectable molecular leukaemia for many years without any therapy. This was a major advance and many clinical trials of drug cessation have followed globally. We have developed more sensitive molecular methods to detect residual leukaemia in the patients who stopped therapy (Ross *et al*, *Leukaemia*, 2018).

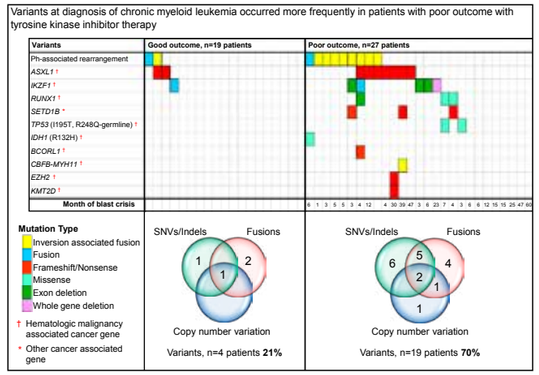
10 Year Highlights

Over the last ten years we developed new international methods to monitor patients with CML.

International reporting scale for *BCR-ABL1* Over the last ten years our laboratory, in collaboration with international researchers, has developed a process and desirable performance criteria that allows consistent interpretation of molecular response. This was achieved by measurement of *BCR-ABL1* levels on a common international reporting scale for patients across the world with chronic myeloid leukaemia (Branford *et al*, *Blood*, 2008; Muller *et al*, *Leukemia*, 2009; White *et al*, *Blood*, 2010; Cross *et al*, *Leukemia*, 2016). The approach is considered the gold standard and has been incorporated into international guidelines and recommendations for monitoring treatment response. Since 2013, the level of *BCR-ABL1* reduction reported on the international scale achieved at milestone timepoints during drug therapy has been used globally to define treatment failure and to guide treatment decisions.

Sensitive detection of *BCR-ABL1* mutations Our work and that of many international researchers has demonstrated that the main mechanism of resistance to targeted drug therapy for patients with chronic myeloid leukaemia is mutation acquired in the *BCR-ABL1* gene. These mutations occur at the drug binding site and interfere with drug binding. We developed more sensitive methods and assessed clinical outcome based on the detection of very low-level mutants that were not detectable by standard methods. For the first time, we demonstrated that certain low level mutants can predict treatment response and guide therapy choices (Parker *et al*, *Journal of Clinical Oncology*, 2011; Parker *et al*, *Blood*, 2012 and 2016).

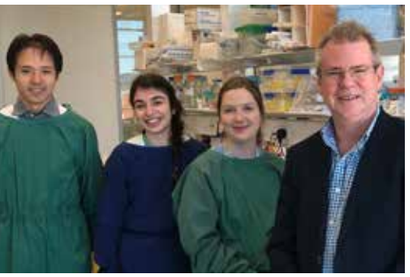
***BCR-ABL1* independent mechanisms of drug resistance** Despite decades of research, biomarkers are lacking to reliably predict treatment response at the time of diagnosis of chronic myeloid leukaemia and to assign appropriate therapy for all patients. Our use of next-generation sequencing coupled with critical bioinformatic analysis of the associated vast amount of generated genomic data has allowed us to identify additional, novel mechanisms of drug resistance (Roberts *et al*, *Bioinformatics*, 2013; Wang *et al*, *Bioinformatics*, 2016; Branford *et al*, *Blood*, 2018). This information should lead to improved treatment outcomes where the incorporation of both clinical and genomic biomarkers will more reliably predict outcome.



Summary of the type of mutations detected at diagnosis.
Massively parallel sequencing of ~20,000 genes was performed at diagnosis for patients with a subsequent good drug response compared to patients with treatment failure. Mutated cancer-associated genes were detected significantly more frequently in patients with subsequent treatment failure. Fusion genes and sequence rearrangements were detected, which provides guidance for the type of sequencing that will be required in future studies. Patients with additional mutations may benefit from more potent drugs or combination therapy to limit the risk of treatment failure.

Outcomes for the Community

Our molecular studies have given patients the opportunity to successfully stop drug therapy in some cases, thereby relieving the burden of long-term side-effects. Our new genomic studies provide the basis for future patient benefit by potentially identifying those at the time of diagnosis who are at the greatest risk of treatment failure. These patients may benefit from more potent drugs or drug combination therapy for better treatment outcome.



Jun Fukihara, Suzanne Maiolo, Jemma Savaglia, 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 FThor 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.

We have investigated a number of approaches to combat COPD-related inflammation, by aiming to improve the function of macrophages and thus the clearance of inflammatory material. New cancer-related projects in 2018 include the establishment of new models whereby human tumour samples are directly harvested to assess the response to novel anti-cancer therapies, particularly addressing the 14-3-3 protein pathway. The blood vessels in the lungs play a critical role in cancer development and respiratory function. Disease processes that narrow the blood vessels restrict flow and lead to heart failure and early death. We have developed gene and cell therapies to combat this process, as well as pulmonary fibrosis, another condition associated with an increased risk of lung cancer. Another arm of our studies seeks to improve the understanding and treatment of graft failure after lung transplantation.

Key discoveries 2018

Engineered cell therapy for pulmonary hypertension

We have further advanced our endothelial progenitor cell (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 and has now been published (Harper *et al*, *Respirology*, 2019).

New insights into lung inflammation

New discoveries concerning the inflammatory pathways involved in the response of lungs to smoke and lung transplant rejection may lead to new strategies in combating these problems.

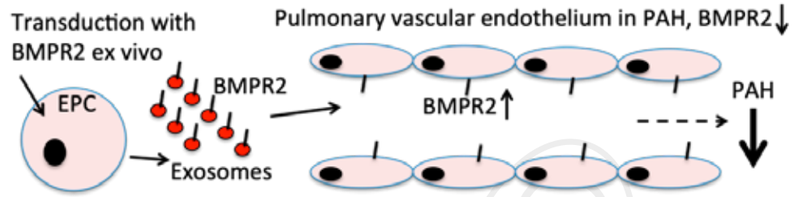
10 Year Highlights

Over the last 10 years the Lung Research Laboratory has explored:

Development of gene / cell therapy for Pulmonary Arterial Hypertension (PAH)
PAH is a fatal disease affecting the blood vessels in the lungs, causing them to narrow and exert a back-pressure effect on the heart, ultimately leading to death from cardiac and respiratory failure. Modern treatments have some benefits, but do not cure the disease. The disease is associated with mutations in a receptor called BMPR2. Over the course of several papers, and with the support of NHMRC funding, we showed that we could deliver the gene for BMPR2 to the lung blood vessels and in so doing achieve a therapeutic response in several pre-clinical animal models of PAH. This work has now culminated in the development of a cell-based therapy using gene-modified EPCs. With ongoing NHMRC support we are now refining the development of cell therapy to include novel nanowire technology to modify the EPCs (Reynolds *et al*, *Am J Physiol Lung Cell Mol Physiol*, 2007; Reynolds *et al*, *Eur Respir J*, 2012; Harper *et al*, *Respirology*, 2019).

Macrophage dysfunction and airways inflammation in Asthma and Chronic Obstructive Pulmonary Disease Our group was the first to identify that smokers and those with asthma have reduced function in airway macrophages, which are the cells that clear dying cells, bacteria and other debris from the airways. Reduced clearance of this material from the airways means it lingers around and causes ongoing inflammation and worsens the disease. We showed that treatments that improve macrophage function, including a macroliode antibiotic (Azithromycin) improved macrophage function and reduced airway inflammation in animal models and in patients with COPD and asthma. This work culminated in a national NHMRC funded collaborative, randomised placebo-controlled trial of Azithromycin for 48 weeks in poorly controlled asthma. The study showed a 40% reduction in asthma exacerbations with Azithromycin compared to the placebo (Hodge *et al*, *Am J Respir Crit Care Med*, 2008; Hodge *et al*, *Am J Respir Cell Mol Biol*, 2010; Gibson *et al*, *Lancet*, 2017).

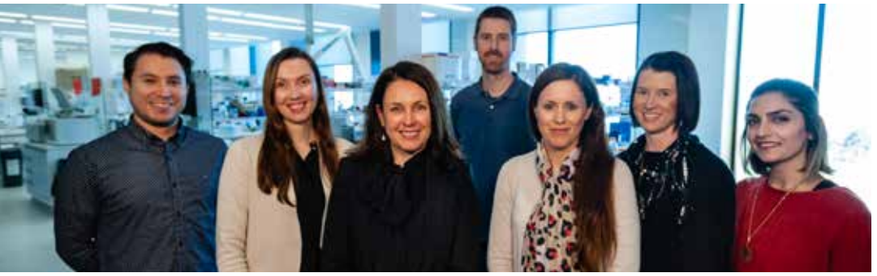
The role of inflammatory processes in lung transplant rejection Of all solid organ transplants, lung transplant outcomes are the poorest, due to chronic lung allograft dysfunction or Bronchiolitis Obliterans Syndrome (BOS). This is thought to be a form of chronic rejection which does not respond well to standard anti-rejection immune-suppressants. Our group has looked at the processes involved in this condition, using broncho-alveolar lavage and blood form lung transplant patients. In this we have identified a number of pro-inflammatory steroid–resistant mechanisms which contribute to the disease and may be useful targets for treatments (Hodge *et al*, *Respir Res*, 2015; Hodge *et al*, *Transplantation*, 2017; Hodge *et al*, *Clin Exp Immunol*, 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. In 2018 we have directly contributed to national guidelines on the management of pulmonary fibrosis.



Luis Arriola-Martinez, Anna Oszmiana, Natasha Harvey, Drew Sutton, Genevieve Secker, Kelly Betterman, Saba Montazaribarforoushi Absent: Jan Kazenwadel

Lymphatic Development Laboratory

Professor Natasha Harvey PhD

Lymphatic vessels are an integral component of our cardiovascular system. These specialised vessels regulate fluid homeostasis, absorb fats from the digestive tract and are an important highway for trafficking immune cells around our bodies. Abnormalities in the growth and development of lymphatic vessels underlie human disorders including lymphoedema, vascular malformations 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 order to gain entry to this vascular highway and spread to other parts of 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.

Key discoveries 2018

Understanding where the building blocks of lymphatic vessels come from during development

The origin of the cells that make up our lymphatic vessels has long been debated. While a substantial proportion of the cells that make up lymphatic vessels (lymphatic endothelial cells) arise from embryonic veins, recent studies have also found additional sources of lymphatic endothelial cells in different tissues. In collaboration with Mathias Francois at the Institute for Molecular Bioscience, Brisbane, we employed advanced imaging technology to 'map' where lymphatic endothelial cells come from during development. We found that in addition to veins, blood capillaries are a source of lymphatic endothelial cells in embryonic skin (Pichol-Thievend *et al*, *Development*, 2018). Our work suggests that a common mechanism of building new vessels from multiple sources might also be employed in pathological settings where lymphatic vessel growth is rapidly promoted.

Understanding how lymphatic vessel valves are built during development

We have a longstanding interest in understanding how the identity of the cells that make up our lymphatic vessels is programmed. We have identified a number of molecular switches called transcription factors that are important for turning genes on or off to control the identity of the cells that are the building blocks of our lymphatic vessels. Following our discovery that one of these switches, the transcription factor GATA2, is crucial for building lymphatic vessel valves (Kazenwadel *et al*, *J Clin Invest*, 2015), we have focussed on defining the 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 targets to which effective therapeutics able to modulate lymphatic vessel function and thereby treat lymphoedema could be designed.

Understanding the genetic and developmental basis of human lymphatic disease

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. Lipoedema, while sharing features with lymphoedema is a distinct, yet very poorly understood condition that is characterised by the accumulation of painful adipose tissue. In collaboration with Hamish Scott's research team at the Centre for Cancer Biology and our clinical partners at Royal Adelaide Hospital and Flinders Medical Centre, we are investigating the genetic basis of human primary lymphoedema syndromes and human lipedema. Ultimately, we aim to develop novel tools that can be employed to aid patient diagnosis, prognosis and treatment.

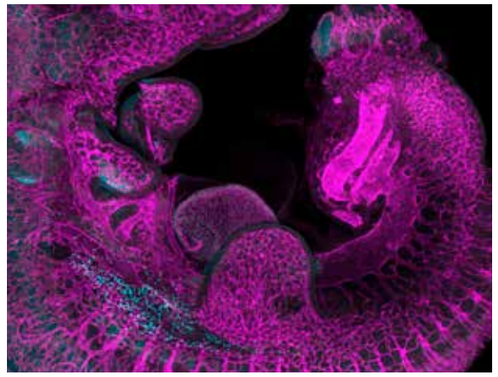
10 Year Highlights

Over the last ten years, we have substantially advanced our understanding of the genetic, cellular and molecular mechanisms that underpin the growth and maturation of lymphatic vessels during development. It has been incredibly exciting to apply this knowledge to defining the genetic and developmental basis of human lymphatic vascular diseases. This couldn't have been achieved without a tremendously talented research team. It has been a real pleasure to see our team grow both in number and expertise, to train talented undergraduate and postgraduate students and to build new collaborative partnerships with national and international scientists and clinicians. It has also been an immense personal privilege to become the mother of two amazing children during this time and together with my treasured colleague Claudine Bonder, to be the first CCB women promoted to Professor. Research highlights of the last ten years include:

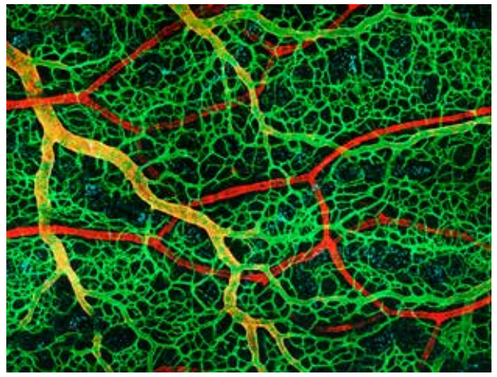
Our discovery, together with Professor Hamish Scott's team, that *GATA2* mutations cause the human primary lymphoedema syndrome, Emberger Syndrome (Kazenwadel *et al*, *Blood*, 2012).

Our discovery that *GATA2* is required to program the growth and development of lymphatic vessels and in particular, to build lymphatic vessel valves, explaining why mutations in *GATA2* cause Emberger syndrome (Kazenwadel *et al*, *J Clin Invest*, 2015).

Our identification of both a novel pool of progenitor cells (Pichol-Thievend *et al*, *Development*, 2018) and key directive signals (Gordon *et al*, *Development*, 2010; Betterman *et al*, *Am J Path*, 2012) important for building the lymphatic vasculature in different tissues during development.



Lymphatic vessel development in the mouse embryo
The first lymphatic vessels (cyan) develop in close association with blood vessels (magenta).

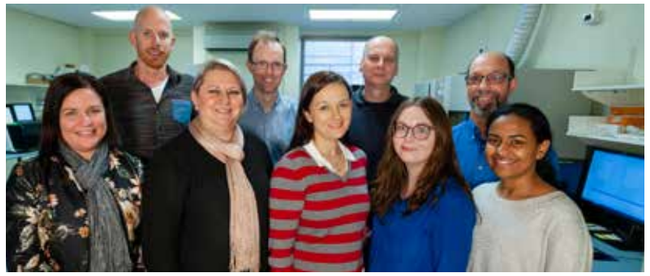


Vascular Highways: Blood vessels (capillaries: green, arteries: red, veins: yellow) and lymphatic vessels (cyan) in the skin.

Outcomes for the Community

Lymphatic vessels are of major importance to cancer patients. Cancer cells exploit lymphatic vessels as a route for metastasis to other parts of the body. Lymphatic vessel damage following cancer surgery results in lymphoedema, a disabling condition for which there are currently no effective, curative treatments. By understanding the signals that control the growth and development of lymphatic vessels, we aim 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 should provide novel therapeutics for the treatment of lymphoedema.

Saba Montazaribarforoushi, Jesse Cheah, Leila Eshraghi, Luis Arriola-Martinez, Hamish Scott, Matilda Jackson, Claire Homan, Thuong Ha



Anna Brown, Peer Arts, Julia Dobbins, Tristan Hardy, Milena Babic, Peter Brautigan, Tamika Burrowes, Chris Hahn, Parvathy Venugopal

Molecular Pathology Research Laboratory

Professor Hamish S Scott PhD FFSc (RCPA) FAHMS
Clinical Affiliates Dr Janice Fletcher PhD Dr Karin Kassahn PhD

The Molecular Pathology Research Laboratory focuses primarily on identifying genetic causes of blood cancer predisposition and progression, and perinatal deaths. There is a strong focus on translation of research findings promptly into the diagnostic and clinical setting, and we are uniquely positioned to do this with co-location of research, diagnostics and genomics facilities.

Genetics and pathologic mechanisms of blood cancer predisposition and progression
As an Australian and New Zealand referral centre for familial cases of haematopoietic malignancies (HM - leukaemias and lymphomas), our laboratory focuses on identifying known and novel genetic causes using the latest genomic/transcriptomic technologies. We have accrued samples from ~200 families with predisposition to HM, and continue to 'solve' the genetic cause through comprehensive bioinformatic and literature interrogation, and interactions with international collaborators and researchers. For select strong candidate genes/mutations, we have generated cell and animal models to show functional consequences of the mutations. Where appropriate, research findings have been translated to the clinical setting to benefit individuals and families.

Genetic autopsy of perinatal death
The causes of perinatal death and genetic termination of pregnancy often cannot be established despite autopsy and extensive investigation, commonly with long term psychological consequences for families. We have used whole genome sequencing of parent/child triplets as a powerful tool for genetic testing, and have more than doubled the diagnostic rate of these cases. We have generated functional cell and animal models for several novel gene mutations to confirm functional phenotypes and aid in characterisation of pathogenic mechanisms. This has led to identification of causal known and novel genes as well as expansion of phenotype for some genes.

Key discoveries 2018

We demonstrated that the mutation profile of Chronic Myeloid Leukaemia (CML) is much more complex that previously recognised with point mutations and small indels as well as large chromosomal rearrangements with deletions and translocations. Some of these can be seen early in disease development and may be predictive of outcome (Branford *et al*, 2018).

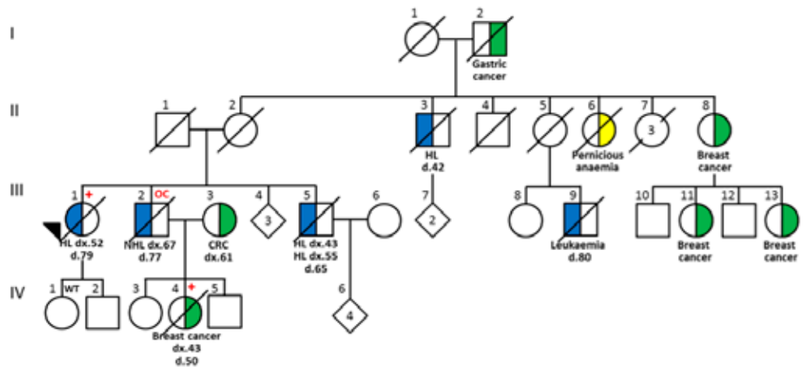
We identified putative mechanisms by which clinically important germline GATA2 mutations predispose to leukaemia (Chong *et al*, 2018; Al Seraihi *et al*, 2018).

10 Year Highlights

Over the last 10 years, we have made discoveries that have impacted families locally and around the world, and translated findings into clinical diagnostic tests and changes in clinical practice.

Familial predisposition to blood cancers Discovery of *GATA2* as a predisposition to myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML) (Hahn *et al*, *Nature Genetics*, 2011) and primary lymphoedema (Kazenwadel *et al*, *Blood*, 2012). Important findings for predisposition genes RUNX1 and DDX41 reporting novel mutations and extended phenotypes (Jongmans *et al*, *Leukemia*, 2010; Lewinsohn *et al*, *Blood*, 2016). Identification of a novel mutation involving bone marrow failure gene RPS26, and a mechanism of somatic mutation reversion (Venugopal *et al*, *Haematologica*, 2017). Unique case of transplantation of bone marrow stem cells harbouring clonal haematopoiesis of indeterminate potential mutations leading to independent cases of AML in the donor and recipient due to independent acquisition of different mutations (Hahn *et al*, *Leukemia*, 2015). Demonstration of complexity in genetic changes in progression of CML (Branford *et al*, *Blood*, 2018). Establishment of first familial RUNX1 mutation database collating next generation sequencing data with comprehensive clinical parameters for 200 individuals from over 70 international collaborators (https://runx1db.runx1.com).

Genomic autopsy project (began 2017) Discovery of new genes and new mutations that lead to perinatal death with extended phenotypes for several known genes. This study has provided genetic diagnoses and recurrence risk of perinatal death for 25/63 (40%) families who would not have had a diagnosis with current practices. To date, this has concluded the diagnostic odyssey for families, given hope for future pregnancies, and enabled healthy births through preimplantation genetic diagnosis.



Pedigree with pan-cancer phenotype including haematological malignancies (HM)
A PALB2 (K142*) mutation, commonly associated with breast and ovarian cancer, is present in individuals with Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) implying a role in HM; mutation carrier (+) and obligate carrier (OC).

Outcomes for the Community

Our discoveries in familial predisposition to blood cancers and genomic autopsy have led directly to changes in the clinical management and treatments of patients and families. Providing families with genetic diagnosis for their disorder is often also comforting, and provides hope for personalised or targeted treatments. Our discoveries in CML have potential to impact clinical practice across the world.

Jantina Manning, Tianqi Xu, Andrej Nikolic, Sharad Kumar, Xin Jiang, Tanya Henshall, Shannon Nicolson, Ammara Farooq

Sonia Dayan, Sonia Shah, Kelly Gembus, Natalie Foot, Julian Carosi, Donna Denton, Yoon Lim, Loretta Dorstyn, Dylan De Bellis, Ian Nicholson

Molecular Regulation Laboratory

Professor Sharad Kumar AM MSc PhD FAA FAHMS

Our research focuses on two essential physiological processes: 'programmed cell death' and 'protein ubiquitination' 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.

Billions of damaged or infected cells in our body die each day in a tightly regulated manner to protect us from the deleterious effects of aberrant cells and to remove harmful pathogens. Understandably, loss of proper cell death or too much cell death are linked to many human pathologies, including cancer, where premalignant cells evade cell death, promoting tumourigenesis. Cell death also plays a critical role during normal fetal development to maintain tissue homeostasis. Regulated cell death can be mediated by a number of mechanistically different processes, including apoptosis, necroptosis, pyroptosis and autophagy-dependent cell death (ADCD). We study the mechanisms and regulation of apoptosis and ADCD, to understand their roles in normal physiology during animal development and in diseases such as cancer and obesity.

Ubiquitination is a common type of protein modification involved in the regulation of protein stability and degradation, and aberrations in the ubiquitin system underpin the pathogenesis of many diseases including malignancies, neurodegenerative disorders and channelopathies. Ubiquitin-protein ligases (E3s) determine the substrate specificity of the ubiquitination process together with adaptor proteins. We are studying the physiological and pathological functions of a group of E3s (the Nedd4 family) and their adaptor proteins (Ndfips and Arrestin-domain-containing proteins, Arrdcs). Our recent work involves understanding their role in regulating the formation and release of extracellular vesicles, which play key roles in cell-cell communication, inflammation and tumour metastasis.

Key discoveries 2018

Spatial regulation of autophagy-dependent cell death (ADCD) Our previous work discovered a mode of cell death that is dependent on autophagy, the process of cellular self-digestion through the lysosome (reviewed in Denton and Kumar, *Cell Death Differ*, 2018). We have now identified a role for Decapentaplegic, Dpp (bone morphogenetic protein/transforming growth factor β ligand) in the correct spatial regulation of ADCD (Denton *at al*, *Cell Death Differ*, 2018). In further studies, we also found that Hedgehog and Wingless signalling are not required for ADCD (Xu *et al*, *Biochem Pharmacol*, 2018). These findings have important implications in understanding autophagy and ADCD in normal development and in disease.

Regulation of genomic stability by caspase-2 We previously discovered a novel role for the cell death protease, caspase-2, in both apoptotic and non-apoptotic signalling pathways including tumour suppression, genomic stability, metabolism and the regulation of oxidative stress pathways associated with premature ageing. Towards its role in regulating genomic stability we found that loss of caspase-2 enhances DNA damage and exacerbates aneuploidy in response to mitotic stress. We have now shown that caspase-2 has cell and context-dependent role in p53-mediated signalling during different mitotic stages (Lim *et al*, *Cell Death Differ*, 2018).

Arrdc1-mediated control of the biogenesis of extracellular vesicles Extracellular vesicles (EVs), are secreted by all cells and mediate the release of proteins and genetic material to facilitate cell-cell communication. We previously found that arrestin-domain containing protein 1 (Arrdc1), an adaptor for the Nedd4 family of ubiquitin ligases, regulates the release of EVs. In a recent study we discovered significant differences in EV cargo released between wild-type and Arrdc1 deficient cells (Anand *et al*, *Proteomics*, 2018: e1800266), suggesting that Arrdc1 function is required for the sorting of protein cargo into EVs. As EV biogenesis and cargo sorting are poorly understood, our work provides new molecular insight into these important processes.

10 Year Highlights

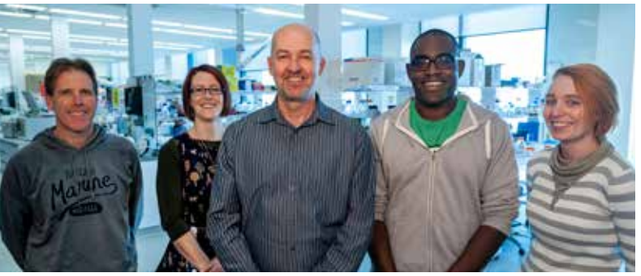
Over the last 10 years we trained 13 PhD students, 16 postdoctoral fellows, obtained >$17M of research and >$10M of research infrastructure funds, and published around one hundred research articles. We discovered and characterised several key biological pathways critical for whole body homeostasis, cancer and other diseases.

- We uncovered an unexpected function for the cell death protease, caspase-2 in tumour suppression (Ho *et al*, *Proc Natl Acad Sci*, 2009; Kumar, *Nature Rev Cancer*, 2009; Puccini *et al*, *Proc Natl Acad Sci*, 2013). We went on to show that caspase-2 prevents genomic instability and aneuploidy, and it regulates oxidative stress response and metabolism (Dorstyn *et al*, *Cell Death Differ*, 2012; Shalini *et al*, *Cell Death Differ*, 2012; Shalini *et al*, *Oncogene*, 2015; Dawar *et al*, *Oncogene*, 2017; Wilson and Kumar, *Cell Death Differ*, 2018). Our work suggests that altered caspase-2 expression or activity may result in susceptibility to certain types of cancer and metabolic disease.
- We discovered that Nedd4-2 is a critical regulator of sodium homeostasis and essential for animal survival (Boase *et al*, *Nature Commun*, 2011; Manning & Kumar, *Trends Biochem Sci*, 2018). We further demonstrated that Nedd4-2 prevents sodium-induced kidney damage (Henshall *et al*, *Cell Death Differ*, 2017). This has important implications for the diagnosis, management and treatment of human kidney diseases, which affect up to 10% of the population.
- In collaborative studies we established Ndfip1 as a critical regulator of iron homeostasis and inflammation (Foot *et al*, *Blood*, 2011; Yip *et al*, *Nature Commun*, 2016; Foot *et al*, *Physiol Reviews*, 2018). Loss or reduced levels of Ndfip1 are now well established to result in inflammatory diseases.
- Our seminal discoveries have shifted the paradigm in understanding the role of autophagy in cell death (Denton *et al*, *Curr Biol*, 2009; Denton & Kumar, *Cell Death Differ*, 2019). Having established a model of autophagy-dependent cell death (ADCD) we also found that hormonal cues and inhibition of growth signalling are important for correct spatial induction of this mode of cell death (Denton *et al*, *Cell Death Differ*, 2012 & 2018; Denton *et al*, *Nature Commun*, 2013; Denton and Kumar, *Cell Death Differ,* 2019). Furthermore, we discovered that the regulation of autophagy during cell death is distinct to that required during cell survival (Xu *et al*, *Cell Death Differ*, 2015). This work has important implications in tumour suppression and treatment.

Cells expressing Dpp (green) are larger in size and show reduced autophagy (red puncta) compared to the neighbouring control cells. Blue staining marks DNA (nuclei). Scale bar represents 25 μm.
Error bars represent SD, ***P<0.0001.

Outcomes for the Community

Our findings provide important insight into cell and tissue homeostasis through the regulation of (i) ADCD, (ii) genomic stability and (iii) the cargo sorting in EVs. As such, we have defined some of the key molecular mechanisms underlying these processes. This will allow us to identify new targets or biomarkers for drug development in the treatment of associated human diseases.



Paul Moretti, Melissa Pitman, Stuart Pitson, Gus Nwosu, Melissa Bennett
Absent: Maurizio Costabile, Alexander Lewis, Craig Wallington-Beddoe

Jason Powell, Lorena Davies, Rhys Hamon, Victoria Pope, Melinda Tea
Absent: Carl Coolen, Briony Gliddon, Jo Woodcock

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 ceramides, sphingosine and sphingosine 1-phosphate, and their dihydro derivatives, regulate a 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 (SK1 and SK2) are key enzymes controlling sphingolipid metabolism, and through this action can regulate central processes such as cell survival and proliferation. Recent work in the Molecular Signalling Laboratory has concentrated on identifying the mechanisms regulating sphingolipid metabolism, the cellular functions controlled by the sphingosine kinases and other enzymes involved in this pathway, and in developing small molecule inhibitors as potential anti-cancer and anti-fibrotic agents. In particular we have made several major breakthroughs in understanding how these enzymes are activated, re-localised in the cell, and deactivated, which have provided novel therapeutic targets to control cancer and other diseases.

Key discoveries 2018

Identification of SK2 as a therapeutic target in glioblastoma Glioblastoma is the most commonly diagnosed malignant brain tumour in adults. With very few treatment options available, patient outcomes are very poor, meaning new therapeutic targets are desperately needed. In work recently published in Oncogene (Neubauer et al, Oncogene) we have found that sphingolipid metabolism is dysregulated in glioblastoma due to the loss of the DYNC protein that normally suppresses SK2. Furthermore, we have demonstrated that SK2 is an attractive target for the potential treatment of glioblastoma, providing impetus for the further development of SK2 inhibitors as anti-glioblastoma drugs.

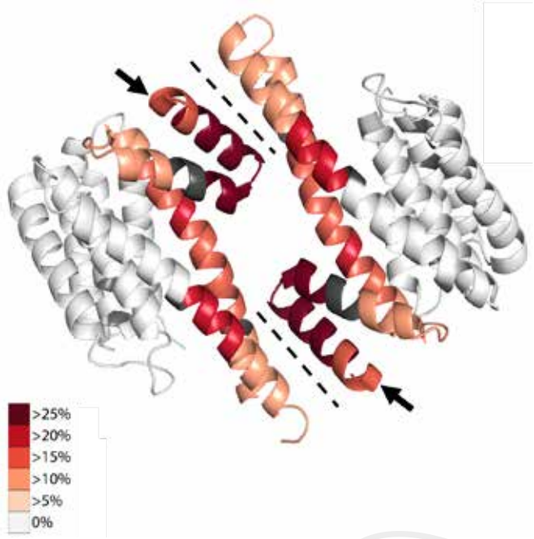
Altering lipid metabolism to combat fibrotic diseases Dysregulated lipid metabolism plays an important role in obesity-related tissue inflammation and subsequent development of fibrotic diseases, which represent a major health burden on society. In collaboration with Associate Professor Bernard Flynn of Monash University, and via a $7 million investment by the Medical Research Commercialisation Fund, we have recently established a spin-out biotechnology company, Cincera Therapeutics, which aims to develop new therapeutics targeting fibrotic diseases through correcting defective lipid metabolism.

Understanding the molecular control of 14-3-3 adaptor protein function The 14-3-3 family of dimeric proteins are sphingosine-regulated adaptor proteins that bind and regulate many important signalling proteins associated with cancer. In studies recently published in the *Journal of Biological Chemistry* (Woodcock *et al*, *J Biol Chem*, 2018), we have defined a number of important structural factors that are critical for the formation and maintenance of 14-3-3 dimers, which are critical for the function of these proteins. These findings not only reveal fundamental insights into the molecular function of the 14-3-3 proteins, but also identify novel avenues to target these proteins for therapeutic benefit.

10 Year Highlights

Over the last 10 years we have gained unique fundamental insights into the regulation and biological functions of sphingolipids in cancer and other diseases, and begun to translate this knowledge towards the clinic.

- Our work on the sphingosine kinases has revealed key regulatory mechanisms of these enzymes that have important implications for acute myeloid leukaemia (Powell *et al*, *Blood*, 2017), glioblastoma (Neubauer *et al*, *Oncogene*, 2019), multiple myeloma (Wallington-Beddoe *et al*, *Oncotarget*, 2017) and ovarian cancer (Zhu *et al*, *Cancer Research*, 2017). Indeed, new sphingosine kinase inhibitors that we have developed show efficacy in advanced pre-clinical models of these cancers, and appear particularly promising in sensitising these tumours to other existing therapies. Our goals are now to translate these to the clinic.
- In 2018 we co-founded Cincera Therapeutics, a spin-out biotechnology company based on our collaborative work with Associate Professor Bernard Flynn of Monash University, and via a $7 million investment by the Medical Research Commercialisation Fund. Cincera Therapeutics aims to develop novel therapeutics that modulate lipid metabolism as anti-fibrotic and anti-cancer agents.
- Translation of cancer research towards the clinic is greatly augmented by high quality, clincially relevant experimental models. In the last decade, in collaboration with key South Australian clinical haematologists and neurosurgeons, we have established such advanced clinically relevant experimental models of acute myeloid leukaemia and glioblastoma, that provide a powerful resource for the cancer research community.
- In the process of our research, in the last ten years we have trained 14 PhD students, two Masters by Research students and 11 Honours students, as well as 11 postdoctoral fellows. In this time we have obtained >$14 million of research and >$4 million of research infrastructure funds, and published >100 research articles.



The ribbon diagram shows a bottom up view of a 14-3-3zeta dimer with the N-termini indicated by arrows and the juxtaposed dimer interfaces delineated by dashed lines. The heat-map colouring of the protein represents the comparative hydrogen-deuterium exchange of D21N 14-3-3zeta relative to wild type 14-3-3zeta at 10 minutes of exchange. The N-terminal helices that form the dimer interface undergo relatively rapid exchange indicating a propensity to be disordered.

Outcomes for the Community

Cancer and fibrosis have major human and economic impacts on the community, with new therapeutic options desperately needed to combat these diseases. Our research has not only helped to determine the molecular basis for the development and progression of these diseases, but also identified new targets and agents for potential use in future therapeutic use.

Xiangjun Xu, Iman Lohraseb, Quenten Schwarz, Markus Tondl, Ellen Potoczky, Ceilidh Marchant, Sophie Wiszniak, Sepideh Azizi Taramsary

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz PhD

In Australia over 20 children are born with a congenital birth defect 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.

The driving force behind the research performed in the Neurovascular Research Laboratory is to identify the cell and molecular mechanisms controlling neuronal and vascular development with the intent of providing novel insight toward the origins and treatment of these debilitating disorders.

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 communicate with 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 different cell types and demonstrate that each cell uses similar molecular pathways to communicate with each other to control tissue morphogenesis.

Our current research projects use 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.

Key discoveries 2018

In 2018 the Neurovascular Research Laboratory had several discoveries that provide novel insight to formation of the peripheral nervous system and the origins of childhood cancers.

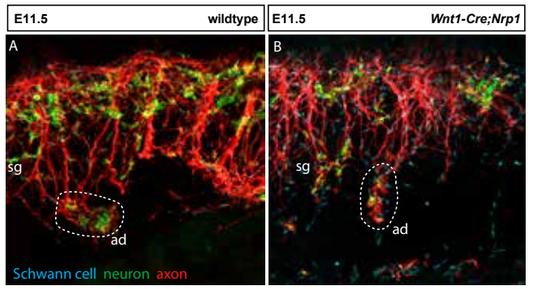
Aberrant development of the peripheral nervous system has significant impact on the body's fight or flight stress response and forms the basis of several childhood cancers, including neuroblastoma and pheochromocytoma. In work published in the journal *Development*, we demonstrated that neural crest cell precursors of adrenal chromaffin cells migrate along the axons with which they will later form connections. This uncovers a novel paradigm by which neurons form connections with their target cells and to how the nervous system is wired (Figure 1). Our work further unlocks part of the molecular mechanisms by which axons navigate to the adrenal gland and how the precursors of chromaffin cells maintain their association with axons. Using genetic mouse mutants we showed that aberrant axonal navigation precludes inappropriate positioning of the adrenal gland. Our current work is testing the possibility that incorrect positioning of chromaffin cells is a precursor to the formation of neuroblastoma and pheochromcytoma.

10 Year Highlights

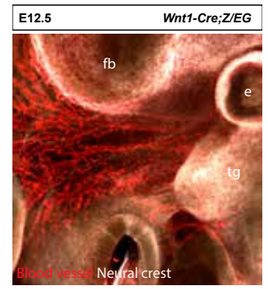
It was a typically wet Wednesday morning in East London when I deleted what I thought was a spam email from someone named Angel Lopez. To my surprise the very next email came from Natasha Harvey who had mentored me during my PhD reiterating what I should have read in the previous email. Thankfully Angel's email was still in the trash folder in which he detailed the recent formation of the Centre for Cancer Biology and the vision of building research capacity and excellence for this new research centre. Following numerous emails and the occasional phone call I was quickly immersed in the double life of being a Post Doc by day and writing Fellowships and Grants by night. With a lot of work in the background from the brains trust in the CCB (thanks to Angel, Sharad, Stuart, Greg, Yeesim and Tash) I was fortunate to receive seed funding from Medvet. Together with an NHMRC Career Development Award this provided the stimulus to initiate the Neurovascular Research Program within the CCB in 2010. What followed was a rapid learning curve of how to lead a research team and how to attempt navigating the Australian grant system. Since 2010 our fledgling lab of 3 has expanded to a group of over 8. We have trained 10 students. We have developed a niche research program focused on the co-dependencies of the neuronal and vascular systems during embryonic development. In this time we have also made some seminal findings into the origins of highly prevalent diseases:

Origins of schizophrenia: Schizophrenia is a devastating neurodevelopmental disorder diagnosed on presentation of debilitating clinical symptoms. Over the past 6 years our laboratory has 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 the onset of schizophrenia. Our work identified a reduction in cortical parvalbumin interneurons as the underlying defect leading to disease symptoms. These findings provide insight to the cell type and molecular pathways which could be targeted to treat the underlying behavioural deficiencies.

Origins and potential treatment of craniofacial birth defects: Craniofacial birth defects are common and require immediate intervention at birth. Our work over the past 5 years demonstrates that blood vessels play an important role in promoting craniofacial development, and that aberrant blood vessel growth underlies a number of common craniofacial disorders. We have recently identified several candidate growth factors secreted by blood vessels that promote chondrocyte proliferation during embryonic development which represent ideal candidates for future therapies to treat craniofacial disorders.



Confocal images of whole E11.5 mouse embryos
(A) Schwann cell precursors (blue) migrate along axons to position themselves in the adrenal primordia (ad; dashed circle) where they give rise to adrenaline secreting chromaffin cells.
(B) When Neuroplin 1 (Nrp1) is removed from Schwann cell precursors they fail to migrate along axons, which results in aberrant formation of the adrenal gland. (sg, sympathetic ganglia)



V-DISCO technique on whole E12.5 mouse embryos identifies interactions between neural crest cells (white) and forming blood vessels (red) in the head. (e, eye; fb, forebrain; tg, trigeminal ganglia)

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 craniofacial disorders, 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.

Amin Shirazi, Mariana Oksdath Mansilla, Guillermo Gomez, Camilo Salazar Hernandez, Chia-Chi Chien, Liky Koide
Absent: Sally Perrin

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez PhD

The last 30 years have seen minimal progress in brain cancer treatment. Some progress relied heavily on discoveries made using cell lines, mouse and patient-derived xenografts (PDXs), which completely fail to model human brain cancer *in vivo*. Hence, to expedite translational impact, we need experimental models of brain cancer that more accurately reflect the physiology and genetics of the human brain.

To attain this, The Tissue Architecture and Organ Function (TAOF) laboratory has now developed a new personalised high-throughput platform to analyse *ex-vivo* the process of cancer cell growth and invasion within human brain tissue using brain organoids as an in-vitro preclinical model. This constitutes a profound technological advance that enables us to target one of the most aggressive types of cancer. For this, the TAOF lab have pioneered a unique combination of:

Brain organoid models We established a collaboration with Dr Madeline Lancaster (MRC Laboratory of Molecular Biology, UK), to successfully grow brain organoids using CRISPR GFP knock-in genome-edited iPSC cells. Co-culture of fluorescently labelled organoids with non-fluorescent cancer cells permits us to identify, track, and analyse different live cell populations.

Culture of patient-derived brain cancer cells In collaboration with Professor Michael Brown, Dr Lisa Ebert, Professor Stuart Pitson and Dr Melinda Tea, we have established protocols for the culture and passage of patient-derived cancer cells obtained post-surgery through the SA Neurological Tumour Bank, and correlated tumour phenotype and the histology of tumour sections with the expression of different markers in these cancer cells when they grow within brain organoids.

High-throughput biomimetic platforms Our laboratory has pioneered the use of 3D printers and Bio-printers for the establishment of high-throughput platforms that better mimic the tumour microenvironment in biopsy samples and that allow better organoid growth. We achieve this by using 'synthetic scaffolds', which define the physical space in which organoids grow and 'biomimetic substrates' that replicate the extracellular matrix on which organoids attach which we also use for bio-printing of different cell types present in the tumour microenvironment.

Deep learning image classification and analysis Together with high-content imaging, we are also developing machine-learning algorithms to extract information from a large dataset of images to gain insight and predictive capacity on the aggressivity of brain cancers in different patients. We are applying this to brain organoid images, pathological images as well as combining it with computational simulations of brain tissue in order to understand morphological features associated with brain cancer progression.

Key discoveries 2018

This paper describes a new method for the analysis of cancer cell morphometry using deep learning: Zadeh Shirazi A, Fornacieri E, Gomez GA. Deep Learning in Precision Medicine. Book chapter in *Artificial Intelligence in Precision Health: From concept to applications*, Elsevier, 2018.

This paper provides a critical review of new synthetic materials for brain organoid growth that mimic the brain extracellular matrix: Oksdath M, Perrin SL, Bardy C, Hilder EF, DeForest CA, Arrua RD, Gomez GA. Synthetic scaffolds to control the biochemical, mechanical, and geometrical environment of stem cell-derived brain organoids. *APL Bioengineering 2*, 2018.

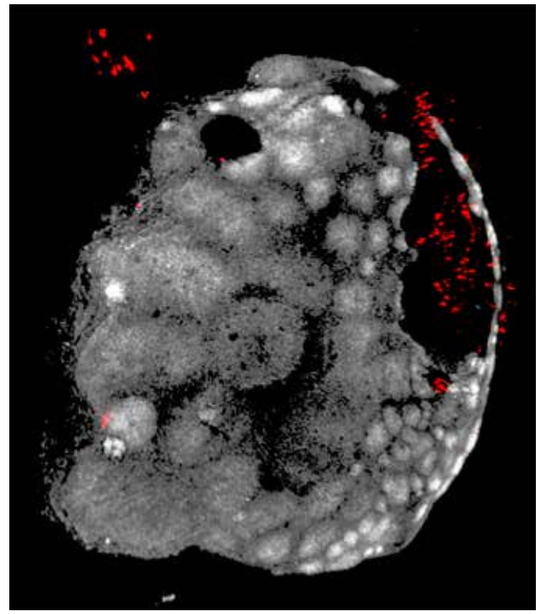
10 Year Highlights

I joined the CCB in 2017 as an ARC Future Fellow to establish the Tissue Architecture and Organ Function Laboratory after finishing postdoctoral training with Professor Alpha Yap at the Institute for Molecular Biosciences, The University of Queensland.

I brought expertise in mechanobiology, stem cell biology, brain organoid technology, imaging, image analysis and computational modelling.

Key highlights since my laboratory started in 2017 are:

- Securing funding to upgrade the CCB's microscope facility with a high content InCell Analyzer 2200 (GE Healthcare) and a multiphoton/FLIM Leica STED SP8 confocal microscope.
- Pioneering the use of 3D printing, bioprinting and use of artificial intelligence for the development of new preclinical models for brain cancer as well as diagnostic tools, for which Tissue Architecture and Organ Function Laboratory obtained funding from the Cure Brain Cancer Foundation, the Neurological Research Foundation, Cancer Council SA Beat Cancer Project and the Hospital Research Foundation.



Confocal fluorescence microscope image of a human brain cancer organoid model Healthy cells that make up the brain (grey) and patient-derived GBM cells (red). Image by Dr Mariana Oksdath (TAOF lab)

Outcomes for the Community

Developments made in the TAOF lab are frequently shared with the community through the media. In particular, in 2018 the lab was interviewed for The Advertiser and ABC radio, about recent developments in brain organoid models for disease including cancer and how to use it for personalised therapies.

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

Although our laboratory research is conducted in the CCB, it is closely aligned with clinical research conducted in the Cancer Clinical Trials Unit of the Royal Adelaide Hospital (RAH), which is the quaternary hospital of South Australia. Consequently, this link enables direct translation of findings at the bench to benefits for cancer patients at the bedside. The main tumour types of interest are melanoma, lung cancer, brain cancer (glioblastoma) and ovarian cancer.

We use the immune system not only to target cancer but also to overcome the immune deficiencies associated with cancer. Our two major research directions are clinical translation of chimeric antigen receptor (CAR)-T cell therapy and antibody-directed cancer delivery of radionuclides and cytotoxins. We already have our own CAR-T cell therapy in clinical trial at RAH, and with collaborators, we are developing two other CAR-T cell therapy protocols. We are preparing for a first-in-human study of radiolabelled chimeric APOMAB (chAPOMAB) as a PET tracer for imaging tumour responses in ovarian and lung cancer patients after anti-cancer chemotherapy. A third recent and promising research direction is our discovery of immune signatures present in the blood before patients receive immune checkpoint (ICI) inhibitor therapy. We are performing additional clinical studies to validate these signatures as a pre-treatment indicator of response to this commonly used anti-cancer therapy.

In the ongoing CARPETS phase 1 clinical trial of autologous, GD2-specific, CAR T-cell therapy in patients with GD2-positive metastatic melanoma, an amendment to the clinical protocol has been approved by the Therapeutic Goods Administration and the Human Research Ethics Committee of the parent organisation to RAH, Central Adelaide Local Health Network (CALHN). This protocol amendment allows broadening of eligibility to include patients with other GD2-positive malignancies together with alteration of the ex vivo CAR-T cell manufacturing method to favour generation of memory CAR-T cells, which in turn favour *in vivo* persistence of CAR-T cells. With new funding, our GD2-CAR T-cell therapy will be extended to adult and paediatric patients with aggressive primary brain tumours, which also express GD2.

Key discoveries 2018

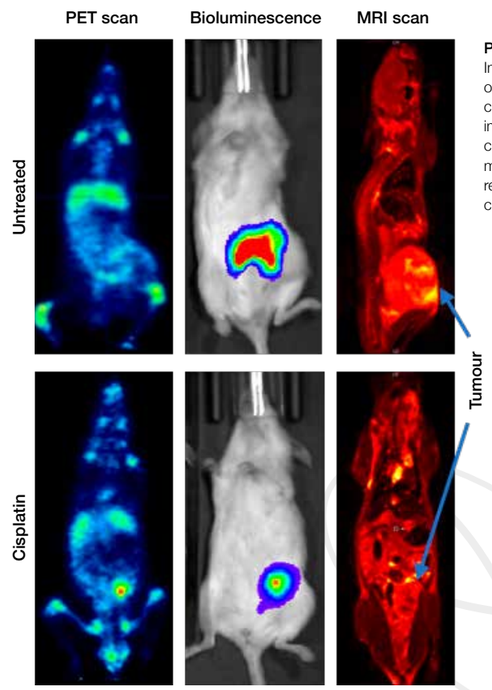
Using an antibody that selectively targets dead tumour cells *in vivo*, APOMAB®, we developed a series of antibody drug conjugates (ADCs) for tumour therapy. ADCs comprise a tumour-targeting antibody chemically coupled via linker to a potent cytotoxin or warhead, which is too toxic to be delivered as a free drug. Unexpectedly, we were able to detect significant anti-tumour activity of these APOMAB-ADCs given as a single dose and particularly after a prior step of DNA-damaging chemotherapy. However, the anti-tumour activity of APOMAB-ADCs was only apparent if the ADCs included a cleavable linker and a cell-permeant warhead drug, which together allow release and diffusion into nearby viable tumour cells of free cytotoxin. Hence, this is the first formal demonstration of an ADC that depends solely on a bystander killing effect for its anti-tumour activity (Staudacher AH *et al*, *Mol Cancer Ther*, published first online November 9, 2018).

10 Year Highlights

Over the last ten years, we have developed two major types of tumour targeting for therapeutic applications:

In an antibody-based approach to tumour targeting, we showed pre-clinical proof of concept by arming the APOMAB® antibody with different kinds of therapeutic modalities. APOMAB is a dead tumour cell targeting antibody, which has the advantage of targeting an invariant aspect of tumour biology, necrosis, which is often increased by standard anti-cancer treatments. Hence, we do not expect that targeting this molecule in dead tumour cells will be affected by genetic instability, a common feature of many cancers. Because it targets dead tumour cells, this antibody has usefully demonstrated the therapeutic potency of an under-appreciated feature of armed tumour-targeting antibodies: bystander tumour cell killing. We have demonstrated these effects for arming APOMAB with therapeutic radionuclides that emit either α-particles (Staudacher *et al*, *Nucl Med Commun*, 2014) or β-particles (Al-Ejeh *et al*, *PLoS ONE*, 2009; Al-Ejeh *et al*, *J Nucl Med*, 2014), which is also known as radiation cross-fire and which amounts to irradiating the tumour from the inside out (Staudacher *et al*, *EJNMMI Res*, 2014). Recently, in the first formal demonstration, we showed that antibody drug conjugates can exert anti-tumour activity solely via bystander killing effects (Staudacher *et al*, *Mol Cancer Ther*, 2019, published first online November 9, 2018).

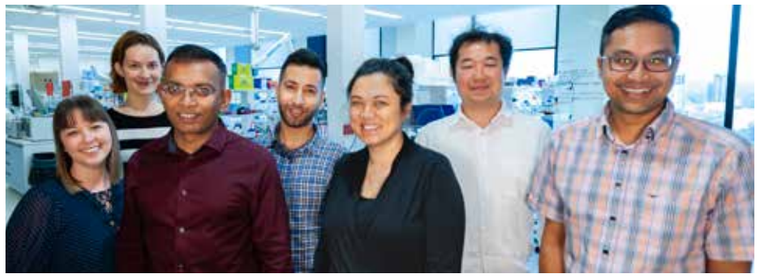
We introduced GD2-specific chimeric antigen-receptor (CAR)-T cell therapy for metastatic melanoma patients (Gargett & Brown, *Front Pharmacol*, 2014; Gargett & Brown, *Cytotherapy*, 2015) and in combination with standard combination BRAF/MEK inhibitor therapy (Gargett *et al*, *J Immunother*, 2015). We demonstrated that the adoptively transferred CAR-T cells had poor expansion and persistence *in vivo* mainly because of a terminally differentiated effector phenotype and activation-induced cell death (Gargett *et al*, *Mol Ther*, 2016). We are developing a dual-targeting CAR-T cell technology for new therapeutic targets in glioblastoma (Ebert *et al*, *Biochem Soc T*, 2018) and extending clinical GD2-CAR-T cell therapy to other GD2-positive malignancies.



Pre-clinical *in vivo* imaging of human ovarian cancer xenograft
Immunocompromised mice bearing ascitic tumour implants of the human ovarian cancer cell line, A2780, were left untreated (upper panels) or given cisplatin (lower panels) followed by ^{89}Zr-labelled chAPOMAB. Live-animal imaging was performed with PET (left lower) to obtain tissue uptake of chAPOMAB, bioluminescence (middle lower) and MRI (right lower) to measure tumour activity and extent, respectively. Treatment with cisplatin reduced tumour growth and increased chAPOMAB uptake because of chemotherapy-induced tumour cell death.

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, Valentina Poltavets, Michael Samuel, Vahid Atashgaran, Natasha Kolesnikoff, Makoto Kamei, Zahied Johan

Tumour Microenvironment Laboratory

Associate Professor Michael Samuel PhD

Tissues of the body have distinct microenvironments that have evolved specifically to facilitate tissue functionality. The extra-cellular matrix (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 together with 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 novel approaches to cancer therapy.

We have previously demonstrated that signalling through the Rho-ROCK pathway promotes tumour cell proliferation in epidermal, breast and colorectal cancers, fundamentally via mechanism that modify the tumour microenvironment. We have also demonstrated that changes in key properties of the microenvironment downstream of ROCK activation promote tumour progression in breast and intestinal cancers. Our lab has established several of the mechanisms by which ROCK activation regulates these tumour-promoting changes in the microenvironment.

Following on from our discovery that the molecular chaperone and 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 regulators of ROCK signalling, which may have utility in accelerating the healing of chronic non-healing wounds or in inhibiting tumour progression.

Key discoveries 2018

A paracrine mechanism downstream of ROCK signalling in tumour cells enhances the tumour-promoting properties of cancer-associated fibroblasts

Rho-ROCK signalling is progressively activated in breast cancers as well as models of mammary cancer. We observed that in mammary cancers in which ROCK is activated, recruitment of fibroblasts into the microenvironment is enhanced. ROCK-educated fibroblasts (i.e. fibroblasts from tumours in which ROCK is activated) are tumour-promoting and are educated by proteins secreted by tumour cells downstream of ROCK activation. We propose that inhibiting or destroying these proteins may be a novel therapeutic modality to slow down or halt tumour progression. We are in the process of identifying this cohort of secreted proteins that may serve as novel targets against breast cancer.

Inhibiting 14-3-3 is a potential therapy to accelerate the healing of diabetic wounds

We recently demonstrated that 14-3-3ζ is a negative regulator of signalling through the Rho-ROCK pathway. We also found that in chronic non- or slow-healing wounds, there were high levels of 14-3-3ζ protein. These wounds are a huge impost on our country's health system. We therefore sought to determine whether inhibiting 14-3-3 in diabetic wounds, a type of slow-healing wound, would accelerate their healing. We have now demonstrated that application of a pharmacological inhibitor developed in the laboratories of Professors Pitson, Lopez and those of their collaborators can indeed accelerate the healing of diabetic wounds. We are now investigating the mechanisms underlying this exciting new discovery.

10 Year Highlights

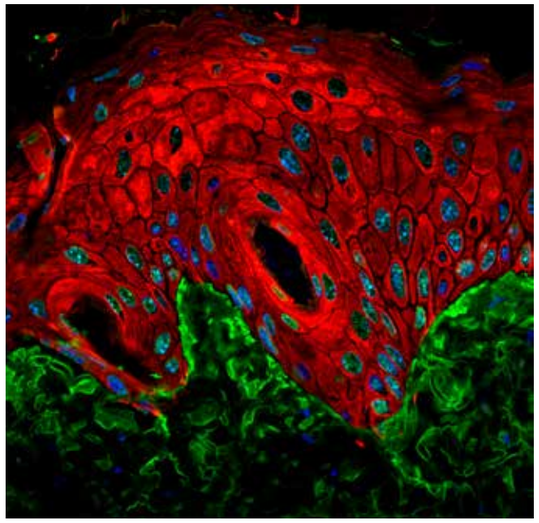
The Tumour Microenvironment Laboratory is younger than the CCB itself, having been established six years ago. Highlights in its lifetime include:

Establishment of the Tumour Microenvironment Laboratory in 2011, which has grown into a cohesive team of 10 researchers in 2018, working to determine how tumours co-opt their microenvironments to promote their growth, invasion and spread. We are particularly interested in the role of the extra-cellular matrix in initiating and transmitting mechanical signals that influence tumour progression and in establishing approaches by which these insights may be utilised to halt tumour progression.

Since then, we have made key contributions to understanding how a tumour promoting microenvironment is established and the mechanisms underlying its maintenance, including:

Demonstrating that aberrant activation of the Rho-ROCK signalling pathway promotes tumour progression in invasive cutaneous squamous cell carcinoma by regulating the production and organisation of ECM collagen (*Cancer Cell*, 2011; *Am J Pathol*, 2013).

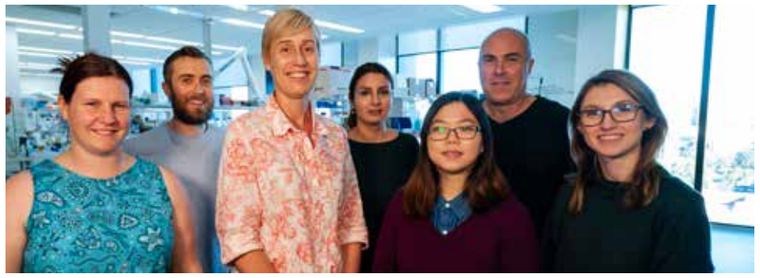
Establishing that this mechanism can indeed be exploited to accelerate the healing of skin wounds by modulating signalling through ROCK by pharmacologically inhibiting the molecular chaperone 14-3-3 and thereby accelerating wound healing (*Developmental Cell*, 2015).



A healing diabetic wound. Immunofluorescence analysis of the hyperproliferative epithelial cell layer (Keratin 14 in red) extracellular matrix (fibronectin in green). Wounds heal slower in diabetic individuals and we are testing a new compound to accelerate wound closure in these patients. (Imaged using a Zeiss LSM 700 confocal system)

Outcomes for the Community

Abnormal changes in the tissue microenvironment can result in cancer, abnormal wound healing and metabolic diseases including obesity. Some of these changes are associated with abnormal production of the collagen-rich scaffold that holds tissues together and provides a milieu within which they can function. We are working to identify the mechanisms underlying this process to discover new approaches to normalise the microenvironment that could lead to new therapies against cancer and other diseases.



Michaelia Cockshell, Eli Moore, Claudine Bonder, Anahita Fouladzadeh, Lih Yin Tan, Mark DeNichilo, Emma Thompson
Absent: Camille Duluc, Kay Khine Myo Min, Samantha Escarbe

Vascular Biology and Cell Trafficking Laboratory

Professor Claudine Bonder PhD

The overarching focus of our research is blood vessels and how they can contribute to disease. A major area of interest for our laboratory is cancer, more specifically, tumour vasculature and vasculogenic mimicry (VM), a process wherein cancer cells mimic endothelial cells to form vascular-like structures for increased blood supply to tumours for growth and metastasis.

We and others have shown that VM content in tumours is associated with poor clinical outcome and we have identified novel elements underpinning VM in breast cancer, melanoma and pancreatic cancer.

In another research program, we are investigating better outcomes for patients with diabetes. With increasing evidence for a critical and intimate relationship between the blood vessel lining endothelial cells and the insulin producing islet cells, our work on the fundamental biology of the pancreatic vasculature aims to provide new opportunities to treat, and possibly even help cure, this prevalent and debilitating disease.

Another of our research programs focuses on the vascular occlusions that contribute to cardiovascular disease (CVD) and are a leading cause of death worldwide. Our attempts to overcome these blockages include the resurfacing of metal stents or other artificial vascular grafts to prevent thrombosis, and reduce restenosis and thus maintain vessel diameter.

Key discoveries 2018

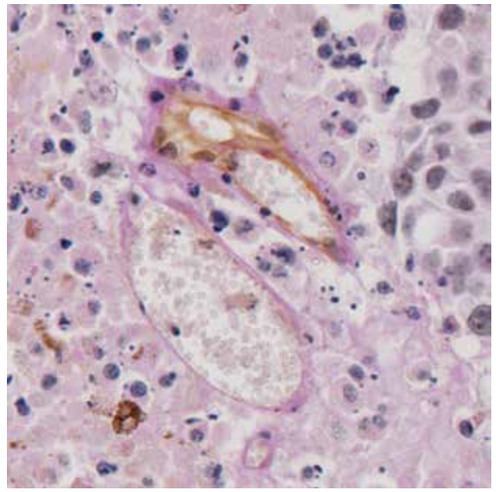
Revolutionising vascular devices Overcoming vascular occlusions is key to combating cardiovascular disease (CVD) and to date the best method to resolve these blockages utilises metal stents to maintain vessel diameter. This has become a multi-billion dollar industry. Despite recent advances in device 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 (CTM-CRC), 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 2018, we established a spin-out company from the CTM-CRC called TekCyte and began pre-clinical animal models with a multi-national industry partner.

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 2018 we were awarded an NHMRC grant to better understand the control of immune cell entry through the tumour vasculature, with a particular focus on VM in melanoma. This built on our previous *Oncotarget* publication that desmoglein-2 (DSG2, an adhesion molecule belonging to the desmosomal cadherin family) is upregulated in ~30% of melanoma patients, that it is used by melanoma cells to form VM channels and that it correlates with poor survival.

10 Year Highlights

Over the last ten years we have built on our understanding of endothelial cell biology with practical implications for debilitating and deadly diseases.

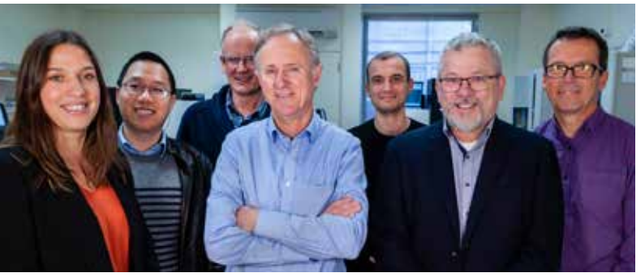
- Identified that sphingosine kinase 1 is important for the activation of endothelial cells by histamine for leukocyte recruitment and that topical application of a repurposed drug may prevent allergic responses in humans (Sun *et al*, *Am J Pathol*, 2012; Sun *et al*, *J Immunol*, 2016).
- Discovered that hyper-branched polyglycerol is anti-adhesive and optimised endothelial cell-material surface interactions (Moore *et al*, *Macromolecular Chemistry and Physics*, 2016; Dalilottojari A *et al, Biomacromolecules*, 2016; Burzava *et al*, *Biomacromolecules* 2017).
- Discovered that endothelial progenitor cells have their survival and function supported by sphingosine kinase 1, proliferate in response to interleukin-3 and can be used as a cell therapy for diabetes and pulmonary arterial hypertension (Bonder *et al*, *Blood*, 2008; Moldenhauer and Cockshell *et al*, *Stem Cell Research*, 2015; Penko *et al*, *Cell Transplantation*, 2015; Parham *et al*, *FASEB J*, 2015; Harper *et al*, *Respirology*, 2019).
- Identified key mediators linking both angiogenesis by endothelial cells and vasculogenic mimicry by cancer cells (Moldenhauer and Cockshell *et al*, *Stem Cell Research*, 2015; Ebert *et al*, *Angiogenesis*, 2016; Tan *et al*, *Oncotarget*, 2016).
- In the last ten years our laboratory has been awarded ~$10M in funding with grants from the NHMRC, Heart Foundation, Cancer Australia and two CRCs (Biomarker Translation and Cell Therapy Manufacturing). We have filed six patents (one granted in US and three under examination), partnered with three multi-national companies and helped establish the start-up company TekCyte Pty Ltd. We have also delivered the highest level of training for young Australian scientists with eight Honours students awarded First class, seven PhD completions (four of whom are now training overseas (eg Stanford) and winning Fellowships) and successful ECRs who are being awarded national Fellowships (eg Heart Foundation). Claudine Bonder was one of the first two females to be promoted to full Professor within the CCB (together with Professor Natasha Harvey), was awarded a Women in Innovation prize in 2016 and has had two children.



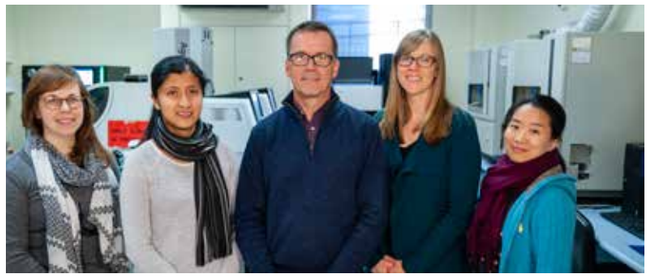
Mouse melanoma section showing endothelial cell lined angiogenesis (brown) and cancer cell lined vasculogenic mimicry (pink)

Outcomes for the **Community**

Our expertise in blood vessels, and the endothelial cells which form their inner lining, allows us to better understand the killer diseases of cancer, cardiovascular disease and diabetes. Our ultimate aim is to harness the information we gain about the blood vasculature in disease states so that new treatment opportunities can be generated to save lives every year, worldwide.



Senior Management Karin Kassahn, Song Gao, Andreas Schreiber, Greg Goodall, Julien Soubrier, Hamish Scott, Rob King



Technology Platform Rosalie Kenyon, Nathalie Nataren, Rob King, Wendy Parker, Ming Lin

The Australian Cancer Research Foundation Cancer Genomics Facility

Professor Greg Goodall, Co-Director Professor Hamish Scott, Co-Director
Mr Joel Geoghegan BSc, MSc and Mr Rob King BSc Facility Managers 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

Developing its strong relationship with the South Australian research community, the ACRF Cancer Genomics Facility performs a key role in providing researchers access to the latest genomics technologies and expertise. The Facility also provides an invaluable testing and validation environment for the translation of research findings into the clinic.

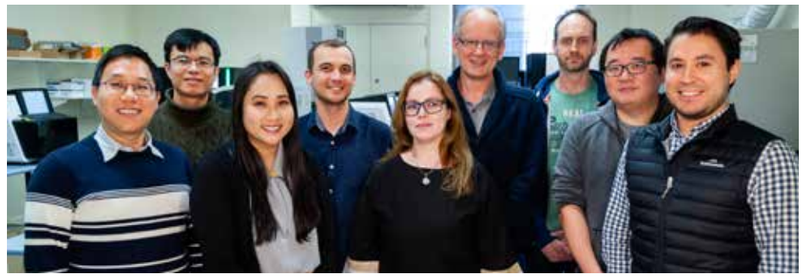
In collaboration with the Genetics and Molecular Pathology Directorate of SA Pathology, the Genome Facility extended its NATA accreditation for diagnostic next generation sequencing in 2018. We applied for and received accreditation to perform copy number variation analysis on whole exome sequencing data, RNA Seq-based testing of splice site mutations and fusion transcript detection, somatic mutation detection for paired tumour-normal samples as well as whole exome sequencing of FFPE samples. The accreditation was received because we were able to demonstrate that we have been developing and successfully implementing these types of tests for research purposes for a number of years. This is an excellent example of the benefits and the considerable financial savings that can be made by conducting both diagnostic and research work side-by-side in the same laboratory. Both the research and diagnostic bioinformatics groups are now working on the necessary software and testing that is required to implement these new diagnostic tests.

Another exciting development was the Genome Facility's acquisition of 10X Genomics Chromium single cell preparation equipment, which permits cell-specific sequencing of the transcriptomes of single cells (see Figure). This technique has great potential benefits, particularly when the relevant sequencing samples contain many different cell types or sub-types. For example, the technique will prove useful in tracking the development of individual clones associated with any number of different leukemias.

For over five years, the Genome Facility has been home to a software development project for a tool permitting interactive mutation analysis of the vast number of potential genetic variants obtained in typical next generation sequencing experiments. In 2018, this tool was used as the foundation for a successful application to the Australian Genomic Health Alliance to create a variant sharing platform — 'Shariant' — for Australia's molecular pathology testing laboratories. We gratefully acknowledge AGHA's funding, which has permitted us to employ another staff member on this important project. Roll-out to the first testing laboratories interstate is now under way.

Integrative analysis of genomic data

Various technology platforms enable genome-wide characterisation of genetic point mutations, chromosomal abnormalities, changes in gene expression and alternately spliced transcripts, as well as amplified chromosomal segments known as copy number variants. While certainly informative on their own, there is significant benefit in a collective integrative analysis of the vast amounts of data generated from each of these platforms. Integrative analysis increases sensitivity and provides a holistic picture of underlying mutational processes. Over five years of development of software tools and integrative bioinformatic analysis culminated, in close collaboration with our Leukemia Unit, in the publication of a landmark study on the full spectrum of genetic variation associated with CML (Branford *et al*, *Blood*, 2018). Apart from the well-known Philadelphia translocation, we found considerable evidence for the presence of numerous other mutation types, certainly at advanced stages of the disease but also at the diagnosis stage.



Bioinformatics Song Gao, Jinghua (Frank) Feng, Thuong Ha, Julien Soubrier, Leila Eshraghi, Andreas Schreiber, James Andrews, Paul Wang, Luis Arriola-Martinez

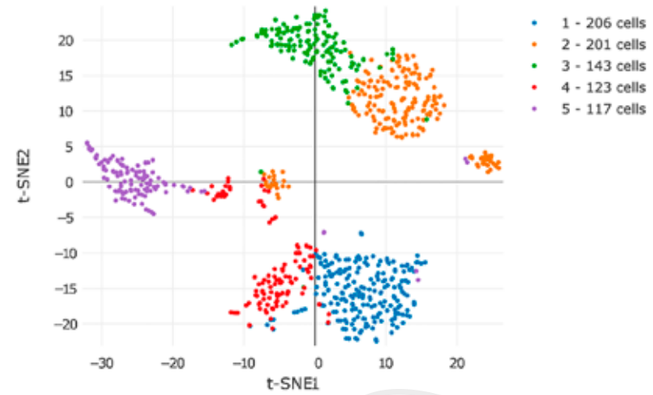
10 Year Highlights

The ACRF Cancer Genomics Facility was opened in 2012 as a partnership between SA Pathology and the University of South Australia, funded by $3.5 million from the ACRF and contributions from the State Government of South Australia, the Federal Government, MedVet Laboratories, the Cancer Council of SA and the CRC for Biomarker Discovery. Over the last eight years the Facility has pioneered the introduction and delivery of new genomics technologies and new research and diagnostic applications.

In 2014, working in close collaboration with the Technology Advancement Unit in the Genetics and Molecular Pathology Directorate of SA Pathology, the Facility achieved NATA accreditation for constitutional and cancer cytogenic screening tests using microarrays, and targeted NGS-based panels for detecting mutations in familial cancers, cardiomyopathy and other inherited disorders. The Facility was the first in Australia to receive accreditation for clinical whole exome sequencing, and later for RNA-seq, in 2018.

2017 saw the introduction of PacBio long read single molecule sequencing to the facility, funded by ACRF. This technology has enabled the sequencing of complex regions of the genome not possible with conventional short read NGS, and identification of chromosomal rearrangements implicated in cancer.

The Facility became the first in South Australia to acquire 10X Genomics Chromium system for single cell genomics in 2018. This ground-breaking technology enables the gene expression profiling of individual cells in a population or tissue, and optional simultaneous identification of cell surface proteins.



The Figure shows gene expression data from blood cells sequenced and analysed in the Genomics Facility, depicted with the help of the t-distributed stochastic neighbour embedding visualization technique. Different cell types are clearly visible as individual expression clusters. Reproduced with permission from Dr G. Cildir, CCB Inflammation and Human Ailments Laboratory.

Outcomes for the Community

The close relationship between the Centre for Cancer Biology and SA Pathology has enabled the rapid translation of new research findings to diagnostic tests. In 2018, the Facility performed over 3,500 diagnostic tests for inherited diseases and cancers, resulting in better informed reproductive choices and improved patient outcomes for South Australians. Researchers connected to the Facility are increasingly active participants in South Australian and national clinical research programs and clinical trials. The Facility is also involved in outreach to the research community providing bioinformatics and technology workshops.

10 Years of Research Excellence: 2009–2019

Research Funding

- **$185 M** Funding
- **450** Grants
- **50** Fellowships

Impact

- **1200** Publications
- **400** Seminars by international and national researchers
- **51** Patents
- **5** International Barossa Meetings

Researchers

- **220** Staff & Students per annum average
- **140** Degrees Undergraduate, Honours, Masters and PhD

Recognition

- **3** AAS Fellows Australian Academy of Science
- **4** AAHMS Fellows Australian Academy of Health and Medical Sciences
- **2** Order of Australia for Medical and Scientific Achievements

Clinical Trials

- **>40** Active Trials in phase 1, 2, 3 & 4 annually

2018 Publications

Professor Natasha Harvey and her team want to halt the spread of cancer by preventing the access of cancer cells to the blood and lymphatic vessel 'highways' in our bodies. They also aim to find ways to repair lymphatic vessels in order to treat lymphoedema, a major problem for cancer patients following the removal of lymph nodes.

Image courtesy of The Hospital Research Foundation

Publications

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Publications continued

Wallington-Beddoe CT, Sobieraj-Teague M, Kuss BJ, Pitson SM. Resistance to proteasome inhibitors and other targeted therapies in myeloma. *British Journal of Haematology*. 182: 11-28, 2018.

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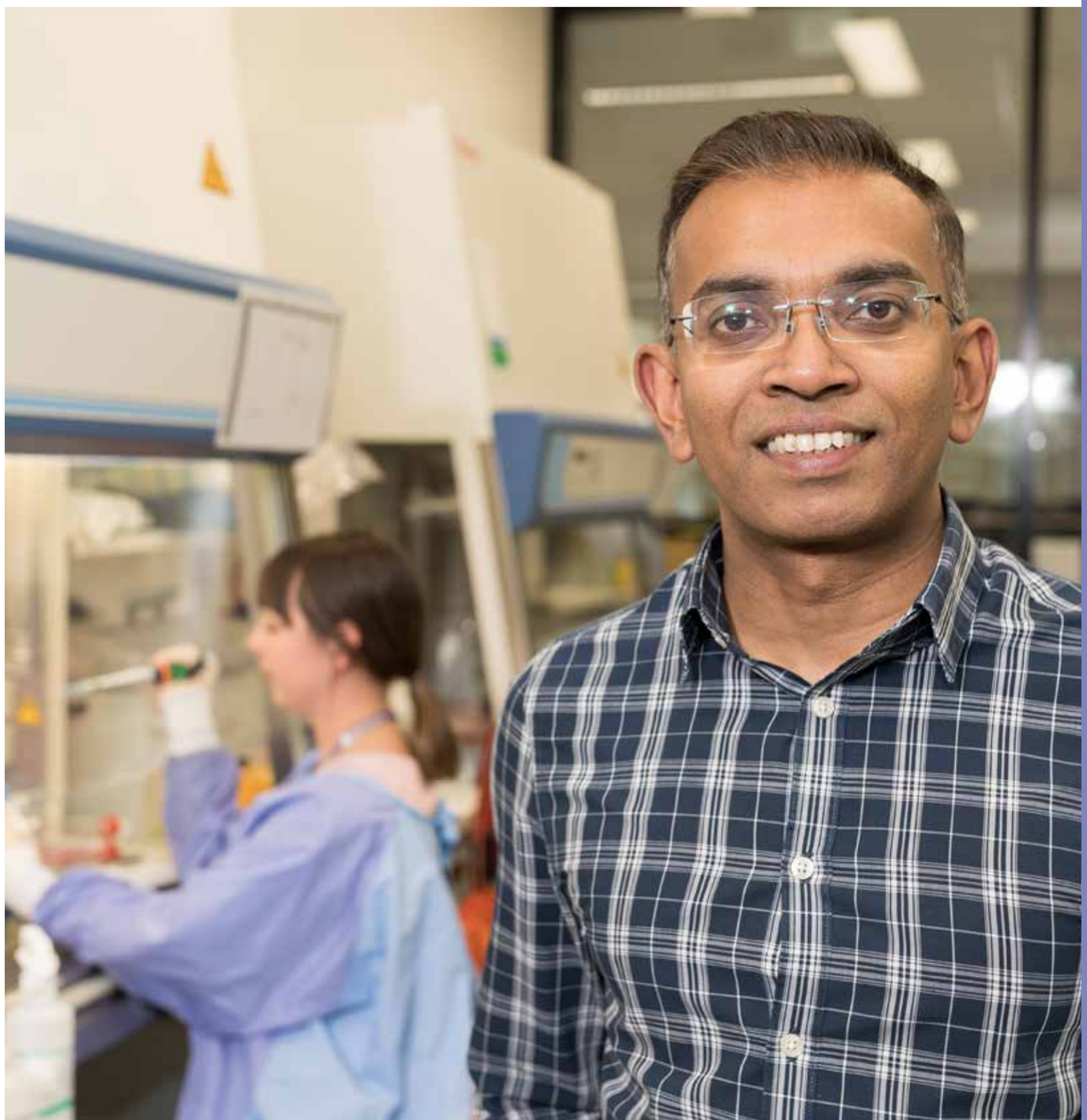
New Grants and Fellowships

Associate Professor Michael Samuel and his team are working to determine how cancers hijack the functions of normal cells in their vicinity to help them grow and spread. This will help them identify new ways to stop cancer in its tracks.

Image courtesy of The Hospital Research Foundation



New Grants and Fellowships

Investigator	Title	Granting Body
Arrua RD, Gomez GA, Hilder EF	New Adventures Fund 2018	University of South Australia
Arts P	Early Career Fellowship: Characterising haematological malignancies through genetic and immunological evaluation	The Hospital Research Foundation
Beattie D, Krasowska M, Benbow N, Tobin M, Vongsvivut J, Samuel MS	Structural signatures of skin and skin cancers from FTIR microscopy studies	Australian Synchrotron
Bonder C	Visualising CAR-T cells in solid tumours *in vivo*	Carina Biotech Pty Ltd.
Bonder C, Voelcker N, Ebert L	Desmoglein-2; an unsuspected regulator of melanoma	National Health & Medical Research Council
Boyle ST	Early Career Researcher Travel Award	The CASS Foundation
Bracken CP, Goodall GJ	MicroRNA combinations as a therapeutic strategy	Worldwide Cancer Research
Bracken CP, Goodall GJ	Transcriptional regulation by microRNAs	Australian Research Council
Branford S, White D, Mercer T, Schreiber A	Towards a new genomic classification of risk for patients with chronic myeloid leukaemia	Cancer Council South Australia
Brooks DA, Dale B, Johnson I, Orgeig S, Parkinson-Lawrence E, O'Leary JJ, Selemidis S, Brooks RD, Logan J, Sorvina A, Martino C, Olver I, Reynolds P, Lazniewska J, Ross D	Developing biomarkers and therapeutics for primary and metastatic lung cancer	University of South Australia, RTIS Seed funding
Brooks DA, O'Leary JJ, Brooks RD, Logan J, Sorvina A, Martino C, Butler L, Johnson I, Selemidis S, Parkinson-Lawrence EJ, Orgeig S, Lazniewska J, Thomas C, Dale B, Reynolds P, Esterman A, Olver I	Companion diagnostics and therapeutics for cancer	Envision Sciences Pty. Ltd.
Brown AL, Scott HS	SA Genomics Health Alliance, Haematological Malignancies Node	Leukaemia Foundation of Australia
Brown AL, Scott HS	RUNX1 mutation data aggregation, analysis and sharing project	RUNX1 Research Program
Brown AL, Scott HS, Hahn C, Schreiber A, Godley L	Biological characterisation and therapeutic options for high risk, DDX41 mutated, haematological malignancies.	RAH Research Foundation
Brown AL, Scott HS, Hahn C, Schreiber A, Godley L	Biological characterisation and therapeutic options for high risk, DDX41 mutated, haematological malignancies	Cancer Council South Australia
Brown MP, Ziegler DS, Gargett T	Clinical testing of new T-cell therapy for adult and paediatric patients with aggressive primary brain cancer	The Hospital Research Foundation, Biomed City Round
D'Andrea R, Gonda T, Moore A	Implications of BRCA1/2 germline variants in childhood AML biology and treatment	Tour de Cure
D'Andrea RJ, Verrills N, Dun MD, Ross D	An integrated proteomics approach to identify novel targets for treatment of Acute Myeloid Leukaemia	Takeda, COCKPI-T Australia
Ebert LM, Brown MP, Tan LY	Scientific correlates of a new triple immuno-oncology combination therapy in metastatic melanoma patients	Royal Adelaide Hospital Research Committee
Flynn B, Kelly D, Wang B, Reid C, Pitson SM	Dihydroceramide desaturase-1 (Des1) inhibitors for the treatment of fibrotic disease	National Health & Medical Research Council
Flynn B, Pitson SM	Establishment and research of Cincera Therapeutics Pty Ltd	Medical Research Commercialisation Fund
Gomez GA, Arrua RD, Ebert LM, Brown MP, Hoffmann P, Samuel MS, Krasowska M	Development of new hydrogels to selectively extract and kill invasive glioblastoma cells from normal brain tissue	University of South Australia, RTIS Scheme
Gomez GA, Bardy C, Arrua RD, Shen C, Pitson SM	A national brain-organoid based high-throughput platform for personalised drug and genetic screening in glioblastoma	Cure Brain Cancer Foundation
Gomez GA, Bardy C, Arrua RD, Shen C, Pitson SM	A national brain-organoid based high-throughput platform for personalised drug and genetic screening in glioblastoma	Tour de Cure Matching Grant
Gomez GA, Samuel MS, Schwarz Q, Khew-Goodall Y, Kumar S, Bonder C, Pitson SM, Dorstyn L, Harvey N, Brooks D, Plush S, Bader C, Butler L, Bardy C, Gecz J, Zannettino A, Jolly L	Deep live-imaging of tumour biology	Beat Cancer Project, Cancer Council South Australia and The Hospital Research Foundation Matching Fund
Gonda T, D'Andrea RJ	Discovery Fast Track Challenge - Targeting MYB in AML	GlaxoSmithKline
Goodall GJ	Direct transcriptional regulation by microRNAs	Beat Cancer Project, Cancer Council South Australia
Gregory PA	Discovery of optimal targets to better diagnose and treat metastatic cancer	Beat Cancer Principal Research Fellowship
Gregory PA, Anderson RL, Goodall GJ, O'Toole S	miR-342 – a novel suppressor of a pro-metastatic gene network in triple-negative breast cancer	National Breast Cancer Foundation
Gregory PA, Goodall GJ, Hollier BG	Characterising an RNA splicing pathway driving prostate cancer metastasis and therapy resistance	National Health & Medical Research Council
Hahn CN, Scott HS, Brown AL, Schreiber AW, Hiwase DK, Poplawski NK, Godley LA, Kassahn KS, Fitzgibbon J, Horsfield JA	Germline mutations in familial haematological malignancies identifies new pan-cancer predisposition genes and may alter clinical decision making, including for known cancer genes	National Health & Medical Research Council
Hogan BM, Harvey NL	Understanding the role of tissue growth pathways in expansion of the lymphatic vasculature	National Health & Medical Research Council
Kolesnikoff N	Theo Murphy Initiative Travel Bursary	Australian Academy of Science
Krasowska M, Beattie D, Benbow N, Samuel MS, Sizeland K	SAXS of collagen structures in healthy and cancerous murine skin	Australian Synchrotron
Kumar S	Ubiquitin-regulated sodium homeostasis in kidney disease	National Health & Medical Research Council
Kumar S, Dorstyn L	Deciphering the mechanisms of caspase-2-mediated suppression of aneuploidy and tumourigenesis.	National Health & Medical Research Council
Kumar S, Manning JA, Finnie J	Dietary sodium as a modulator of kidney disease.	The Hospital Research Foundation
Lawrence D, King-Smith S, Scott H, Schreiber A, Kassahn K, Geoghegan J	Australian Genomics – Variant Sharing Platform	Australian Genomic Health Alliance
Lock R, Haber M, Marshall G, Norris M, Moore A, Ekert P, D'Andrea R, Lopez A, Arndt G	A personalised medicine approach to the treatment of acute myeloid leukaemia in children	Tour de Cure
Lynn D, Rogers G, Marshall H, Tumes D	How does the microbiota modulate vaccine responses in human infants: A systems vaccinology approach	National Health & Medical Research Council
Olver IN, Joshi R, Brown MP, Karapetis C, Price T, Singhal N, Osborn M, Proprawski D, Brown A, Sharplin G	Establishing the South Australian Cancer Trials Network	Cancer Council South Australia
Orgeig S, Parkinson-Lawrence E, Reynolds P, Stringer A, Hoffman P, Brooks DA, Logan J, Martino C, Sorvina A, Johnson I, Olver I, O'Leary J, Pursey P, Selemidis S, Bozinovski S	Understanding the biology of lung cancer initiation and progression	University of South Australia Cancer Research Institute Strategic Funding Grant
Perkins A, Ross D, Lane S, Forsyth C, Wei A, Curtis D, Shortt J, Erber W, Stevenson W	Improving survival in myelofibrosis	MRFF Clinical Trials, Low Survival Cancers and Diseases (LSCD) Grant Opportunity
Pitman M, Oehler M, Pitson SM	Harnessing sphingosine kinase regulation of Mcl-1 to re-sensitise chemoresistant ovarian cancer	Royal Adelaide Hospital Research Fund
Pitman MR	Florey Fellowship	Royal Adelaide Hospital Research Fund
Pitson SM	Targeting sphingosine kinase in acute myeloid leukaemia	Fay Fuller Foundation
Pitson SM	Targeting sphingosine kinase in acute myeloid leukaemia	The Hospital Research Foundation

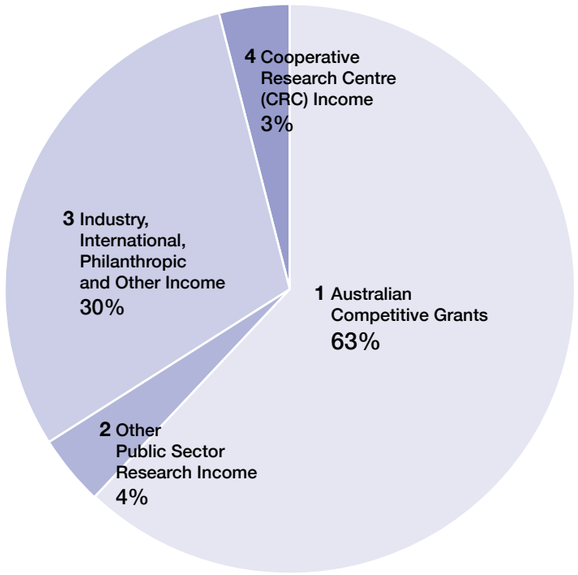
New Grants and Fellowships continued

Investigator	Title	Granting Body
Pitson SM, Powell JA, Tea M	Stereotactic alignment and injection system for the generation of orthotopic xenografts of human brain tumours	Neurosurgical Research Foundation
Pitson SM, Spencer A, Wallington-Beddoe C	A new therapeutic target for proteasome inhibitor resistant multiple myeloma	National Health & Medical Research Council
Powell JA	Developing new therapies for the treatment of acute myeloid leukaemia	Royal Adelaide Hospital Research Fund
Ross D, D'Andrea RJ, Lopez AF	A new immune therapy targeting the myelofibrosis stem cell with CD123 antibody treatment	The Hospital Research Foundation
Samuel MS	Rho-ROCK signalling in the promotion of intestinal cancer progression	Vonbri Foundation/The Hospital Research Foundation
Seyfang J, Reynolds PN	Characterisation of endothelial cells and exosome biology in patients with secondary PH from chronic thrombosis and emphysema.	Royal Adelaide Hospital
Shanmuganathan N, Branford S, Hughes T	Identify if second-generation tyrosine kinase inhibitors modify the effect of genomic events observed in chronic-phase chronic myeloid leukaemia	Royal Adelaide Hospital Research Fund
Tumes D	Towards personalised medicine for allergic airway disease and harnessing allergic pathways to treat cancer	The Hospital Reseach Foundation
Yip D	Establishing the clinical potential of sphingomimetics in children's eczema	Channel 7 Children's Research Foundation
Yip D	Mast cells and inflammation	The Hospital Research Foundation

Financial Highlights

Research Income 2018 Calendar Year

1	Australian Competitive Grants	7,821,102
2	Other Public Sector Research Income	418,075
3	Industry, International, Philanthropic and Other Income	3,740,305
4	Cooperative Research Centre (CRC) Income	390,092
	Total	AUD 12,369,574



Seminar Program

Dr Jayantha Gunaratne
Principal Investigator, Translational Biomedical Proteomics, Institute of Molecular and Cell Biology (IMCB), Agency for Science, Technology and Research (A*STAR); Adjunct A/Prof, Yong Loo Lin School of Medicine, National University of Singapore (NUS)
Advanced proteomics mass spectrometry in biomedical research: from discovery to translation 7/2/2018

Associate Professor Julia Horsfield
Director, Genetics Otago; Associate Dean Postgraduate, Department of Pathology, Dunedin School of Medicine, The University of Otago, New Zealand
Zebrafish models for chromatin architecture in gene transcription and developmental syndromes 15/2/2018

Dr Duncan Sparrow
British Heart Foundation Senior Research Fellow, University of Oxford
Environmental influences on mouse embryonic development 13/4/2018

Dr Marina Pajic
Group Leader, Personalised Cancer Therapeutics, Cancer Division, Garvan Institute of Medical Research
Characterisation of mechanisms behind treatment failure in pancreatic cancer: the long road to precision medicine 24/5/2018

Dr Damon Tumes
Head, Allergy and Cancer Immunology Laboratory, Centre for Cancer Biology
Epigenetic and microbiome-mediated regulation of adaptive immunity 31/5/2018

Professor Mike Ryan
Biochemistry and Molecular Biology, Monash Biomedicine Discovery Institute, Monash University
Mitochondria, dynamics and disease 14/6/2018

Associate Professor Phil Darcy
NHMRC Principal Research Fellow, Laboratory Head, Cancer Immunotherapy, Peter MacCallum Cancer Centre
Development of CAR T cell therapy for cancer 28/6/2018

Associate Professor Kristen Radford
Cancer Immunotherapies Group Leader, Mater Foundation; Principal Research Fellow, Mater Research Institute, The University of Queensland
Targeting human CD141+ dendritic cells for cancer immunotherapy 5/7/2018

Professor David Vaux
Deputy Director and Joint Division Head, Cell Signalling and Cell Death, Walter and Eliza Hall Institute of Medical Research
Researchers behaving badly 19/7/2018

Dr Morgan Huse
Laboratory Head, Memorial Sloan Kettering Cancer Center, USA
Mechanical regulation of cytotoxic T cell function 24/7/2018

Professor Peter Leedman
Director, Harry Perkins Institute of Medical Research; Laboratory Head, Laboratory for Cancer Medicine
Keynote speaker, CCB Staff Meeting 26/7/2018

Associate Professor Meredith O'Keeffe
Biochemistry and Molecular Biology, Monash Biomedicine Discovery Institute, Monash University
Dendritic cells, interferon-lambda and immunotherapy 2/8/2018

Dr Leonie Quinn
Cancer Models Group, ACRF Department of Cancer Biology and Therapeutics, John Curtin School of Medical Research, The Australian National University
Surprising roles for single stranded DNA binding proteins in germline and neuroblast stem cell fate 9/8/2018

Associate Professor Jeff Babon
Laboratory Head, Structural Biology, Cancer and Haematology, Walter and Eliza Hall Institute of Medical Research
Regulation of cytokine (JAK/STAT) signalling 16/8/2018

Professor Merlin Crossley
Deputy Vice-Chancellor Academic, University of New South Wales
The slow road to curing genetic diseases by CRISPR gene editing 23/8/2018

Associate Professor James Murphy
Laboratory Head, Cell Signalling and Cell Death, Walter and Eliza Hall Institute of Medical Research
Dawn of the dead: cell death by the zombie protein, MLKL 6/9/2018

Associate Professor Oliver Sieber
Acting Division Head, Systems Biology and Personalised Medicine, Walter and Eliza Hall Institute of Medical Research
Defining the molecular basis of chromosome instability in colorectal cancer 13/9/2018

Dr Kate Poole
School of Medical Sciences, University of New South Wales
A cellular sense of touch: mechanotransduction at the cell-substrate interface 4/10/2018

Professor Helen Rizos
Head, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Macquarie University
Treatment response and resistance in melanoma 18/10/2018

Professor Richard Iggo
Professor of Cell Biology, University of Bordeaux
Intraductal and organoid models of human breast cancer 25/10/2018

Dr Maté Biro
EMBL Australia Group Leader – Cell Motility and Mechanobiology, The University of New South Wales
Mechanobiology of cytotoxic T cell and tumour cell movements and interactions 1/11/2018

Professor Nicole La Gruta
ARC Future Fellow, Biochemistry and Molecular Biology, Monash Biomedicine Discovery Institute
CD8+ T cell immunity: what makes it and what breaks it 8/11/2018

Professor Simon Barry
Head, Molecular Immunology Group, Robinson Research Institute; Member, RRI Executive, Theme Leader, Healthy Adolescents and Children, Co-Director, Gene Silencing and Expression Facility, The University of Adelaide
Using 3D Immunogenomics to map autoimmune disease risk to its target genes and developing CAR-T immunotherapies for cancer 15/11/2018

Professor Glenn Marshall
Paediatric Haematologist/Oncologist, Kids Cancer Centre, Sydney Children's Hospital; Professor of Paediatrics, University of New South Wales; Head, Molecular Carcinogenesis Program and Translational Research, Children's Cancer Institute Australia; Director, Kids Cancer Alliance, Cancer Institute NSW
Therapeutic and prevention strategies for high speed carcinogenesis in early life 22/11/2018

Professor Joe Trapani
Group Leader, Cancer Immunology Program, Peter MacCallum Cancer Centre
Effector functions of CTL/NK cells. Friend or foe? 29/11/2018

Dr Guillermo Gomez
Head, Tissue Architecture and Organ Function Laboratory, Centre for Cancer Biology
Cross-disciplinary approaches for preclinical assessment and possible treatment of aggressive brain cancers 6/12/2018

Professor Matthias Ernst
Scientific Director, Olivia Newton-John Cancer Research Institute
Towards new therapies – manipulating the tumour microenvironment 13/12/2018

Invited Presentations

ACRF Genomics Facility

Dr Andreas Schreiber

Co-convenor and Session Chair

Australasian Genomic Technologies Association 2018, Adelaide, Australia, November

Acute Leukaemia Laboratory

Professor Richard D'Andrea

Session Chair

8th New Directions in Leukaemia Research (NDLR), Brisbane, Australia, March

Invited Speaker

Hunter Medical Research Institute, Regulation and targeting of DNA repair in AML, Newcastle Australia, September

Associate Professor David Ross

Session Chair

60th American Society of Hematology (ASH) Annual Scientific Meeting and Exposition, San Diego, CA, USA, December

Invited Speaker

Blood 2018, Haematology Society of Australia and New Zealand (HSANZ), Brisbane, Australia, May

National Haematology Expert Meeting, Malaysian Society of Haematology, Malaysia, July

Allergy and Cancer Immunology Laboratory

Dr Damon Tumes

Invited Speaker

80th Chiba University Leading Graduate School Seminar, Chiba, Japan, November

Centre for Cancer Biology Seminar Program, Adelaide, Australia, May

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall

Invited Speaker

18th Hunter Cell Biology Meeting, Hunter Valley, Australia, March

FASEB Protein Phosphatase, Snowmass, USA, July

FASEB Protein Phosphorylation Networks, Snowmass, USA, July

Cytokine Receptor Laboratory

Professor Angel Lopez AO

Invited Speaker

CSL Limited, Melbourne, March

From Receptors and Kinases towards Transcriptional Regulators: Cancer Genome Landscapes and their Therapeutic Targets, Styria, Austria, May

EMBO Conference: Cellular Signalling and Cancer Therapy, Cavtat, Croatia, September

9th Garvan Signalling Symposium, Sydney, November

Dr Tim Hercus

Invited Speaker

Australian Institute of Medical Scientists, Adelaide, Australia, May

Blood Club, Adelaide, Australia, June

Dr Winnie Kan

Session Co-Chair

8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, Australia, November

Dr Denis Tvorogov

Invited speaker

Basil Hetzel Institute, Adelaide, Australia, April

The Haematology Society of Australia & New Zealand (HSANZ, 2018), Adelaide, Australia, September

Gene Regulation Section

Professor Greg Goodall

Plenary Speaker

2nd Japan-Australia RNA Meeting, Sapporo, Japan, November

Guest Speaker

Julian Wells Medal Lecturer, 39th Annual Lorne Genome Conference, Lorne, Australia, February

Gene Regulation in Cancer Group

Dr Philip Gregory

Session Chair

ASMR SA meeting, Adelaide, June

Invited Speaker

ONJCRI institute seminar, Melbourne, July

Inflammation and Human Ailments Laboratory

Professor Vinay Tergaonkar

Invited Speaker

First International (Shenzhen) Forum of Da Meisha Regenerative Medicine, China, January

Trends in Biochemical and Biomedical Research: Advances and Challenges (TBBR), Benaras, India, February

University of Macau, Faculty of Health Sciences, (Host, Deng Chuxia), Macau, March

EMBO: workshop on pseudo-enzymes, Sardinia, Italy, May

University of Zurich, Department of Molecular Mechanisms of Disease, (Host, Michael Hottiger), Switzerland, October

Biozentrum, University of Basel, (Host, Mihaela Zavolan), Switzerland, October

Cold Spring Harbor Asia Conference, Suzhou, China, October

9th international symposium on DNA Damage Response & Human Disease, Shenzen, China, November

Keynote speaker

4th European NF-kappaB subunit workshop, Grasse, France, October

Dr Nirmal Robinson

Invited Speaker

70th Indian Pharmaceutical Congress, New Delhi, India, December

JSS Academy of Higher Education and Research, Mysuru, India, December

2nd International Symposium on the future of regenerative medicine, Ostuni, Italy, October

Basil Hetzel Institute for Translational Health Research, (Host: Ehud Hauben), Adelaide, Australia, August

University of Helsinki, (Host: Vidya Velagapudi), Helsinki, Finland, May

Keynote Speaker

Gene Manipulation Using CRISPR-Cas9, Ooty, India, December

Leukaemia Unit, Genetics and Molecular Pathology

Associate Professor Susan Branford

Invited Speaker

Mater Hospital Seminar, Brisbane, Australia, April

Journal Club Meeting, Austin Hospital, Melbourne, Australia, May

Blood Cancer Genomics Symposium, Peter MacCallum Cancer Centre, Melbourne, Australia, June

Post European Hematology Association Meeting, Adelaide, Australia, August

CML Opinion Leaders Training Program, Adelaide, Australia, August

The Master Clinician Alliance of Canada Speaker Tour on Chronic Myeloid Leukaemia, Ontario, Canada, October

Oncology, Haematology, Palliative Care Meeting, Royal Hobart Hospital, Hobart, Australia, October

Molecular Monitoring, Singapore, November

CML Genomics Alliance Meeting, San Diego, USA, December

Session Chair

Inaugural CML Genomics Alliance Meeting, Stockholm, Sweden, June

American Society of Hematology, San Diego, USA, December

CML Genomics Alliance Meeting, San Diego, USA, December

Lung Research Laboratory

Professor Paul Reynolds

Session Chair

Advances in Interstitial Lung Disease, Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide, Australia, September

Lymphatic Development Laboratory

Professor Natasha Harvey

Invited Speaker

Gordon Research Conference: Lymphatics, Barga, Italy, March

Olivia Newton John Cancer Research Institute Seminar Series, Melbourne, Australia, May

International Vascular Biology Meeting, Helsinki, Finland, June

University of Turku, Turku, Finland, June

Walter and Eliza Hall Institute Postgraduate Seminar Series, Melbourne, Australia, July

Peter MacCallum Cancer Centre Seminar Series, Melbourne, Australia, August

Institute for Molecular Bioscience Seminar Series, Brisbane, Australia, September

Adelaide Blood Club, Adelaide, Australia, September

Lymphoedema Education Day, Adelaide, Australia, September

Indian Society for Developmental Biology Meeting, Kanpur, India, December

Lipedema Foundation Scientific Retreat, Washington DC, USA, December

Penn Cardiovascular Institute Seminar Series, University of Pennsylvania, Philadelphia, USA, December

Session Chair

International Vascular Biology Meeting, Helsinki, Finland, June

Australian Vascular Biology Meeting, Adelaide, Australia, November

Convenor

18th Hunter Cell Biology Meeting, Hunter Valley, Australia, March

Conference Vice-Chair

Gordon Research Conference: Lymphatics, Barga, Italy, March

Dr Genevieve Secker

Session Chair

8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, November

Dr Drew Sutton

Session Chair

8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, November

Ms Jan Kazenwadel

Session Chair

Gordon Research Seminar: Lymphatics, Barga, Italy, March

Molecular Pathology Research Laboratory

Professor Hamish Scott

Invited Speaker

DBA Conference, Atlanta, USA, March

International Clinical Cardiovascular Genetics, Brisbane, Australia, May

Australian Precision Oncology Symposium, Sydney, Australia, September

JCSMR Friday Seminar Series, Canberra, Australia, September

RUNX1 Research Program Scientific Meeting, California, USA, November

Third Annual Australian Clinical Genomics Symposium, Brisbane, Australia, November

60th ASH Annual Meeting & Expo (Spotlight), San Diego, USA, December

Organising Chair

RCPA Pathology Update 2018, Sydney, Australia, March

Third Annual Australian Clinical Genomics Symposium, Brisbane, Australia, November

Chair

Australian Precision Oncology Symposium, Sydney, Australia, September

RUNX1 Research Program Scientific Meeting, California, USA, November

Third Annual Australian Clinical Genomics Symposium, Brisbane, Australia, November

Lipedema Foundation 2018 Research Retreat, Washington DC, USA, December

Dr Chris Hahn

Invited Speaker

Molecular genetics and strategies for mutation detection, RCPA AACB Chemical Pathology Course, Adelaide, Australia, February

Chair

15th Annual Human Genetics Society of Australasia Symposium (SA Branch), Genomics Session, Adelaide, Australia, September

Dr Anna Brown

Invited Speaker

7th New Directions in Leukaemia Research Meeting, Brisbane, Australia, March

Novartis Molecular Haematology Meeting, Brisbane, Australia, October

2nd RUNX1 Research Program Annual Meeting, Santa Barbara, USA, November

3rd American Society of Hematology, Friday Inherited Hematological Malignancies Workshop, San Diego, USA, December

Ms Alicia Byrne

Invited Speaker

Human Genetics Society of Australasia 42nd Annual Scientific Meeting, Sydney, Australia August

Leena Peltonen School of Human Genomics, Les Diablerets, Switzerland, August

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

Australasian Genomic Technologies Association 2018 Annual Conference, Adelaide, Australia, November

Dr Sunita De Sousa

Invited Speaker

Molecular Genetics in Endocrinology, RCPA AACB Chemical Pathology Course, Adelaide, Australia, February

Molecular Regulation Laboratory

Professor Sharad Kumar AM

Invited Speaker

30th Lorne Cancer Conference, Cumberland Lorne Resort, Lorne, Australia, February

18th Hunter Cell Biology Meeting, Hunter Valley, Australia, March

The John Curtin School of Medical Research (JCSMR) Director's Seminar, Australian National University, Canberra, Australia, May

Australia-Japan Meeting on Cell Death, University of Tokyo, Japan, May

International Cell Death Society Meeting, About canonical, non-canonical, and immunogenic cell death: basic mechanisms and translational applications, Seoul, South Korea, May

9th CDD Meeting on Gene and Environment in Cancer, Clare College, Cambridge, UK, September

Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Symposium, Canberra, Australia, November

Indian Society for Developmental Biologists Biennial Meeting 2018 (InSDB2018), Kanpur, India, December

Invited Lecture

Institute of Immunology, University Medical Center, Mainz, Germany, September

IGER, Nagoya University, Nagoya, Japan, May

Invited Session Chair

18th Hunter Meeting, Crowne Plaza, Hunter Valley, Australia, March

Dr Donna Denton

Invited Speaker

2018 Australian Fly Meeting, Warburton, Australia, August

Dr Loretta Dorstyn

Chair

Plenary talk, 8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, November

Dr Natalie Foot

Session Chair and Judge

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

Dr Yoon Lim

Session Chair

8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, Australia, November

Selected Speaker

ECR Session, Australia-Japan Meeting on Cell Death, Tokyo, Japan, May

Dr Jantina Manning

Invited Speaker

Department of Physiology, University of Otago, Otago, New Zealand, December

Selected Speaker

Australian and New Zealand Society of Nephrology (ANZSN): Nephrology: from the Laboratory to the Clinic, Blenheim, Marlborough, New Zealand, December

Ms Cindy Xu

Selected Speaker

ECR Session, Australia-Japan Meeting on Cell Death, Tokyo, Japan, May

Molecular Signalling Laboratory

Professor Stuart Pitson

Invited Speaker

Australia and New Zealand Gynaecological Oncology Group (ANZGOG) Annual Conference, Brisbane, Australia, April

Cutaneous Biology 2018 Annual Scientific Meeting, Stradbroke Island, Australia, October

9th Garvan Signalling Symposium, Sydney, Australia, November

Session co-chair

Ross Wishart Medal Symposium, ASMR SA Conference, Adelaide, Australia, June

Invited Presentations continued

Cutaneous Biology 2018 Annual Scientific Meeting, Stradbroke Island, Australia, October
9th Garvan Signalling Symposium, Sydney, Australia, November

Dr Thao Nguyen
Session Co-chair
ASMR Annual Scientific Meeting, Adelaide, Australia, June

Dr Melissa Pitman
Invited Speaker
Royal Adelaide Hospital Research Showcase, Adelaide, Australia, November

Dr Jason Powell
Invited Speaker
Haematology Society of Australia and New Zealand, Adelaide, Australia, August
Royal Adelaide Hospital Research Fund, Adelaide, Australia, July
Session Co-chair
ASMR Annual Scientific Meeting, Adelaide, Australia, June

Dr Melinda Tea
Invited Speaker
Neurosurgical Research Foundation Annual General Meeting, Adelaide, Australia, September

Dr Joanna Woodcock
Invited Speaker
ComBio 2018, Sydney, Australia, September

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz
Invited Speaker
ComBio 2018, Sydney, Australia, October
HUPO human brain proteome project, Adelaide, Australia, November
Session Co-chair
18th Hunter Cell Biology Meeting, Hunter Valley, Australia, March
ASMR Ross Wishart award seminar 2018, Adelaide, Australia, April

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez
Invited Speaker
Thinking beyond the dish: taking *in vitro* neural differentiation to the next level, Company of Biologist, Wiston House, UK, February
18th Hunter Meeting, Crowne Plaza, Hunter Valley, Australia, March
Session Co-Chair
18th Hunter Cell Biology Meeting, Hunter Valley, Australia, March

Translational Oncology Laboratory

Professor Michael P Brown
Invited Speaker
Eradicate Cancer Conference, Melbourne, Australia, March
US-Australia Cancer Moonshot Roundtable, Canberra, Australia, March
2018 Current Trends in Immuno-Oncology, Sydney, Australia, May
CAR-T Summit @MRCF, Melbourne, Australia, June
Medical Oncology Group of Australia Annual Scientific Meeting, Adelaide, Australia, August
First Australian Precision Oncology Symposium, Sydney, Australia, September
NSW Agency for Clinical Innovation Blood and Marrow Transplant Network Symposium, Sydney, Australia, September
US-Australia Cancer Moonshot Roundtable, Sydney, Australia, October
Session Co-Chair
Eradicate Cancer Conference, Melbourne, Australia, March
First Australian Precision Oncology Symposium, Sydney, Australia, September
Merck, Sharp & Dohme, Conversations in Immuno-Oncology, Adelaide, Australia, September

Dr Lisa Ebert
Invited Speaker
Australasian Cytometry Society Conference, Adelaide, Australia, October
Session Co-chair
Australian Society for Medical Research (ASMR) SA Scientific Meeting, Adelaide, Australia, June

Dr Tessa Gargett
Invited Speaker
Eradicate Cancer Conference, Melbourne, Australia, March
Australasian Melanoma Conference, Melbourne, Australia, August
Australasian Cytometry Society Conference, Adelaide, Australia, October
International Society for Cell Therapy, Regional Meeting, Sydney, Australia, November
Session Co-chair
Eradicate Cancer Conference, Melbourne, Australia, March

Dr Alex Staudacher
Invited Speaker
9th Annual World ADC summit, San Diego, USA, November

Tumour Microenvironment Laboratory

Associate Professor Michael Samuel
Invited Speaker
18th Hunter Cell Biology Meeting, Hunter Valley, Australia, March
Mechanobiology Down Under 2018, Sydney, Australia, May
The Francis Crick Institute Special Seminar, London, UK, June
Walter and Eliza Hall Institute Special Seminar, Melbourne, Australia, July
20th Annual Scientific Meeting of the Australasian Gastro-Intestinal Trials Group (AGITG), Brisbane, Australia, August
Australia and New Zealand Society for Cell and Developmental Biology, ACT state meeting, Canberra, Australia, November
9th Garvan Signalling Symposium, Sydney, Australia, November
Selected Speaker
Cutaneous Biology 2018, North Stradbroke Island, Australia, October
Plenary Chair
Plenary by Prof Val Weaver, UCSF, USA at ComBio 2018, Sydney, Australia, September
Session Chair
Lorne Cancer Conference, Lorne, Australia, February
9th Garvan Signalling Symposium, Sydney, Australia, November

Dr Sarah Boyle
Selected Speaker
Mammary Gland Biology Gordon Research Conference Seminar, Lucca, Italy, May
Australian Society for Medical Research, Annual Adelaide Meeting, Adelaide, Australia, June
ComBio 2018, Sydney, Australia, September
South Australia Breast Cancer Study Group, Scientific Symposium, Adelaide, Australia, October
Convener
8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, November

Dr Natasha Kolesnikoff
Selected Speaker
Cutaneous Biology 2018, North Stradbroke Island, Australia, October
8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Meeting, Adelaide, November

Ms Valentina Poltavets
Selected Speaker
EMBL Australia Postgraduate Course 2018, Sydney, Australia, July

Vascular Biology and Cell Trafficking Laboratory

Professor Claudine Bonder
Invited Speaker
Walter and Eliza Hall Institute postgraduate lecture series, cell and developmental biology, Melbourne, Australia, March
University of Amsterdam, Amsterdam, The Netherlands, June
Australasian Melanoma Conference, Melbourne, Australia, October
Australian and New Zealand Society for Immunology, Perth, Australia, December
Australian Network of Cardiac and Vascular Developmental Biologists, Melbourne, Australia, December

Centre for Cancer Biology 2018 Awards

Professor Claudine Bonder and her team want to stop blood vessels from being 'hijacked' by cancer cells to spread and metastasize to vital organs such as the lungs and brain.

Image courtesy of The Hospital Research Foundation

Awards

Allergy and Cancer Immunology Laboratory

Dr Dave Yip

Best Abstract Prize, The European Academy of Allergy and Clinical Immunology (EAACI) Congress

Cytokine Receptor Laboratory

Dr Winnie Kan

Winner, Most Outstanding Postdoctoral Poster Presentation award, 8th ANZSCDB Meeting, Adelaide, Australia

Gene Regulation Section

Professor Greg Goodall

Julian Wells Medal, Lorne Genome Conference, Lorne, Australia

Fellow of the Australian Academy of Science

Inflammation and Human Ailments Laboratory

Dr Nirmal Robinson

Outstanding Researcher Award presented by JSS Academy of Higher Education and Research, Mysuru, India, December

Lymphatic Development Laboratory

Dr Kelly Betterman

Runner Up, Carl Zeiss Image Competition, 8th ANZSCDB Meeting, Adelaide, Australia

Dr Anna Oszmiana

Winner, Carl Zeiss Image Competition, 8th ANZSCDB Meeting, Adelaide, Australia

Dr Genevieve Secker

Runner Up, Best Postdoctoral Poster, 8th ANZSCDB Meeting, Adelaide, Australia

Ms Jan Kazenwadel

Lymphatic Education & Research Network (LE&RN) Young Investigator Travel Award to attend Gordon Research Conference: Lymphatics, Barga, Italy

Molecular Pathology Research Laboratory

Ms Alicia Byrne

Karen Snow-Bailey Award, Best oral presentation by an ASDG member, Human Genetics Society of Australasia, 42nd Annual Scientific Meeting, Sydney, Australia

Best Student Oral Presentation, Australasian Genomic Technologies Association 2018 Annual Conference, Adelaide, Australia

Human Genetics Society of Australasia Annual Scientific Meeting Travel Award

Molecular Regulation Laboratory

Professor Sharad Kumar AM

Member of the Order of Australia (AM)

President's Award, South Australian Indian Medical Association (SAIMA)

Honoured by Indian Australian Association of South Australia for significant service to medical research in South Australia

Dr Natalie Foot

Winner, Poster Award, Australasian Extracellular Vesicles Conference, Sydney, Australia

Dr Yoon Lim

Travel Grant, Australia-Japan Meeting on Cell Death, Tokyo, Japan

Dr Jantina Manning

Most outstanding Oral Presentation (Post-graduate), 8th ANZSCDB Meeting, Adelaide, Australia

Early Career Researcher Prize, Sparrho Travel Grant, London, UK

Travel Grant, The Hospital Research Foundation, Adelaide, Australia

Ms Cindy Xu

Travel Grant, Australia-Japan Meeting on Cell Death, Tokyo, Japan.

Molecular Signalling Laboratory

Dr Thao Nguyen

Travel Grant, Australasian Society for Stem Cell Research and the National Stem Cell Foundation of Australia

Dr Joanna Woodcock

Finalist, Unsung Heroes, SA Science Excellence Awards

Translational Oncology Laboratory

Dr Alex Staudacher

Australian Scholarship and Science (CASS) Foundation Travel Grant

Tumour Microenvironment Laboratory

Dr Sarah Boyle

Centre for Cancer Biology Early Career Researcher Award for 2017

ANZSCDB Toshiya Yamada Prize for Best Postdoctoral Symposium Presentation, ComBio Conference, Sydney, Australia, September

Best Overall Presentation, South Australia Breast Cancer Study Group Scientific Symposium, Adelaide, Australia, October

Winner of 2018 GE Healthcare Cell Image Contest

Dr Zahied Johan

Winner of 2018 GE Healthcare Cell Image Contest

Dr Natasha Kolesnikoff

Runner Up, Most Outstanding Postdoctoral Oral Presentation, 8th ANZSCDB Meeting, Adelaide, Australia

Ms Valentina Poltavets

Awarded participation, EMBL Australia Postgraduate Course 2018, Sydney, Australia, July

Best Oral Presentation, The School of Pharmacy and Medical Sciences Bi-annual Symposium, Adelaide, Australia, September

Runner Up, Most Outstanding Student Oral Presentation, 8th ANZSCDB Meeting, Adelaide, Australia

Vascular Biology and Cell Trafficking Laboratory

Dr Camille Duluc

Winner, ASMR (Adelaide) Best Oral Presentation by an Early Career Researcher

Dr Eli Moore

Winner, CCB image competition for 2017 Annual Report cover

Winner, University of South Australia Images of Research Competition

Ms Kay Khine Myo Min

University of South Australia Presidential Award for Division of Health Sciences

Ms Danielle King

Winner, ASMR (Adelaide) Best Oral Presentation by an Honours student

Top Honours student in B Lab Med Sci course

Ms Emma Thompson

Winner, best presentation for New Ideas Grant at South Australian Breast Cancer Study Group annual meeting

Professor Peter Leedman presents the 2017 CCB Early Career Researcher Award to Dr Sarah Boyle

Dr Eli Moore wins the 2017 CCB Annual Report Cover Image Competition and the UniSA Images of Research Competition

Dr Sarah Boyle presents Dr Winnie Kan with the ANZSCDB award for the Most Outstanding Postdoctoral Poster Presentation

Dr Arvind Sehgal presents Professor Sharad Kumar AM with the President's Award from the South Australian Indian Medical Association (SAIMA)

The Hon Steven Marshall MP presents an award to the Genetics and Molecular Team at the Premier's Excellence Awards

Dr Sarah Boyle presents Ms Ellen Potoczky with the ANZSCDB award for the Most Outstanding Student Oral Presentation

Mr Benjamin Ung presents Dr Anna Oszmiana with the ANZSCDB award for the Carl Zeiss Image Competition

Professor Claudine Bonder congratulates Dr Lih Tan as she graduates with her PhD

Professor Peter Leedman presents the 2017 CCB Best Primary Research Publication Award to Dr Jason Powell

Service to the Community

ACRF Cancer Genomics Facility

Dr Andreas Schreiber

Co-convenor for Australasian Genomic Technologies Association 2018

Australasian Genomic Technologies Association Executive

Acute Leukaemia Laboratory

Professor Richard D'Andrea

NHMRC Grant Review Panel

Australasian Leukaemia Lymphoma Group (ALLG) Scientific Committee on Laboratory Sciences

Celgene Advisory Board on AML

South Australia Cancer Research Biobank (SACRB) Executive Committee

Australian Familial Hematological Cancer Study Executive Committee

Centre for Cancer Biology, Mentoring Committee

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

Associate Professor David Ross

Associate Editor of Leukemia Research

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

Examiner, Royal College of Pathologists of Australasia

for familial haematological malignancies

International RUNX1 Research Foundation Sequencing Project Steering Committee

Allergy and Cancer Immunology Laboratory

Dr Damon Tumes

World Day of Immunology SA Branch Co-chair

NHMRC External Reviewer

Australian and New Zealand Society for Immunology South Australia and Northern Territory Branch councillor

FIVEaa radio interview with Rilka Warbanoff

Dr Dave Yip

Television interview on Seven News

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall

RAH Fellowships committee

University of South Australia HDR scholarships committee

Cytokine Receptor Laboratory

Professor Angel Lopez AO

Cancer Council Victoria Grant Interview Panel

ACRF Grant Interview Panel

Cure Brain Cancer Foundation Grant Interview Panel

Sylvia and Charles Viertel Charitable Foundation Interview Panel

Dr Winnie Kan

Secretary and committee member, Adelaide Protein Group

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

Gene Regulation Section

Professor Greg Goodall

Associate Editor, Oncogene

Associate Editor, Oncogenesis

NHMRC Assigners Academy

NBCF Peer Review Committee

AAHMS Mentorship Committee

Gene Regulation in Cancer Group

Dr Philip Gregory

Cancer Australia Grant Review Panel

Ambassador for Australian Prostate Cancer Research

Master of Ceremony for SASTA Oliphant Science Awards

Secretary of The EMT International Association (TEMTIA)

Gene Regulation Networks Group

Dr Cameron Bracken

NHMRC Grant Review Panel

National Breast Cancer and Ovarian Cancer Foundation Grant Review Panel

Guest Lecturer, School of Medicine, University of Adelaide

Inflammation and Human Ailments Laboratory

Professor Vinay Tergaonkar

NHMRC Assigners Academy

Cancer Australia Grant Review Panel

National Breast Cancer Foundation (NBCF) Grant Review Panel

Associate Editor, Oncogene

Dr Nirmal Robinson

External Assessor, NMHRC

Grant reviewer, French National Research Agency

Visiting Faculty at JSS Academy of Higher Education and Research, Mysuru, India

Visiting Faculty at Uni Campania, Naples, Italy

Leukaemia Unit, Genetics and Molecular Pathology

Associate Professor Susan Branford

Abstract Reviewer, American Society of Hematology Conference

Board Member, Blood Research

Qiagen Global Scientific Advisory Board

Novartis Pharmaceuticals International Molecular Advisory Board

International Chronic Myeloid Leukaemia Foundation Scientific Advisory Board

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

Novartis Pharmaceuticals Emerging Global Market Molecular Monitoring Steering Committee

Lung Research Laboratory

Professor Paul Reynolds

NHMRC Grant Review Panel, Centres of Research Excellence

Lymphatic Development Laboratory

Professor Natasha Harvey

NHMRC Grant Review Panel

Australian Academy of Science National Committee for Cell and Developmental Biology Member

Chair, Royal Adelaide Hospital Research Committee Scholarships and Fellowships Committee

Big Science Adelaide Panel Member: The Future of Cancer Research in Australia

University of South Australia Division of Health Sciences Research Management Committee Member

Host of Girls in STEM CCB Tour

A Career in Science Presentation at Linden Park Primary School

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 Genomics, Genetics and Druggable Targets pillar, South Australian Comprehensive Cancer Consortium

Celgene Advisory Committee

Dr Chris Hahn

Institute Biosafety Committee, SA Pathology

Dr Anna Brown

Clingen Myeloid Malignancy Variant Curation Expert Panel

International Society for Experimental Hematology Annual Scientific Meeting organising committee

Dr Parvathy Venugopal

Conference Organising Committee - Australasian Cytometry Society 41st Annual Meeting, Adelaide

Science Mentor, Frontiers for Young Minds

Ms Alicia Byrne

Secretary, Human Genetics Society of Australasia SA Branch

Mentor, South Australian Department for Education STEM Aboriginal Student Congress

Volunteer, Still Aware

Molecular Regulation Laboratory

Professor Sharad Kumar AM

President, ANZSCDB

Member, Australian Academy of Science (AAS) Sectional Committee

Member, AAS National Committee on Biomedical Sciences

Member, NHMRC Assigners Academy

Member, Beat Cancer Project Research Strategy Group, Cancer Council SA

Board Member, International Cell Death Society

Member, Faculty of 1000

Editorial Board, Cell Death & Differentiation

Editorial Board, Science Open

Editorial Board, Oncotarget

Editorial Board, Cell Stress

Associate Editor, Molecular and Cellular Oncology

Member, Hunter Cellular Biology Meetings Committee

Dr Donna Denton

Associate Member Faculty of 1000

Dr Loretta Dorstyn

Associate Member Faculty of 1000

Dr Natalie Foot

University of South Australia Animal Ethics Committee

Dr Yoon Lim

Co-Organiser of the 8th Australia and New Zealand Society for Cell and Developmental Biology (ANZSCDB) Adelaide Meeting

SA State Representative, ANZSCDB

Representative for CCB 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 for the Adelaide Protein Group Student Awards

Dr Jantina Manning

RAH Research Showcase, Royal Adelaide Hospital

Molecular Signalling Laboratory

Professor Stuart Pitson

NHMRC Grant Review Panel

SA Academic Health Science and Translation Centre Grant Review Panel

Chris Adams University of South Australia Research Grant Review Panel

PhD thesis examiner, University of Melbourne

Ross Wishart Medal judge, Australian Society for Medical Research SA

Editorial Board member, Cellular Signalling

Editorial Board member, Journal of Bioenergetics and Biomembranes

Associate Editor, Prostaglandins & Other Lipid Mediators

Dr Jason Powell

Executive committee member, South Australian Cancer Research Biobank

Dr Melissa Pitman

Chair, Adelaide Protein Group

Dr Thao Nguyen

Editorial Board Member, StemJournal

Junior Investigators Committee Member, International Society for Stem Cell Research

Abstract Review Panel, International Society for Stem Cell Research Annual Meeting

Neurovascular Research Laboratory

Associate Professor Quenten Schwarz

NHMRC Assigners Academy

Series Editor Methods in Molecular Biology

University of South Australia PMB Research Executive Management Committee

Dr Sophie Wiszniak

Series Editor Methods in Molecular Biology

Dr Zarina Greenberg

Committee member of the Connectome Project

Tissue Architecture and Organ Function Laboratory

Dr Guillermo Gomez

Associate Editor Bio-Protocol, Cogent Biology, Frontiers in Bioengineering and Biotechnology and Frontiers in Cell and Developmental Biology

Translational Oncology Laboratory

Professor Michael P Brown

Guest speaker, Melanoma Patients Australia Education Day

NHMRC Fellowship Review Panel

Victorian Cancer Agency Mid-Career Research Fellowships Panel

Health Research Council New Zealand Review Panel, Wellington

NSW Government Office of Health and Medical Research Cell and Gene Therapy Grant Review Panel

Board director, Australian Genomic Cancer Medicine Centre

Medical Research Advisory Committee, Australian Cancer Research Foundation

Medical Research Advisory Committee, Cure Cancer Australia

Lead Facilitator, Therapeutic Innovations Pillar, South Australian Comprehensive Cancer Consortium

Dr Lisa Ebert

Guest Editor, Journal of Clinical Medicine (JCM) Special Issue: 'Targeted Therapies and Immuno-Oncology in Melanoma'

Member, Organising Committee, Australasian Cytometry Society (ACS) 41st Annual Meeting

Member, Local Organising Committee, Australian and New Zealand Society for Immunology (ASI) Annual Scientific Meeting

Dr Tessa Gargett

Day of Immunology Public Seminar, SAHMRI

Science in the Pub: Cell Therapy, Rob Roy Hotel

Flinders Centre for Innovation in Cancer College of Medicine and Public Health Lecture Series

Tumour Microenvironment Laboratory

Associate Professor Michael Samuel

NHMRC Project Grant Review Panel

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

University of South Australia Core Animal Facility Management Advisory Committee

Centre for Cancer Biology Consumer Advocacy Committee

Dr Vahid Atashgaran

Science in the Pub Adelaide Committee Member

Adelaide Immunology Retreat Committee Member

Science Alive Adelaide, Volunteer.

Dr Sarah Boyle

Centre for Cancer Biology Consumer Advocacy Committee

SA State Representative, ANZSCDB

Ms Valentina Poltavets

Member of Organising Committee, EMBL Australia Postgraduate Symposium 2019

Vascular Biology and Cell Trafficking Laboratory

Professor Claudine Bonder

NBCF Grant Review Panel (project grants)

Heart Foundation Grant Review Panel (fellowship scheme)

Chair, CCB Consumer Advocacy Group

University of South Australia, Leadership Group for Cancer Theme

University of South Australia, Leadership Group for Aboriginal Research Strategy

Conference organising committee, South Australian Breast Cancer Study Group (Scientific Chair)

Conference organising committee, Australian Society for Medical Research, National Scientific (Conference co-chair)

Conference organising committee, International Society on Thrombosis and Haemostasis: 'Immunothrombosis and Vascular Biology'

Conference organising committee, Australasian Society of Immunology, Annual Scientific Meeting

Ambassador, Bridging the Gap Foundation

Scientific presenter for NBCF, Mother's Day Classic launch

9 News Adelaide, headline article on Heart Health Month

9 News Adelaide, headline article on The Longest Table

FIVEaa radio interview with Rilka Warbanoff

Research Staff and Students

Acute Leukaemia Laboratory
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Dr Winnie Kan
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Ms Mara Dottore
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Ms Pannapa Pinweha (PhD)
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Professor Sandra Hodge
Professor Mark Holmes
Professor Hubertus Jersmann
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Ms Debra Sandford (PhD)

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Dr Drew Sutton
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Dr Natalie Foot
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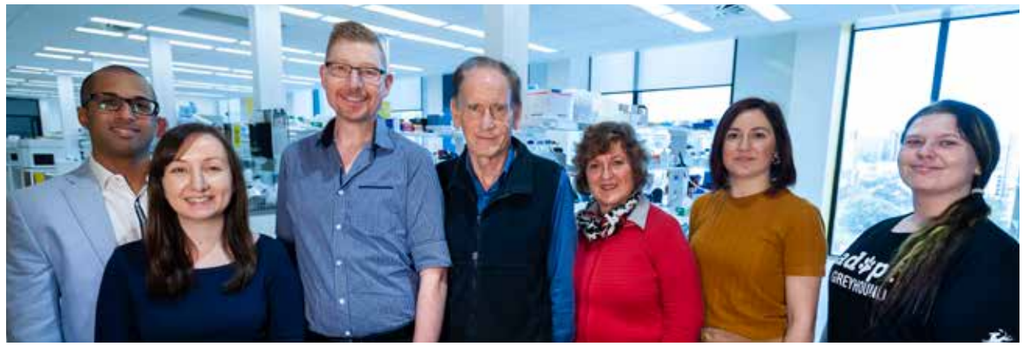

Research Support Staff Russell D'Costa, Angela Ziaei, Tim Murphy, David Tregear, Cathy Lagnado, Selin Cildir, Kadie Bonman
Absent: Marianne Oosterwegel, Geraldine Penco, Natasha Pyne

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Dr Sophie Wiszniak
Ms Celidh Marchant
Mr Markus Tondl
Mr Xinagjun Xu
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Ms Ellen Potoczky (PhD)
Ms Tess Redden (Placement)

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Mr Andrew Blake (Vacation Scholarship)
Ms Hannah Marie Dharmapalan (Vacation Scholarship)
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Dr Katherine Pillman
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Mr Klay Saunders
Mr John Toubia

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Ms Cathy Lagnado
Ms Marianne Oosterwegel
Ms Geraldine Penco
Ms Natasha Pyne
Mr David Tregear
Ms Angela Ziaei

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ERSA

NRF

Riding to Cure Cancer

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

Centre for Cancer Biology Logo

The Brief

Develop a visual identity that portrays the Centre for Cancer Biology as an internationally renowned, innovative hub of scientific discovery with a human face

Design Rationale

Layering and interplay of the two pathways is an abstracted expression of: strands of dna; overlapping systems of cellular signal transmission; mapping and exploration, with the nodes representing interconnectivity and collaboration

The cyclical, intertwining nature of the pathways conveys movement, energy and complexity, and evokes the idea of a centralised hub

A detail of the pathways is reversed from the circle, travelling beyond its boundary, suggesting expansiveness and new frontiers

The detail is positioned off-centre within the circle, creating visual tension, further reinforcing the energetic and positive aspect of the logo

The precision of the geometric forms makes reference to scientific and professional rigour befitting an organisation of international stature, while their curvilinear nature presents an organic, humanistic interface

Used as a watermark, a further layer to the imagery is developed, with a visual play between the *in vivo* aspect of the logo and the body as a whole

The colour is a reference to wright's stain, and a classic sans serif font is used for its enduring elegance and legibility

Catherine Buddle April 2009