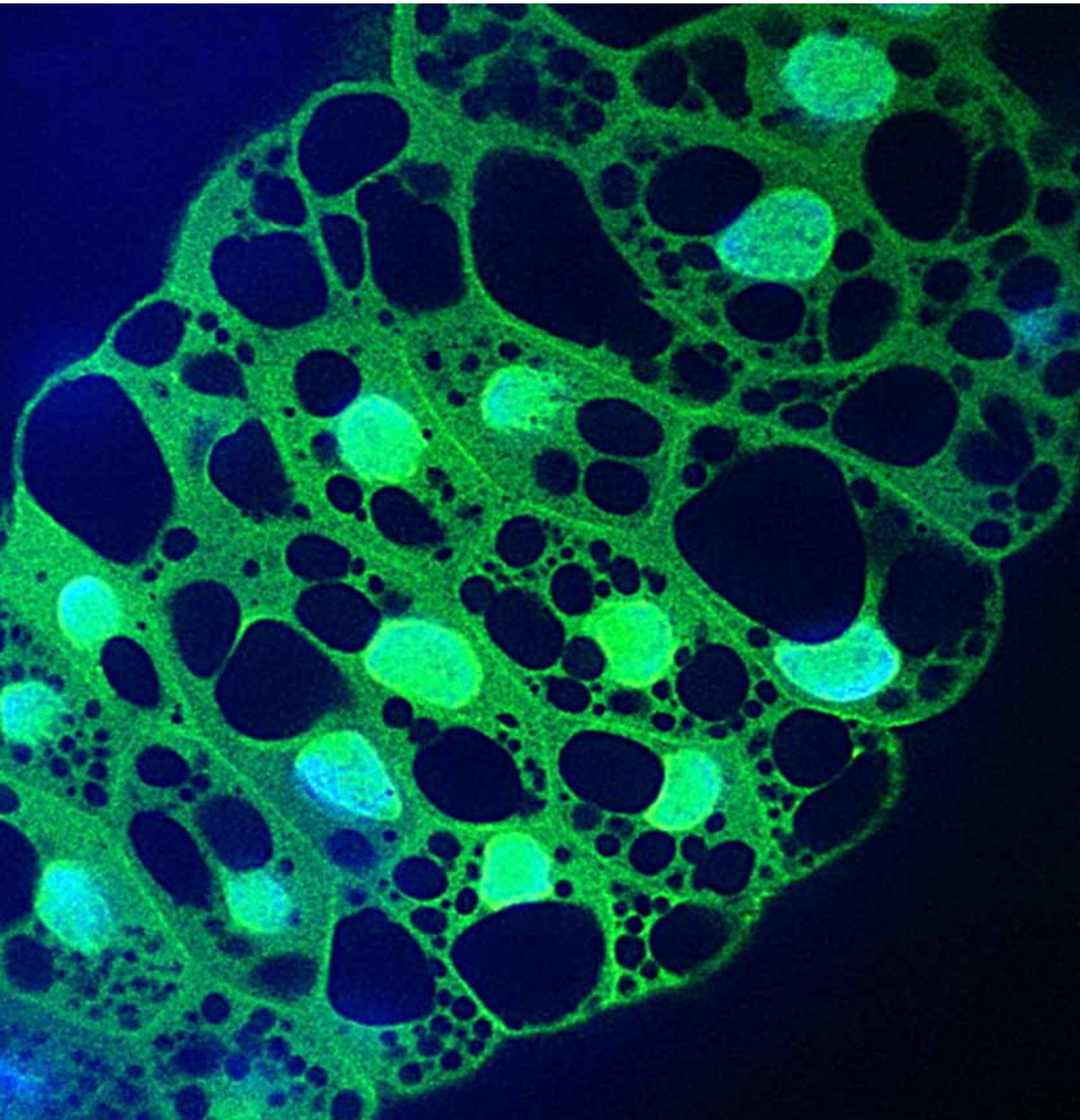
2013
Annual Report

Centre for Cancer Biology



Centre for Cancer Biology
SA Pathology
Frome Road, Adelaide
South Australia 5000
Australia

T +61 8 8222 3422
F +61 8 8232 4092

General Enquiries
Ms Anna Nitschke
Executive Assistant to Professor Angel Lopez
Anna.Nitschke@health.sa.gov.au

Postal Address
PO Box 14 Rundle Mall
Adelaide South Australia 5000
Australia

www.centreforcancerbiology.org.au

Publication Coordination
Anna Nitschke
Centre for Cancer Biology

Design and Production
Catherine Buddle
Buddle Design

Photography and Art Direction
Mark Fitz-Gerald and Peter Dent
SA Pathology Photo & Imaging

cover image
Drosophila salivary glands expressing GFP show vacuolisation in UTX mutants

2013
Annual Report

Centre for Cancer Biology

Organisation

SA Pathology Executive Director's Report

It gives me great pleasure to present the fourth Annual Report of the Centre for Cancer Biology (CCB) of SA Pathology and to reflect on its successes in 2013.

Since its establishment in 2009 as the South Australian hub of cancer research excellence, the CCB has steadily grown in size and success. New key staff have been recruited, new technologies brought in and new facilities have been established. This recurrent growth has energised a virtuous cycle with a significant rise in competitive research grants, Fellowships and infrastructure funding for the CCB.

As you will see in this Annual Report, 2013 has been yet another highly successful year for the CCB. The membership of its Faculty has grown, several new Fellowships and research grants have been won, and the CCB has earned and received awards and donations for much needed state-of-the-art equipment. The prestigious NHMRC grants for instance, ensure our researchers continue to be competitive which facilitates the translation of discoveries into better cancer treatments and outcomes

I have been in charge of SA Pathology for two years now and I am delighted with the research partnerships and alliances the CCB and other SA Pathology researchers have formed with our universities and the South Australian Health and Medical Research Institute (SAHMRI) which will provide even richer sharing of ideas and infrastructure. In particular the insipient alliance between SA Pathology and the University of South Australia over the CCB promises to strengthen and facilitate the CCB growth into the future. Of course the close association of our clinical pathologists with CCB researchers helps maintain the high quality of our diagnostic pathology services whilst giving our CCB researchers access to the most relevant pathology samples needed to make their cancer discoveries. The essential integration of the CCB work with our own clinicians and clinicians at the Royal Adelaide Hospital provides reciprocal benefits to research and the clinical care of our patients.

This close association between diagnostic and research activities continues to be boosted with the growing reputation and success of the ACRF Cancer Genomics Facility, creating wonderful integrated research and teamwork. Together, this integrated approach is helping further advance the personalised cancer care provided by SA Pathology, as well as boosting cancer, genomics and bioinformatics research for the CCB, for the benefit of the SA research community in general.

As you will also see in this Annual Report the CCB enjoys a wonderful association with the rest of the research community and in particular with the two neighbouring universities: the University of Adelaide and the University of South Australia, with which it shares students, equipment, library facilities and seminar programs. Of note also are the CCB links to industry that facilitates the commercialisation of many of its inventions and their development for clinical use.

As I reflect on the future of health care for the State, I greatly appreciate how well SA Pathology and the CCB fit with the wider SA research community. SA Pathology strongly supports the McKeon Report with its motto of 'Better health through research' as this could not epitomise better what we value in SA Pathology as part of our comprehensive commitment to research, teaching and education for the benefit of our patients and our population.

Ken Barr
Executive Director, SA Pathology

Angel Lopez

Sharad Kumar

Professor Doug Hilton, Director of the Walter and Eliza Hall Institute, Melbourne, was keynote speaker at the CCB's 2013 Annual General Meeting.

Co-Director Sharad Kumar with Prime Minister Julia Gillard, UniSA Vice-Chancellor David Lloyd (left) and Premier Jay Weatherill (right), following the announcement of a $40 million Federal Government grant to UniSA towards a new building to house and grow the CCB.

Centre for Cancer Biology Directors' Report

Professor Angel Lopez MBBS PhD FRCPA FAA
Professor Sharad Kumar MSc PhD FAA

We are delighted to present the 2013 Annual Report of the Centre for Cancer Biology. As you will see below, the CCB has had a highly successful year as measured by publications, peer reviewed grant funds awarded and new advances in cancer diagnostics and treatments. But what has really stood out this year is the alliance being forged between the Department of Health (through SA Pathology) and the University of South Australia to strengthen the CCB in the long term. This new alliance is the product of the realisation that additional resources were needed to grow the CCB and is designed to bolster existing resources to enhance the human potential of the CCB and support cancer research excellence.

Fresh support is being invested in the CCB and new research fellowships are being created to enhance critical mass and bring new cancer expertise into the CCB. We are delighted to note that as part of this overall endeavour, a new facility to accommodate the CCB will be built. This has been possible thanks to funding by the University of South Australia and matching funds provided by the Federal Government to provide the CCB with state-of-the-art new facilities that will ensure its future growth. At a ceremony in June 2013, Prime Minister Julia Gillard announced $40 million federal funds towards this endeavour. The University has recognised the opportunity to create a flagship building and has added significant new funding so that the building can accommodate major complementary facilities. The new building will be erected on the west end side of North Terrace in what is rapidly being known as the SA Health and Innovation Precinct. The design of the building has begun in earnest and we will be updating the community of its progress and no doubt asking for help as we seek to maximise this opportunity. These are truly exciting times for cancer research in South Australia and we would like to thank all those involved in taking the CCB into this new and promising phase.

In 2013, the CCB has continued to make inroads into discovering the causes of certain cancers and through new research and the rapidly expanding ACRF Genomics Facility, has made significant advances in personalised medicine. In terms of discovery, in 2013 we reported in the Proceedings of the National Academy of Sciences how caspase-2, a gene thought to be involved in cell death, suppresses lymphoma; in a paper published in Nature Communications, that a gene often mutated in multiple cancer types controls cell death; and in two papers in Oncogene we reported the discovery of genes involved in tumour initiation and metastasis. Our translational efforts to bring our discoveries closer to patients have been boosted by further involvement of the pharmaceutical industry. The recent agreement between CSL and Jenssen on CSL 362 will now enable this candidate drug, based on our antibody 7G3 against acute myeloid leukaemia cells, to be tested in patients worldwide. This example of personalised medicine is rapidly being followed by new tests and analyses being developed with our ACRF Genomics Facility. The application of genomics to cancer patients in the setting of the CCB embedded in the health system promises to revolutionise how we diagnose and treat individual cancer patients. SA Pathology and the CCB have changed the standard way we test many tumours. Instead of testing for one mutation at a time, we now test for almost 200 mutations in five genes: each one of these gives the clinician treatment options. This is resulting in more patients being enrolled in clinical trials.

In 2013, we published 141 scientific articles encompassing studies on various solid and blood cancers. Our work continues to be well received as indicated by frequent invitations that our Faculty and other staff receive from interstate cancer institutes and major international scientific meetings. Our younger members are thriving and it is pleasing to see the growing number of graduate students seeking to enroll in Honours and PhD programs at the CCB.

We are pleased to report that in 2013 we continued to receive new peer reviewed funding and fellowships from local, national and international sources. Importantly, many of our new investigators received research grants as well as the more established ones. In the latest round of the highly competitive NHMRC Project Grants, CCB researchers Sharad Kumar, Natasha Harvey, Greg Goodall, Quenten Schwarz, Andrew Zannettino, Tim Hughes, Michael Beard, Richard D'Andrea and Michele Grimbaldeston were successful, bringing in over $6 million of research funds. The CCB was also successful in winning a prestigious Program Grant. The Program Grant, led by Professors Angel Lopez, Michael Parker (St Vincent's Institute of Medical Research) and Timothy Hughes, was awarded $6.7 million over five years to investigate the causes of and seek better treatments in leukaemia.

We take much pleasure in reporting that Co-Director Professor Sharad Kumar was recognised for his scientific contributions through the ASBMB Lemberg Medal, the FAOBMB Research Excellence Award and by being elected a Fellow of the Australian Academy of Science, one of the highest honours bestowed for scientific work in Australia. Associate Professor Natasha Harvey received a prestigious Future Fellowship from the Australian Research Council. Drs Claire Wilson and Craig Wallington-Beddoe received NHMRC Early Career Fellowships to work with Professor Kumar and Professor Pitson respectively.

In 2013 we welcomed as a new member to the CCB Faculty, Associate Professor Ian Lewis. Ian already has established collaborations with CCB scientists and the strong translational impact of his work in leukaemia and bone marrow transplantation is already improving the lives of many cancer patients.

On 20 June 2013, the CCB held its Annual General Meeting. Professor Doug Hilton, Director of the Walter and Eliza Hall Institute, Melbourne, was the invited keynote speaker. He emphasised the importance of resilience and dedication in medical research and noted how the CCB fulfils the mission of the first two pillars of the National Health and Medical research Council, namely achieving transformative discoveries and implementing their translation into better health care. We were referred to as WEHI's 'SA sister' organisation, a compliment that energises our enthusiasm and commitment to perform at the highest level. Professor Hilton presented a number of research excellence awards to the staff and students of the CCB, including the 'Best Primary Research Publication Award' to Associate Professor Susan Branford, the 'Best Student Primary Research Publication Award' to Ms Wai Yan Sun and the 'CCB Early Career Investigator Award' to Dr Melissa Pitman. The CCB takes special pride in training and mentoring junior scientists and graduate students who are our colleagues of tomorrow.

In 2013, we held the 6th Barossa Meeting on Cell Signalling which once again attracted full participation from interstate colleagues. The showcasing of excellent science in South Australia's premier region continues to be a winning formula to attract the best speakers to this state and promote CCB research achievements on an international stage.

Professor Pitson was the lead convenor of the meeting (see separate report) and did a fantastic job in continuing with the tradition of high standards for these meetings.

This report gives us the opportunity to thank the government agencies, charity organisations and commercial companies that support our research: the NHMRC, ARC, SA Health, UniSA, the Australian Cancer Research Foundation, the Health Services Charitable Gift Board, eResearch SA, Novartis, CSL Limited, Cancer Council SA, Cancer Australia, Leukaemia Foundation, RAH Research Foundation, Channel 7 Foundation, Therapeutic Innovation Australia, The Kids' Cancer Project SA and Medvet. Their support for Fellowships, projects and infrastructure is essential for our research and is therefore greatly appreciated.

As in previous years, we have had strong support from SA Pathology and this is an opportunity for both of us to thank Mr Ken Barr, Executive Director of SA Pathology, as well as the other two members of the SA Pathology Executive, Mr Quinton Swann and Dr Janice Fletcher. A big thanks goes to Professor Heddy Zola, Research Director of SA Pathology, for his unabated commitment to the CCB. At the end of 2013, Professor Zola retired from SA Pathology which gave us an opportunity to thank him publicly for all his thoughtfulness and hard work. We wish Heddy all the best for the future and we hope he can continue to be involved in the next phase of the CCB with his wisdom and sound advice. We are grateful to the University of SA team that has worked hard to materialize the CCB alliance between the University and SA Health, especially Professors David Lloyd, Allan Evans, Leanna Read, Sakkie Pretorius, Terry Evans and Dr Stephen Rodda.

Our thanks also go to the RAH Research Fund team, led by Mr Mark Goldsmith, for their enthusiasm and support. As Hanson founders and beneficiaries, we appreciate the continuous hard work by Mark and his team in raising valuable funds for the work of the CCB. We look forward to continuing our long association well into the future.

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

Professor Arul Chinnaiyan presents the 2013 Clifford Prize oration

Ms Jenny Richter awarded Professor Arul Chinnaiyan with the 2013 Clifford Prize for Cancer Researdh

6th Barossa Meeting

On the 21–23 November 2013 we hosted the 6th Barossa Meeting on the theme of Cell Signalling in the Omics Era. As with previous instalments in this biennial series, the 2013 Barossa Meeting had a strong focus on cutting-edge discoveries in cell signalling and how this knowledge can be exploited to improve human health.

The meeting hosted an array of high profile international speakers including Thomas Brabletz, Arul Chinnaiyan, Vishva Dixit, Ulf Eriksson, Richard Flavell, Wanjin Hong, Richard Moriggl, Luke O'Neill, Nigel Pyne, Veronica Sexl and James Wells. A further 13 invited interstate speakers rounded out a stellar program that attracted the maximum capacity of 130 delegates to the meeting.

The meeting was comprised of ten scientific sessions, including those entitled Cancer Genomics and Epigenetics, VEGFs: the Vasculature and Beyond, Cell Signalling Architecture, Mechanisms of Tumour Progression, Metabolism and Disease, Molecular Therapeutics, Cell Signalling Modules, and Novel Therapeutics. Approaches to meet the challenge of analysing large scale 'omic' data sets to answer both specific and global biological questions was a major theme throughout the meeting. This was no better exemplified by the work of Professor James Wells (University of California at San Francisco) who described cutting-edge tools towards understanding apoptosis via global identification of caspase substrates.

In addition to highlighting the latest trends in cell signalling in disease, the Barossa meetings also provide a vehicle for the presentation of the Clifford Prize for Cancer Research. The 2013 recipient was Professor Arul Chinnaiyan of the University of Michigan for his outstanding work in understanding the genetic lesions that contribute to cancer development and progression. The Prize, presented by Ms Jenny Richter, Deputy Chief Executive for System Performance of SA Health, comprised a perpetual trophy crafted by South Australian glass artist Nick Mount, and a magnum of Grange Hermitage donated by Penfolds. With this award Professor Chinnaiyan joins an illustrious list of past winners that include Axel Ullrich (Munich), Tony Hunter (San Diego), John Dick (Toronto) and Vishva Dixit (San Francisco).

As always the 2013 Barossa Meeting provided an intense three and a half days of quality science, complemented by equally impressive food and wine. The gastronomic highlight of the meeting was the food of Elli Beer at the Clifford Prize Dinner held at The Farm, Barossa Function Centre. Delegates at this function were also treated to an impressive list of carefully selected, high quality wines, introduced by wine expert John Leydon.

The Barossa meetings continue to provide outstanding opportunities for students, early career and more established researchers to mix with world class scientists in a convivial, but scientifically rigorous atmosphere conducive to the development of collaborations. As always, the meeting also showcased the quality of South Australian science and continues to develop as one of the premier biomedical research meetings on the scientific calendar.

Professor Stuart Pitson
Convenor, 6th Barossa Meeting

Michelle Perugini | Debora Casolari | Nur Hezrin Shahrin | Nenad Petrovic
Saumya Samaraweera | Anna Brown | Richard D'Andrea

Ian Lewis | Teresa Sadras | Jesse Cheah | Kyaw Ze Ya Maung | Ka Leung Li
Sarah Bray | Mahmoud Bassal

Acute Leukaemia Laboratory

Professor Richard D'Andrea PhD
Associate Professor Ian Lewis MBBS PhD FRACP FRCPA

Acute Myeloid Leukaemia (AML) accounts for 20% of leukaemia in children and is the most common form of acute leukaemia in adults. AML results from the accumulation of immature myeloid cells in the bone marrow and peripheral blood, and is heterogeneous in nature, with many different subtypes classified according to molecular aberrations.

Overall survival for adult AML is still only 30-40% with median overall survival for some high-risk patient groups as low as 10 months. The molecular basis for many subtypes is still largely unclear. With new therapies becoming available there is a clear need to improve patient stratification in order to select the best available treatment for each patient. A better understanding of AML biology is also important to develop new treatments that can be targeted to the specific patient groups that are associated with poor outcomes on standard therapy.

A major focus is understanding the mechanisms underlying normal blood cell development, and the changes associated with haematological malignancy, in particular AML and pre-leukaemic diseases including Myeloproliferative neoplasms and bone marrow failure syndromes. A significant research focus of our laboratory is the investigation of receptor signalling mechanisms that control stem and progenitor cell responses to a number of key growth factors, and which are commonly up-regulated or mutated in AML. Additionally we have an interest in the genetic changes that lead to altered metabolism in cancerous cells, and the identification and testing of novel therapeutics that target these changes. We also use genetic and epigenetic approaches to identify new genes and mutations that contribute to myeloid disease.

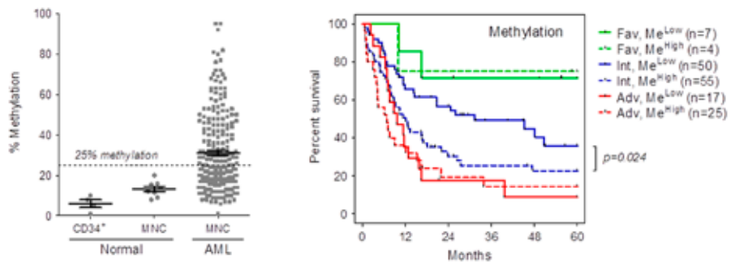
During 2013, the research activities of the Acute Leukaemia Laboratory focused on:

- Promoter methylation status of the GADD45A gene—we showed that this can be used as a prognostic marker in identifying a subset of AML patients who experience a poor outcome from standard therapy.
- Identification of novel mutations in families of genes using high-throughput sequencing for 100 AML samples. Work is ongoing to determine frequency and overlap of mutations in these genes with common AML mutations, and to correlate these mutations with gene expression signatures, altered properties of AML cells, and clinical outcomes.
- Identification of novel pathways that may be targeted in disease cells, and preliminary investigations of selective inhibitors of these pathways using cell line models and primary disease material. This line of research has the potential to identify effective targeted treatments to improve patient outcomes.

Key discoveries 2013

Role of KLF5 and Methylation in AML
We have used a mouse gene-ablation model of KLF5 to show that this transcription factor plays an important role in differentiation of myeloid cells. We have also demonstrated that hyper-methylation of KLF5 contributes to reduced KLF5 expression in AML (Diakiw *et al*, 2013). Patient survival analyses showed that methylation of intron 1 of KLF5 is associated with poor prognosis (particularly for the 'intermediate risk' patient group).

Prognostic Significance of GADD45A promoter hyper-methylation in AML
In 2013 we reported that GADD45A is silenced by methylation in approximately 40% of AML patients. We tested the clinical significance of GADD45A promoter hyper-methylation in a large AML patient cohort (167 AML patients). This showed that GADD45A promoter methylation is predictive of poor survival overall in AML, and particularly in normal karyotype AML. This is the first study to link GADD45A promoter methylation to patient outcome in cancer. We also showed that GADD45A methylation is associated with a DNA hypermethylation profile, and with selected mutations in a number of key genes that are frequently mutated in AML. These findings suggest a treatment strategy for these patients with current and emerging hypo-methylation agents.

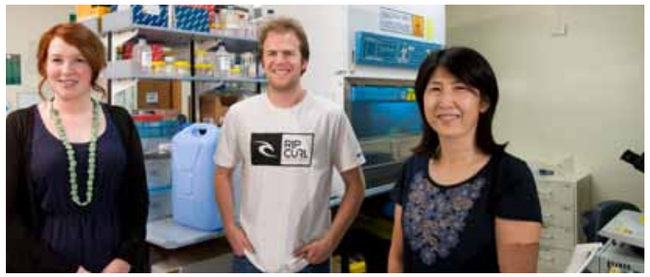


Hyper-methylation of KLF5 intron 1 in AML patients and its correlation with poor overall survival, particularly in the intermediate risk group

Outcomes for the Community

Our research has provided new insights into the biology of AML and important leads for improving treatment of patients with myeloid malignancies. The identification of prognostic markers that may allow identification of subsets of AML patients that will benefit from targeted hypomethylation therapy has potential to improve patient outcomes. The identification of novel pathways that can be targeted with inhibitors to induce death of diseased cells in AML is also important and we will directly test these approaches using animal models.

Yeesim Khew-Goodall | Ana Lonic



Hannah Thomas | James Paltridge | Xiaochun Li

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall PhD

The interest of the Cell Signalling Laboratory is to understand how signals that are normally generated to maintain homeostasis, give rise to disease when dysregulated.

Our primary research interest is to understand how a cancer cell progresses from a benign state, with good prognosis, to a malignant state resulting in metastatic disease. In solid cancers, which constitute 80% of human cancers, the vast majority of deaths are due to metastasis.

The two main areas of research are:

Regulation of protein trafficking by tyrosine phosphorylation

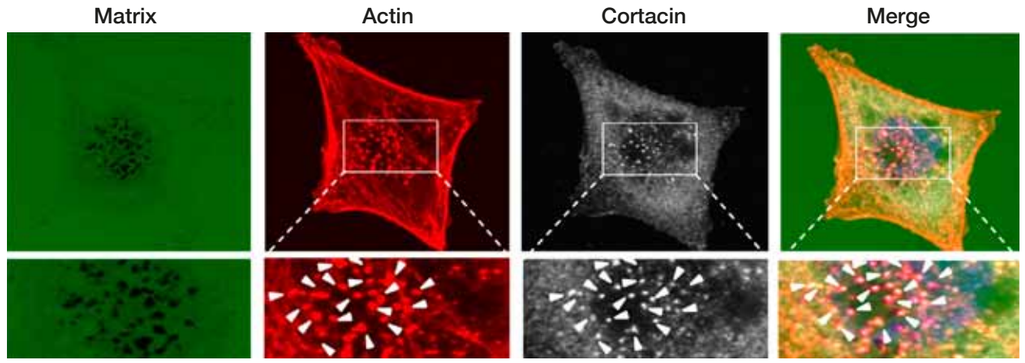
Cells express a range of surface receptors and secrete a range of cytokines and growth factors that influence their growth and the activities of neighbouring cells. However, the spectrum of secreted proteins and cell surface receptors are often vastly altered in cancer cells relative to their cell of origin. These vast changes to the secretome and plasma membrane proteome of cancer cells which can make them grow better, more metastatic or chemoresistant are seemingly coordinated but how this occurs is not understood. We are interested in elucidating the signal transduction pathways that regulate trafficking of receptors and secreted proteins and how these are dysregulated in cancer cells to promote growth and metastasis.

Molecular regulation of cell invasion

The ability of cancer cells to invade their surrounding tissue is critical for their spread to secondary organs. We are identifying molecules critical for assembly and regulation of the invasive machinery in breast cancer and in neuroblastoma, how they act to promote invasion and how they are regulated.

Key discoveries 2013

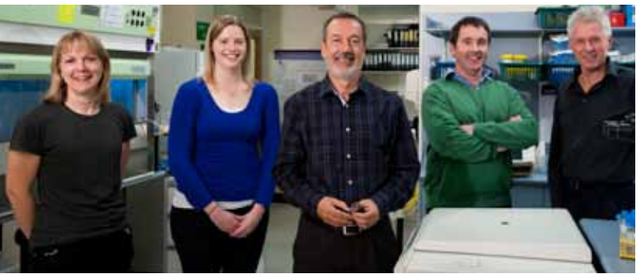
This year we published works showing that the miR-200 family of microRNAs are critical regulators of cell invasion involved in colon cancer (Paterson et al) and in breast cancer we also identified a key target of miR-200 not associated with its role in regulating epithelial-mesenchymal transition that regulates metastasis *in vivo* (Li *et al*).



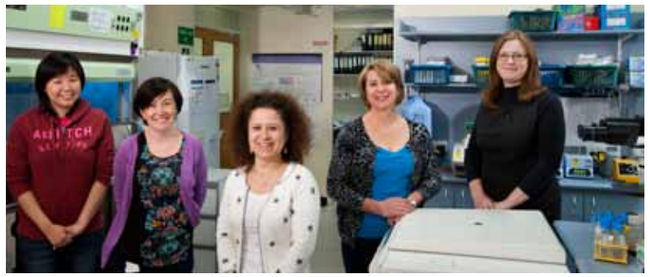
Degradation of extracellular matrix (black holes) by MDA-MB-231 breast cancer cells at sites of invadopodia formation marked by actin and cortactin colocalisation

Outcomes for the Community

Solid tumours make up the majority of human cancers whereby the progression to metastasis is the main cause of morbidity and mortality in these patients. Currently, there is little effective treatment for metastatic diseases. Our studies aim to increase knowledge of the molecules driving metastasis using multiple strategies so that we may identify and open up avenues for new therapeutics to be developed.



Hayley Ramshaw | Nicole Wittwer | Angel Lopez
Tim Hercus | Frank Stomski



Winnie Kan | Emma Barry | Mara Dottore | Anna Sapa | Barbara McClure

Cytokine Receptor Laboratory

Professor Angel Lopez MBBS PhD FRCPA

Cytokine receptors are important membrane proteins that transduce signals from the immediate environment to elicit a cellular response. As cytokines are released in the extracellular space, cytokine receptors on the cell surface recognize them, initiating a process which ultimately determines whether cells will divide, differentiate or perform other specific functions.

This is a tightly controlled process which, when dysregulated, leads to diseases such as chronic inflammation and cancer. The focus of this laboratory is to understand how a discrete subset of cytokine receptors, termed the βc cytokines, function in health and disease. In particular our work is relevant in diseases such as leukaemia which exhibit abnormalities in βc cytokine receptor expression, and in asthma where excessive βc cytokine receptor stimulation of myeloid cells in the lung causes recurrent damage.

A major aspect of our work is to understand how βc cytokines recognize their receptors and initiate cellular activities. To facilitate these studies, we have an ongoing need to develop effective methods for the large-scale production of the protein components (PLoS ONE 8, 2013). In collaboration with Prof Parker's group at St Vincent's Institute of Medical Research in Melbourne, we are determining the 3-D structure of βc cytokine receptors in complex with the βc cytokines themselves and with antibodies specific to functionally important epitopes. This in turn will guide us in the development of novel molecules that by modulating cytokine receptor function can help control some myeloid leukaemias as well as inflammatory conditions such as asthma.

As cytokine receptors are activated on the cell surface they trigger a variety of biochemical responses within the cell. We are characterizing these in collaboration with Prof Pitson's and Dr Guthridge's laboratories and finding that cytokine receptors themselves can be phosphorylated and activated by the lipid kinase PI-3 kinase leading to extended cell survival with clear implications in leukaemia (PLoS Biology 11, 2013).

As part of this signalosome, the 14-3-3 adaptor proteins are emerging as key regulatory molecules. We are finding that their exquisite modulation using compounds that alter the 14-3-3 dimer interface have profound consequences on whether cells will live or die.

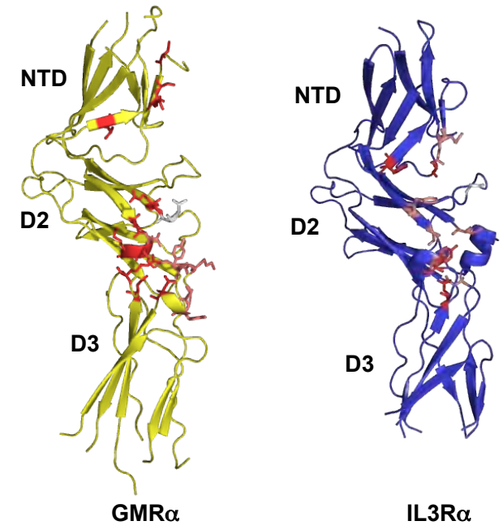
Interestingly, this 14-3-3 family of proteins so critical in myeloid cell function appear to be important in some brain functions and are linked to dopamine transport activities (Transl Psychiatry 3:e327, 2013).

The influence of βc cytokines in human disease is being pursued in a variety of settings. In allergic inflammation models, we are finding in collaboration with Associate Professor Grimbaldeston and with CSL Limited that βc cytokines are powerful activators of mast cell function and that the pro-inflammatory activity of most cells can be tamed with new compounds that we are developing. In autoimmune diseases, we have found in collaboration with Professor J Schrader (Vancouver) and Professor J Hamilton (University of Melbourne) that autoantibodies against GM-CSF are pathogenic (PNAS 110, 2013). In several experimental cancer models, we have succeeded in controlling tumour growth with new compounds that inhibit 14-3-3 function. Lastly, in collaboration with Professor T Hughes and CSL Limited, we found that certain human myeloid leukaemias can be controlled in vitro by appropriately targeting CD123 (Br J Haematol 161, 2013). As we understand more and more the mechanism of action of βc cytokines, new opportunities arise to better control some forms of cancer and other diseases.

Key discoveries 2013

Structure of the human IL-3 receptor
In collaboration with Professor Parker (St Vincent's Institute Medical Research) and CSL Limited, we have solved the structure of the human IL-3 receptor in complex with the Fab fragment of the blocking antibody 7G3/CSL362. Crystal structures of the IL-3 receptor showed the N-terminal domain existing in an 'open' and a 'closed' state, probably a reflection of the mobility of this domain. In turn, this suggests a dynamic process whereby the 'closed' receptor leads to optimal engagement of the βc subunit allowing sustained receptor activation and cellular signalling.

Anti-leukaemic activity of the anti-CD123 antibody CSL362
In collaboration with CSL Limited we have found that the antibody CSL362, optimized for antibody-dependent cell-mediated cytotoxicity, is a strong enabler of NK cell killing of acute myeloid leukaemia cells *in vitro* and in *in vivo* animal models. We have also extended these observations to chronic myeloid leukaemia in collaboration with Professor T Hughes, Professor D White and CSL Limited in which leukaemia stem-like cells over-express CD123 and are susceptible to CSL362-mediating NK cell killing.



X-ray crystallography was used to determine structures of the cytokine binding subunits for GM-CSF (yellow) and IL-3 (blue) to help understand how these cytokines function
Each subunit contains three distinct domains, NTD, D2 and D3. Functional studies have been used to identify regions of the receptor that allow specific binding of the appropriate cytokine (residues shown in red, pink or white).

Outcomes for the Community

We have continued to uncover the molecular basis of βc receptor activation. This understanding is essential for generating breakthroughs that can then be exploited to devise new therapeutics. We are delighted that after many years of work on the human IL-3 receptor, the antibody CSL362 against this receptor is currently in clinical trials in the USA and Australia for the treatment of acute myeloid leukaemia.

Andrew Ruszkiewicz | Maria Caruso

Teresa Tin | Jing-Song Chen

Gastroenterology Research Laboratory

Associate Professor Andrew Ruszkiewicz MD FRCPA

The research work conducted in our laboratory focus on gastroenterology pathology including malignancies of the colorectum, oesophagus and pancreas. We are particularly interested in colorectal cancers arising through so called 'serrated pathways' and their precursor lesions, including serrated colorectal polyps.

Until recently, the serrated polyps were regarded as innocuous, non-neoplastic lesions with no malignant potential. We are particularly interested in characterization of colorectal cancers bearing somatic BRAF V600E mutation as these tumours are particularly aggressive and do not respond to conventional chemotherapy treatment.

We have recently demonstrated elevation of Claudin1 expression in colorectal serrated polyps with BRAF V600E mutation. This findings significantly widen the serrated polyp spectrum and provide additional support for a close relationship between BRAF mutated hyperplastic polyp and sessile serrated adenoma which may, in fact, represent a continuous spectrum of the same neoplastic process.

We are also involved in discovery and validation of biomarkers of colorectal neoplastic lesions and actively working on the development of accurate non-invasive blood based test for detection of colorectal cancer cancer and its precursors.

Our research work on the serrated pathwayand biomarkers of colorectal cancer is conducted in close collaboration with researches from CSIRO, gastroenterologists and colorectal surgeons.

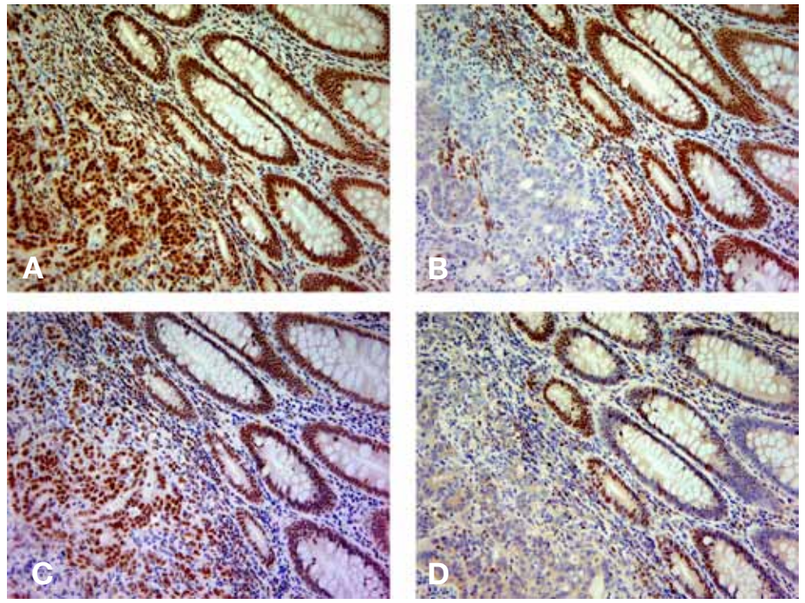
Our interest in familial colorectal cancer including Hereditary non-Polyposis Colorectal Cancer (HNPCC, Lynch syndrome) resulted in several publications including international multicenter collaborative studies evaluating practicality of various approaches in clinical practice. Our laboratory (NATA accredited) was one of the first in Australia to offer testing for mismatch repair genes immunohistochemistry in a diagnostic setting.

Our laboratory staff are responsible for operations of the Colorectal Cancer Tissue Bank which holds samples of colorectal cancers and other gastrointestinal tumours, colorectal polyps, normal tissues, matching blood and clinical data from patients treated in various hospitals in Adelaide. This material is used for research projects conducted by us and other laboratories of the Centre for Cancer Biology.

Key discoveries 2013

Using Next Generation Sequencing we have identified a group of genes which are frequently mutated in sessile serrated adenomas and serrated pathway colorectal cancers including a particularly aggressive form of this disease characterised by BRAF V600E mutation and intact mismatch repair system.

After successfully adopting a novel technique of detection of cell-free circulating tumour DNA in patients with colorectal cancer we are evaluating this method as a potential tool for detection of early recurrence of cancer and response to chemotherapy. This non-invasive method allows detecting tumour specific somatic mutations in patient's bloodstream potentially eliminating the need for repeated tumour biopsies.

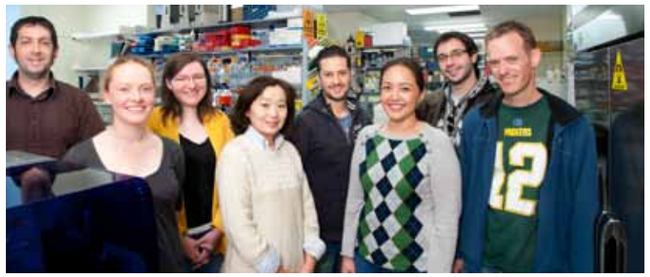


Mismatch repair genes immunohistochemistry is used to screen for hereditary colorectal cancer (Lynch syndrome, HNPCC)
Loss of nuclear protein expression indicates inactivated gene prioritising gene mutation analysis. This case demonstrates concomitant loss of MSH2 and MSH6 proteins (B and D respectively) in the cancer tissue and preserved expression of MLH1 and PMS2 proteins (A and C respectively). Subsequent mutation study revealed a germ line mutation in the MSH2 gene.

Outcomes for the Community

Our studies aim to advance the knowledge of biology of bowel cancer and its precursor lesions including conventional adenomas and serrated polyps. This is a necessary step to improve early detection and treatment options of the disease which is the second most common cause of cancer related death in Australia, killing 4000 patients each year.

Marika Salmanidis | Anna Tsykin | Greg Goodall
Caroline Phillips | Cameron Bracken | Andrew Bert



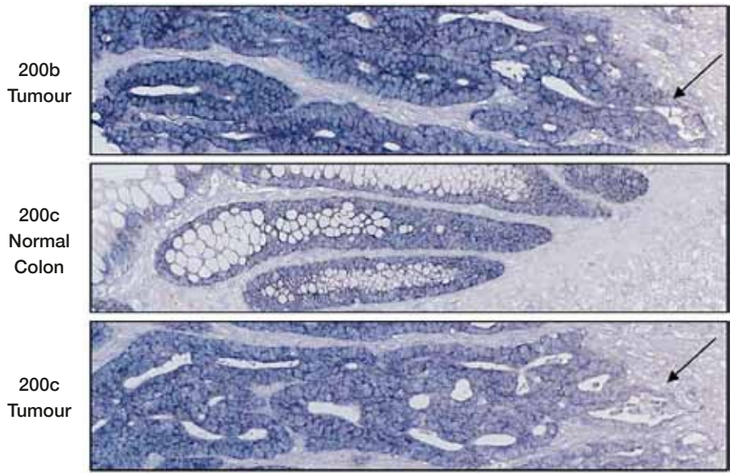
Simon Conn | Katherine Pillman | Victoria Arnet | Kimi Honma | John Toubia
Suraya Roslan | Francisco Sadras | Philip Gregory

Gene Regulation Laboratory

Professor Greg Goodall PhD

Several years ago in collaboration with the Khew-Goodall lab, we made the fortunate discovery of a microRNA family that has remarkably potent effect on controlling epithelial to mesenchymal transition (EMT), a process now recognised to be crucial for solid cancers such as breast, colon and prostate cancer to metastasise and thereby be lethal.

Since our report on this in 2008 (Gregory *et al*, Nature Cell Biol, now cited over 1500 times) we have been investigating how this family of microRNAs (called miR-200) has its inhibitory effects on cancer metastasis and how the microRNAs themselves are regulated. We have developed methods to detect where the microRNAs are located in tumours, allowing us to confim the role that miR-200 has in colon cancer invasion; we have used laboratory models of breast cancer to identify the pathways through which miR-200 has its effects; and we have studied the molecular mechanisms that act on the miR-200 gene to determine its activity.



MicroRNA-200 expression is reduced in cells invading the adjacent tissue at the invasive front of a colon cancer
Sections from a colon cancer with invasive region, and a section from normal colon, were stained for miR-200 by in situ hybridisation with tagged antisense probes that were then detected with antibody to the tag. Arrows point to the invasive front of the tumour.

Key discoveries 2013

MiR-200 can repress breast cancer metastasis through ZEB1-independent, but moesin-dependent pathways
We have identified a key molecule, called Moesin, that is regulated by miR-200 which in turn has a major role in allowing breast cancers to metastasise to bone and lung. Using an orthotopic model of breast cancer metastasis we found that ectopic expression of miR-200b or miR-200c reduces tumour cell invasion and breast cancer metastasis. Surprisingly, these effects were not mediated directly by the loss of ZEB1 but rather through the repression of the cytoskeletal remodelling protein moesin, which has previously been shown to be targeted by miR-200c and to influence the ability of miR-200c to repress cell migration. Moesin was verified to be directly targeted by miR-200b, and restoration of moesin in miR-200b expressing cells was sufficient to alleviate metastatic repression. In breast cancer cell lines and patient samples, the expression of moesin significantly inversely correlated with miR-200 expression, and high levels of moesin were associated with poor relapse-free survival. These findings highlight the context-dependent effects of miR-200 in breast cancer metastasis and demonstrate the existence of a moesin-dependent pathway, distinct from the ZEB1-E-cadherin axis, through which miR-200 can regulate tumour cell plasticity and metastasis. (Li *et al*, Oncogene, 2013)

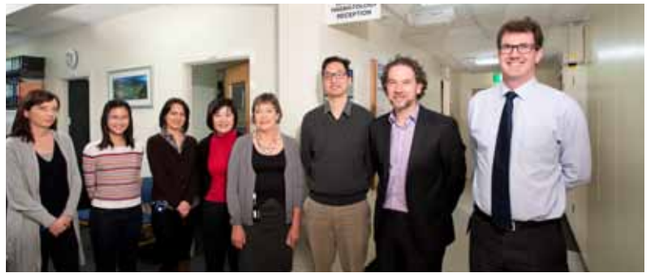
Epigenetic modulation of the miR-200 family is associated with transition to a breast cancer stem cell-like state.
Because breast cancer stem cells resemble cells that have undergone epithelial–mesenchymal transition, and the miR-200 family is a key regulator of EMT, we investigated whether miR-200 has a role in controlling the transition between cancer stem cell-like and non-stem-cell-like states. We found immortalized human mammary epithelial (HMLE) cells can undergo spontaneous conversion from a non-stem to a stem-like phenotype and this conversion was accompanied by the loss of miR-200 expression. Stem-like cells isolated from metastatic breast cancers also displayed loss of miR-200 indicating similar molecular changes may occur during breast cancer progression. The phenotypic change observed in HMLE cells was directly controlled by miR-200 because restoration of its expression decreased stem-like properties while promoting a transition to an epithelial phenotype. Investigation of the mechanisms controlling miR-200 expression revealed both DNA methylation and histone modifications were significantly altered in the stem-like and non-stem phenotypes. In particular, in the stem-like phenotype, the miR-200b-200a-429 cluster was silenced primarily through polycomb group-mediated histone modifications whereas the miR-200c-141 cluster was repressed by DNA methylation. These results indicate that the miR-200 family plays a crucial role in the transition between stem-like and non-stem phenotypes and that distinct epigenetic-based mechanisms regulate each miR-200 gene in this process. Therapy targeted against miR-200 family members and epigenetic modifications might therefore be applicable to breast cancer. (Lim *et al*, J Cell Sci, 2013).

Identification of an enhancer that controls miR-200b~200a~429 gene expression in breast cancer cells
To better understand how expression of the miR-200 family of microRNAs in regulated, we analyzed the miR-200 gene region for epigenetic modifications that are likely to influence activity of the miR-200 gene in breast cancers. We discovered a region of the gene that has the epigentic modifications typical of a regulatory region that enhances gene activity. We constructed chimeric reporter genes incorporating this region and found it could increase gene activity 27-fold in breast epithelial cells. Furthermore, we found that a region of this activity enhancer was itself active at producing RNA, although ectopic over-expression of this enhancer RNA did not affect the miR-200b~200a~429 gene activity. While additional investigations of the miR-200b enhancer RNA function will be necessary, it is possible that it may be involved in interactions with the the miR-200b~200a~429 gene that control its activity. (Attema *et al*, Plos One, 2013)

Outcomes for the Community

Our discoveries indicate potential avenues towards development of drugs that block cancer metastasis. They have influenced many labs around the world to take up investigation of the role of miR-200 in cancer metastasis, with our publications receiving 1260 citations in 2013.

Stanley Cheung | Cindy Lee | Chandrika Rajapaksha | Carine Tang
Kerry Munro | Safoorah Sagheer | Luen Bik To | David Ross | Rakchha Chetri



Monika Kutnya | Amilia Wee | Ljiljana Vidovic
Agnes Yong | Pam Dyson | Chee Wee Tan | Simon McRae | Ian Lewis

Haematology Clinical Research Unit

Professor Luen Bik To, MBBS (HK), MD (Adel), MRCP (UK), FRCPA, FRACP
Associate Professor Ian Lewis, MBBS (Adel), PhD (Adel), FRCPA, FRACP

The Haematology Clinical Research Unit focuses on disease and treatment directed research. It encompasses several research teams in the RAH Department of Haematology, including the Therapeutic Product Facility, Haemostasis Laboratory and the Clinical Trials Unit.

Research endeavours focus on clinical trial participation, which allows patients access to novel treatments, as well as provision of infrastructure to facilitate fundamental research and clinical trial activity. Two particularly important grant funding successes have enabled the establishment of the South Australian Cancer Research Biobank and a negative pressure clean room facility. Both are vital for building research infrastructure to enable further development of campus strength in leukaemia and myeloma research.

Understanding the molecular heterogeneity of leukaemia is leading to the identification of new targets for therapy in a disease where current treatments are unsatisfactory. The clinical input from the Unit has been critical for the characterisation of hypermethylation of the KLF5 and GADD45A in subsets of AML patient samples at diagnosis. This work has provided new prognostic information and potential for establishment of trials to investigate the use of hypomethylation agents to treat particular patient subsets. Similarly, recent research in collaboration with Professor Zannettino (Myeloma Research Laboratory) has identified a negative prognostic indicator (circulating N-cadherin levels) for patients with multiple myeloma (Vandyke *et al*, BJH). Collaborative studies with Professor Charles Mullighan (St Judes Research Institute, Memphius, USA) has defined the genomic landscape of a subtype of ALL associated with poor outcome.

Outcomes for the Community

The Haematology Clinical Research Unit has a core translational focus of improving the treatment of patients with malignant and non-malignant diseases of the blood. This is achieved through collaborations with fundamental research groups, involvement in clinical trials utilising novel agents and provision of key infrastructure to facilitate these activities. A key outcome for 2013 is the establishment of the South Australian Cancer Research Biobank which is now processing and banking leukaemia samples from patients across major hospitals in Adelaide.

Clinical Trials 2013

1 Therapeutic infusion of most closely HLA-matched third party donor-derived virus-specific cytotoxic T-lymphocytes in patients with active viral reactivation post-allogeneic stem cell transplantation. R3ACT
Principal Investigator: Dr Agnes Yong

2 A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of Idelalisib (GS-1101) in Combination with Rituximab for Previously Treated Indolent Non-Hodgkin Lymphomas. GS-US-313-0124
Principal Investigator: Dr Pratyush Giri

3 A Phase 3, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Efficacy and Safety of Idelalisib (GS-1101) in Combination with Bendamustine and Rituximab for Previously Treated Indolent Non-Hodgkin Lymphomas GS-US-313-0125
Principal Investigator: Dr Pratyush Giri

4 A Phase 3, Multicentre, Randomized, Double-Blind Study to Compare the Efficacy and Safety of Oral Azacitidineplus Best Supportive Care versus Placebo plus Best Supportive Care in Subjects with Red Blood Cell Transfusion-dependent Anaemia and Thrombocytopenia Due to IPSS Lower-Risk Myelodysplastic Syndromes. AZA-MDS-003
Principal Investigator: Dr Devendra Hiwase

5 A Randomized, Double-Blind, Placebo-Controlled, Phase 3 Trial to Evaluate the Protective Efficacy and Safety of a Therapeutic Vaccine, ASP0113, in Cytomegalovirus (CMV)-Seropositive Recipients Undergoing Allogeneic, Haematopoietic Cell Transplant (HCT)
Principal Researcher: Associate Professor Ian Lewis

6 A phase II multi-centre, open label, randomized study to assess safety and efficacy of two different schedules of oral LDE225 in adult patients with relapsed/refractory or untreated elderly patients with acute leukaemia. CLDE225X2203
Principal Investigator: Associate Professor Ian Lewis

7 An Open-label, Single arm, Multicenter Phase 2 Study of the Bruton's Tyrosine Kinase Inhibitor PCI-32765 (Ibrutinib) in Patients with Relapsed or Refractory Chronic Lymphocytic Leukemia or Small Lymphocytic Lymphoma with 17p Deletion. PCYC-1117-CA
Principal Investigator: Professor Bik To

8 A Randomized, Open-label Phase 3 Study of Carfilzomib, Melphalan, and Prednisone versus Bortezomib, Melphalan, and Prednisone in Transplant-ineligible Patients with Newly Diagnosed Multiple Myeloma. 2012-005
Principal Investigator: Dr Noemi Horvath

9 A Randomized, Double-blind, Placebo-controlled Phase 3 Study of the Bruton's Tyrosine Kinase (BTK) Inhibitor, PCI-32765 (Ibrutinib), in Combination with Bendamustine and Rituximab (BR) in Subjects With Newly Diagnosed Mantle Cell Lymphoma. PCI-32765MCL3002 (SHINE)
Principal Investigator: Dr Pratyush Giri

10 A Phase II, single arm, open label study of treatment-free remission in Chronic Myeloid Leukaemia (CML) chronic phase (CP) patients after achieving sustained MR4.5 on nilotinib. CAMN107A2408
Principal Investigator: Professor Timothy Hughes

11 A Phase 3, randomised, double-blind, placebo-controlled study to compare the efficacy and safety of oral azacitidine plus best supportive care as maintenance therapy in subjects with Acute Myeloid Leukaemia in complete remission. CC-486-AML-001
Principal Investigator: Associate Professor Ian Lewis

12 An open-label, multicentre, single-arm, phase 2 study of PCI-32765 (Ibrutinib) in subjects with refractory follicular lymphoma. PCI-32765FLR2002 (DAWN)
Principal Investigator: Dr Pratyush Giri

13 An Open-Label Bosutinib Treatment Extension Study for Subjects With Chronic Myeloid Leukaemia (CML) Who Have Previously Participated In Bosutinib Studies B1871006 Or B1871008. B1871040.
Principal Investigator: Professor Tim Hughes

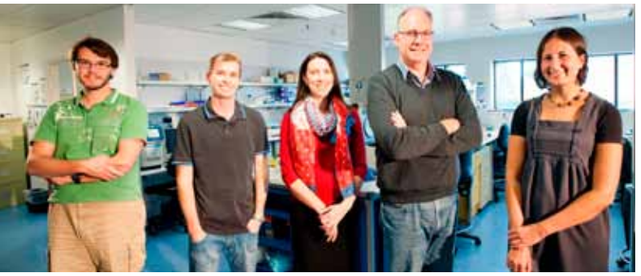
14 A randomised, double-blind, placebo-controlled phase 3 study of the Bruton's Tyrosine Kinase Inhibitor, PCI-32765 (Ibrutinib) in combination with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone in subjects with newly diagnosed non-germinal centre B-cell subtype of diffuse large B-cell lymphoma.
Principal Investigator: Dr Pratyush Giri.

15 A prospective randomised Phase II study of single agent pomalidomide maintenance versus combination pomalidomide and low dose dexamethasone maintenance following induction with the combination of pomalidomide and low dose dexamethasone in patients with relapsed and refractory myeloma previously treated with Lenalidomide. ALLG MM14
Principal Investigator: Dr Noemi Horvath

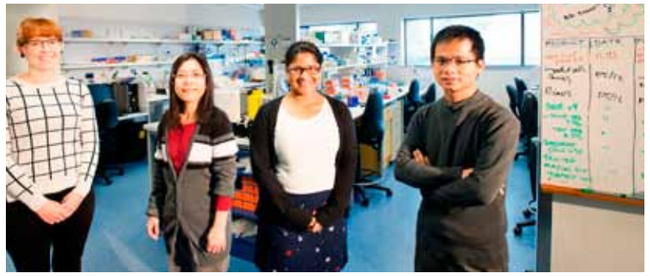
16 A Phase 2/3, Multi-Center, Open Label Study of Efficacy, Safety, and Pharmacokinetics of PEGylated Recombinant Factor VIII (BAX 855) Administered for Prophylaxis and Treatment of Bleeding in Previously Treated Patients with Severe Hemophilia A. 261201
Principal Investigator: Dr Simon McRae

17 A pilot study exploring the impact of nursing case management and comprehensive geriatric assessment on patients with MDS.
Principal Investigator: Dr Devendra Hiwase.

18 A Phase 3 Randomized, Double-Blind, Multicentre Study Comparing Oral MLN9708 plus Lenalidomide and Dexamethasone versus Placebo plus Lenalidomide and Dexamethasone in Adult Patients with Relapsed and/or Refractory Multiple Myeloma. C16010
Principal Investigator: Dr Noemi Horvath



Guillaume Fiches | Nicholas Eyre | Karla Helbig | Michael Beard | Amanda Aloia



Erin McCartney | Onruedee Khantisitthiporn | Sumudu Narayana | Viet Hoang

Hepatitis C Virus Laboratory

Associate Professor Michael R Beard PhD

The hepatitis C virus (HCV) that infects over 170 million people worldwide results in significant liver disease (fibrosis/cirrhosis) and liver cancer (hepatocellular carcinoma) in many of those infected.

In fact, infection with HCV is now the leading indication for liver transplantation in many countries including Australia. Recent development of direct acting antiviral (DAA) compounds show great promise in the treatment of hepatitis C, however these are often expensive, have significant side effects and are not available to all infected with HCV. Thus new therapies and a greater understanding of the pathogenesis of hepatitis C are required. HCV specifically infects liver cells (hepatocytes) and the main focus of our laboratory is to define the host response to infection with HCV using both laboratory based models and clinical samples. Through these approachs we hope to add to our understanding of how HCV causes disease and identify novel therapeutic targets. Specific areas of research include:

- Investigating the interferon stimulated gene response (ISG) in HCV infection and the identification and characterization of novel antiviral ISGs. We are specifically interested in ISG control of the positive RNA strand flavivirus family.
- Understanding the dynamics of viral replication at the cellular level using a live cell imaging approach to study HCV replication in real time. We are also interested in visualising HCV RNA in real time and have engineered HCV genomes containing the bacteriophage MS2 detection system that allows us to track RNA in living cells.
- Exosomes are small membrane vesicles that contain cellular RNA and protein and represent a novel mechanism of cellular communication. We are interested in how viral infection may change the composition of exosomes that may in turn impact pathogenesis.

Outcomes for the Community

Chronic hepatitis C often results in serious liver disease including the development of liver cancer and places a significant burden on our health system. Our work investigating the host response to infection with HCV has significant implications in that a greater understanding of how the liver combats HCV infection is essential for the development and implementation of new therapeutic strategies. Furthermore, our work with with the new HCV DAAs will inform therapeutic strategy in particular with HCV genotype 6 that predominates in Asia.

Key discoveries 2013

Control of the innate immune response

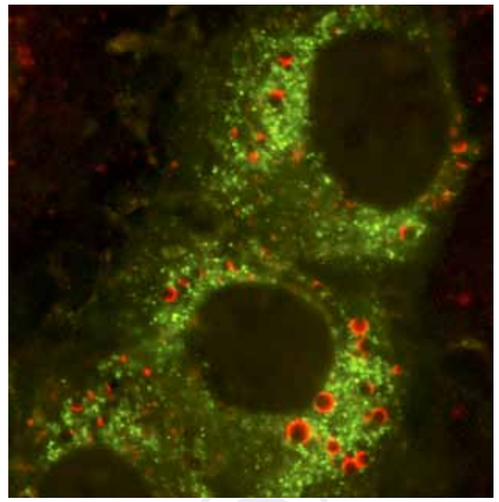
The early cellular innate response to a viral infection involves various signalling cascades that culminate in the production of hundreds of interferon-stimulated genes (ISGs), most with unknown function. Work in our laboratory looks at defining which ISGs are important anti-viral effectors, and delineating their function. We have previously demonstrated the ISG viperin to be anti-viral against HCV, HIV and Dengue virus. Recent data from our laboratory has been able to show that viperin is also able to modulate a number of innate immune signalling cascades, as well as impact the bacterial lifecycle. This is the first time that an interferon stimulated gene has been shown to limit such a wide variety of pathogens, including both RNA and DNA viruses, as well as bacteria, and also play a role in control of cellular innate signalling in response to pathogens, making viperin one of the most potent ISGs described to date. We have recently developed a knockout murine model of viperin to continue examining its role in early innate immunity.

HCV genotype 6 replication and antivirals

The hepatitis C virus (HCV) is classified into six genotypes according to the specific sequence of the virus. Genotype-6 HCV is particularly common in the Asia-Pacific region, especially in Thailand and Egypt. However, as the majority of hepatitis C infections globally are classified as genotype-1 or -2, genotype-6 hepatitis C virus is a neglected area of research. For example, the new direct acting antivirals (DAAs) targeting the HCV NS3 serine protease are only licensed to treat patients with genotype-1 infection. A major reason for this is the lack of models to study genotype-6 HCV replication in the laboratory. We developed a new model for genotype-6 HCV that allows us to study the effect of DAAs specifically targeting the HCV NS3 protease. We have used this model to investigate the effectiveness of a currently available NS3 specific DAA (boceprevir) and found that it is able to inhibit HCV replication with similar efficacy to that of HCV genotype 1. These studies are significant in that they suggest that the HCV NS3 inhibitor, boceprevir can significantly impact genotype 6 HCV replication, which will form the basis for clinical trials in regions where HCV genotype 6 is endemic.

Dynamic imaging of HCV replication complexes:

Like all positive strand RNA viruses, HCV infection induces cytoplasmic membrane rearrangements that support and compartmentalise the replication of its genome. Using a combination of fluorescent labelling approaches (tetracysteine tags, fluorescent proteins and SNAP tags) we have developed techniques to image the localization and dynamics of HCV proteins NS5A and core, HCV RNA and relevant host cell factors in living virus-producing cells. We have demonstrated that the traffic of NS5A positive cytoplasmic structures throughout the cytoplasm depends on an intact microtubule network and the dynein motor protein complex. Furthermore we have demonstrated that both relatively static and highly motile NS5A structures are enriched with fluorescently labelled HCV RNA and the host cell factors VAP-A and Rab5A. Finally we have visualised the association of NS5A-positive RCs with core-coated lipid droplets in the context of a productive infection and demonstrated the interaction of these proteins by proximity ligation assays. Through the use of pharmacological inhibitors of cellular pathways and viral protein function we are now in a position to further dissect aspects the HCV life cycle in real-time.



Live cell imaging of the hepatitis C virus NS5A and core proteins during a productive infection
HCV core protein (tetracysteine-tagged and labeled with ReAsH; red) predominantly localized to cytoplasmic lipid droplets (LDs), while motile NS5A foci (GFP-tagged; green) were infrequently juxtaposed to core-capped LDs.

Sue Branford | Zoe Donaldson | Linda Fletcher | Alex Yeoman, | Stuart Phillis
Jasmine Georgievski | Wendy Parker

Bradley Chereda | Justine Moran | Daris Stongl | Emme Chennon
Bronte Jamison | May Leong | David Yeung

Leukaemia Unit, Department of Molecular Pathology

Associate Professor Susan Branford PhD, FFSc (RCPA)

The introduction of tyrosine kinase inhibitor therapy over a decade ago has changed the course of disease for patients with chronic myeloid leukaemia (CML) and most can now enjoy a normal life expectancy. However, most patients will need to take their medication every day for the rest of their lives and some do suffer from ongoing side effects. Stopping therapy could lead to a poor outcome.

Our laboratory investigates the molecular response to therapy by an examination of the BCR-ABL1 oncogene. This abnormal gene causes the leukaemia and can be effectively treated by kinase inhibitor drugs in most patients. However, drug resistance can occur in 10 to 20% of patients. We investigate factors associated with clinical response and resistance to the targeted therapy. The rate of leukaemic cell death may be an important factor for response. Those with a very rapid initial response have been identified as having the best long term prospects, whereas those with a slow response may need a change of therapy to avoid disease progression and death. Optimisation of therapy is frequently needed for the best outcomes.

Biological factors, such as a patient's inherited genetic makeup, may play a role in the dynamics of leukaemic cell death (apoptosis) and hence affect an individual's response to therapy. We are investigating genes involved in the apoptotic process to determine if inherited factors modulate treatment response. Our aim is to identify biomarkers at the time of diagnosis that will predict response and to guide the most appropriate type of drug the patient should receive. We are also using new technology to search all genes for acquired, harmful mutations that may be present at the time of diagnosis that could lead to rapid disease progression. This only occurs in a few patients but can lead to devastating consequences. Our research continues to offer guidance to haematologists in terms of appropriate monitoring of treatment response and the early prediction of drug resistance.

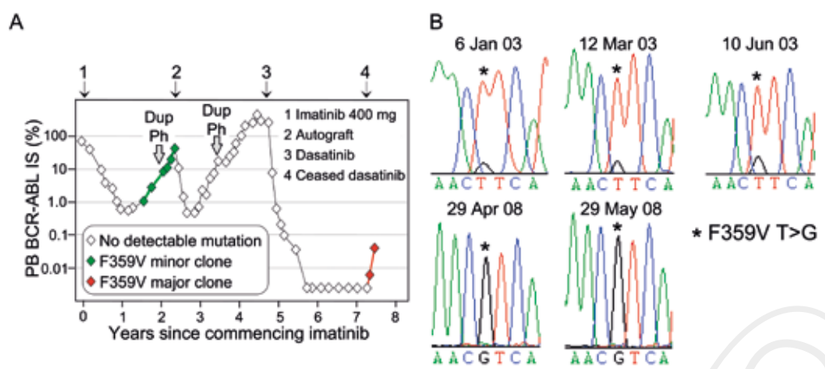
Outcomes for the Community

Our research has benefited some patients with CML by identifying the factors that may lead to a trial of drug cessation. Although side effects in some patients may be minor, they can impact the long term quality of life. Stopping therapy successfully means that patients may be able to lead a normal life. Additionally, the cost saving of drug therapy for the community is substantial and millions of dollars could be saved annually.

Key discoveries 2013

The early molecular response to drug therapy can identify patients who may be able to stop taking their medication
Tyrosine kinase inhibitor drugs have made a remarkable difference to survival for patients with CML. Most patients can now enjoy a normal life expectancy as long as they continue to take their medication regularly. This year the results of an Australian study that commenced in 2006 was published that investigated the possibility of stopping medication without relapse. Patients were carefully selected and had received therapy for at least 3 years and had a very good response during that time. Their leukaemia was not detected using sensitive techniques. About 40% of the patients who enrolled in the study did not relapse. Those who did relapse were very quickly and safely rescued by restarting their medication. The study demonstrated that it is safe to stop therapy under very controlled conditions for some carefully selected patients. Another study of more than 400 patients identified the factors that predict which patients may eventually be able to undertake a trial of stopping therapy. We found that very few patients actually achieve the criteria for stopping. Females and those patients who had a very rapid initial response to therapy are more likely to be able to stop. The outcome from this study is that more patients may be able to reach the criteria for stopping if they are treated with a more potent kinase inhibitor. This will benefit patients who currently face the prospect of life long therapy with ongoing side effects.

Drug resistance causing BCR-ABL1 mutations can remain dormant for many years and lead to drug resistance with a change of therapy
Some patients develop resistance to kinase inhibitor therapy. The main mechanism is a mutation within the gene that causes CML: BCR-ABL1. These mutations interfere with drug binding, but for most mutations a change of therapy restores sensitivity. The new therapy needs to be carefully selected to ensure that the mutation does not cause resistance to the new drug as well. By carefully monitoring patients with mutations over many years who had changed therapy, we found that some sensitive mutations are not eradicated by the new drug, but remain dormant and undetectable. These patients should not receive another therapy change if their historical mutation causes resistance to the next drug. In these cases, the dormant mutation can rapidly grow, cause resistance again and lead to a very poor outcome. Our study demonstrated for clinicians the importance of knowing the patient mutation history and considering the history when making therapeutic decisions.



Selection and de-selection of a resistant mutant subclone over the course of more than seven years of therapy according to the selective pressure of therapy.
(A) BCR-ABL1 mRNA levels showing rise and fall corresponding to times of response, resistance and therapy cessation.
The patient acquired a mutation resistant to the kinase inhibitor imatinib.
(B) Sequencing chromatograms. When the mutation was first detected it was a minor clone. The patient received an autologous transplant and the kinase inhibitor dasatinib. The F359V mutation is sensitive to dasatinib and became undetectable by direct sequencing but existed as a subclonal mutation, which emerged as the predominant clone in the absence of kinase inhibitor nearly five years later. The F359V mutation is resistant to the inhibitor nilotinib. This case is an example where a mutation can remain dormant for many years and could cause disease progression if the patient received nilotinib therapy.

Natasha Harvey | Jan Kazenwadel | Genevieve Secker

Kelly Betterman | Drew Sutton

Lymphatic Development Laboratory

Associate Professor Natasha Harvey PhD

Lymphatic vessels are a key component of the cardiovascular system. These specialised vessels maintain fluid homeostasis, absorb fats from the digestive tract and are an important highway for immune cell traffic. Defects in the growth and development of lymphatic vessels underlie human disorders including primary lymphoedema, lymphangiectasia, and lymphangioma.

Cancer cells exploit the lymphatic vasculature as a route for metastasis and in some cases, promote the growth of new lymphatic vessels within the tumour environment as a means to gain entry to this vascular highway and thereby spread throughout the body. The focus of our laboratory is to understand how the lymphatic vascular network is constructed during development.

We are interested in identifying and characterising genes that are important for lymphatic vessel growth, patterning and maturation. Once we understand how lymphatic vessel growth and development is normally controlled, we will gain new insight into how this process 'goes wrong' in human disease and moreover, will be afforded the opportunity to rationally design novel therapeutics able to block or promote lymphatic vessel growth and/or function and thereby treat human lymphatic vascular disorders.

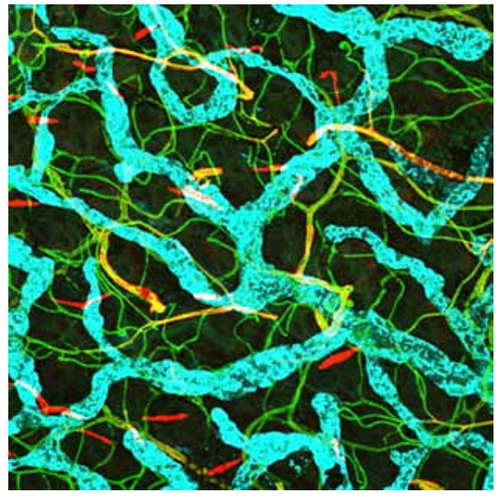
Outcomes for the **Community**

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

Key discoveries 2013

Defining the role that GATA2 plays in lymphatic vessel development

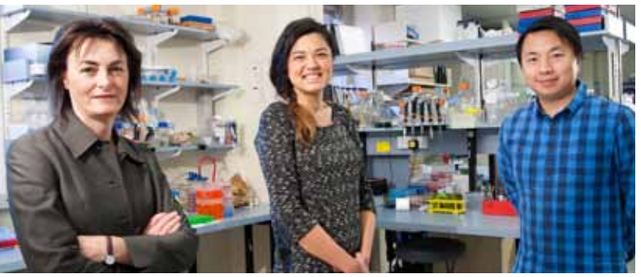
In collaboration with Professor Hamish Scott's team at the Centre for Cancer Biology, we recently discovered that heritable mutations in the transcription factor GATA2 predispose carriers to lymphoedema and myelodysplasia syndrome (MDS)-acute myeloid leukaemia (AML) (Kazenwadel *et al*, Blood, 2012). This discovery revealed a key role for GATA2 in lymphatic vessel growth, maturation and/or function. We have subsequently shown that GATA2 is present at high levels in lymphatic vessel valves and that GATA2 regulates the expression of genes required for valve development. Our current work aims to define precisely how GATA2 regulates the development of lymphatic vessel valves, in order to understand how GATA2 mutations result in lymphoedema. Ultimately, we aim to identify new therapeutic targets to which effective therapeutics for the treatment of lymphoedema could be designed.



Lymphatic vessels (cyan) and blood vessels (green) in adult skin

Precise control of retinoic acid levels is important for development of the lymphatic vasculature

During lymphatic vascular development in the mammalian embryo, a subset of endothelial cells in the cardinal veins is programmed to adopt a lymphatic endothelial fate once they 'switch on' the transcription factor Prox1. However, very little is known about how the size of this progenitor pool is programmed. In collaboration with Dr Mathias Francois at the Institute for Molecular Bioscience, Brisbane, we have shown that genetic modulation of retinoic acid levels has a dramatic impact on lymphatic endothelial progenitor cell specification and lymphatic vascular development (Bowles *et al*, Dev Biol, 2013). Increased levels of retinoic acid resulted in many more lymphatic endothelial progenitor cells present within the cardinal veins and accordingly, in greatly enlarged lymphatic vessels. Conversely, reduced levels of retinoic acid resulted in smaller lymphatic vascular structures. This work revealed that precise regulation of retinoic acid levels in important for normal development of the lymphatic vasculature.



Michelle Grimbaldeston | Natasha Kolesnikoff | Dave Yip

Viera Stanekova | Svetlana Vassilieva | Nicholas Hauschild

Mast Cell Laboratory

Associate Professor Michele Grimbaldeston PhD

Mast cells are unique immunocytes that normally reside in tissues, particularly those that are exposed to the external environment such as the skin, gut and lung. Historically, they are depicted as major effector cells of asthma and other IgE-associated allergic disorders and immune responses to parasites.

However, in addition to their ability to initiate and amplify inflammation, mast cells can also regulate such responses to protect against pathological effects of excessive inflammation and aide the processes of restoring tissue homeostasis.

Research being undertaken by the Mast Cell Laboratory focuses on the novel regulatory abilities of mast cells, with an emphasis on how this dynamic cell contributes to the regulation of inflammation associated with allergy and skin cancer development. In collaboration with Dr Michael Samuel (CCB), Dr Thomas Gebhardt (University of Melbourne) and Professor Gunnar Pejler (Uppsala, Sweden), we are investigating the important question of whether mast cell function at the peri-lesional interface provides a permissive tumourigenic environment or guards against rapid neoplastic progression during skin carcinogenesis. At the molecular level we have identified that at certain stages of UVB-induced neoplastic progression, mast cells protect against detrimental inflammation and tissue changes by secreting IL-10 and the chymotrypsin-like protease, mast cell protease 4.

Another important aspect of our studies is to identify agents that can harness the negative regulatory ability of mast cells and thereby alter their activation state from a nefarious pro-inflammatory one to that of a beneficial anti-inflammatory one. In 2012, CSL Ltd and my laboratory, together with Professor Angel Lopez (CCB), formed a partnership to develop therapeutics that specifically target the overactivity of mast cells without causing loss of their viability. Already we have identified a number of molecules (Commercial in Confidence) with such efficacy in vitro and we are now investigating them for their therapeutic potential utilising humanised mouse models of nasal polyp growth, and thereby establishing proof of principle prior to engagement in Phase I clinical trials.

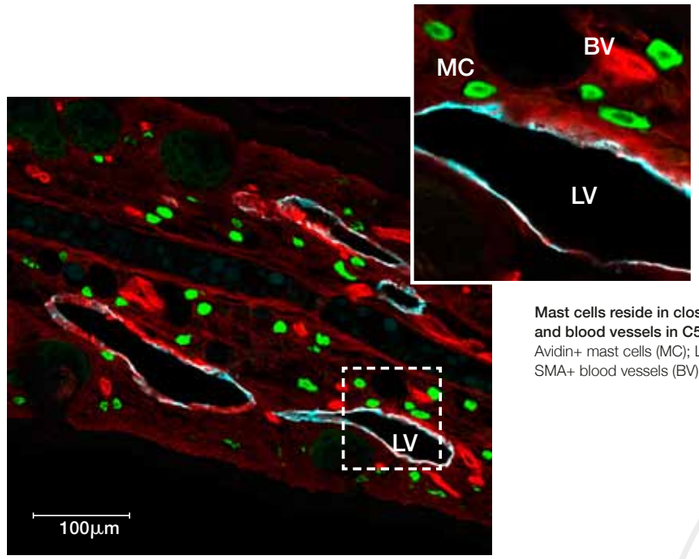
Outcomes for the **Community**

Our research extends from basic discovery in mouse models through to drug development for clinical settings. The emergence of the notion that mast cells also possess ‘anti-inflammatory’ potential and that they exhibit a level of ‘plasticity’ in response to the signals they receive from the tissue in which they reside, points to the possibility that ‘harnessing’ mast cell functions will be clinically beneficial. Our finding that vitamin D3-induced mast cell activation can initiate anti-inflammatory responses, suggests that by identifying potential druggable targets that engage the negative regulatory propensity of mast cells will enable new therapies to emerge. Such endeavours will be of paramount importance, for example, to people who suffer with allergic disease, a setting where mast cells can exacerbate the extent of the pathology.

Key discoveries 2013

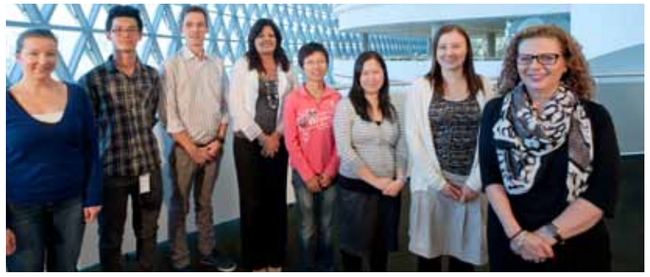
Vitamin D3 metabolites repress IgE-mediated mast cell activation

Mast cells have long been recognized as active participants of the allergic response at specific sites. Whether in the skin or the lung, the binding and cross-linking of IgE on the surface of mast cells stimulates the release of inflammatory mediators that exacerbate the allergic response. Our new findings demonstrate that the pro-inflammatory properties of MCs in certain IgE-dependent immune settings can be reduced upon vitamin D3 metabolite administration. Utilizing the powerful tool of mast cell-deficient c-kit mutant mice, that can be successfully repaired of their mast cell deficiency by selective engraftment of bone marrow-derived cultured mast cells, we observed that topical cutaneous application of biologically active (1a,25(OH)2D3) or inactive (25OHD3) vitamin D3 significantly curtails ear swelling responses associated with IgE-mediated passive cutaneous anaphylaxis. Notably, this effect required the presence of dermal mast cells and their expression of vitamin D receptors (Journal Allergy Clinical Immunology, in press).



Mast cells reside in close proximity to lymphatic vessels and blood vessels in C57BL/6 mouse ear pinnae
Avidin+ mast cells (MC); Lyve1+ dilated lymphatic vessels (LV) SMA+ blood vessels (BV)

Timothy Hughes | Tamara Leclercq | Chung Kok | Dale Watkins | Jenny McLean
Liu Lu | Kartini Asari | Paul Mathew



Laura Eadie | Ben Leow | Jarrad Goyne | Janey Nicholson
Jackie Wang | Phuong Dang | Eva Nievergall | Deborah White

Melissa White Memorial Laboratory

Clinical Laboratory: Professor Timothy Hughes MD FRACP FRCPA MBBS
Research Laborartory: Professor Deborah White PhD FFSc (RCPA)

The primary focus of this laboratory is translational research into Chronic Myeloid Leukaemia (CML), characterised by the constitutively active tyrosine kinase Bcr-Abl, and more recently also Acute Lymphoblastic Leukaemia (ALL).

While the majority of patients with these malignancies respond well to current therapies, there is no real cure and a significant proportion of patients are likely to develop resistance to these therapies leading to relapse and/or persistent disease.

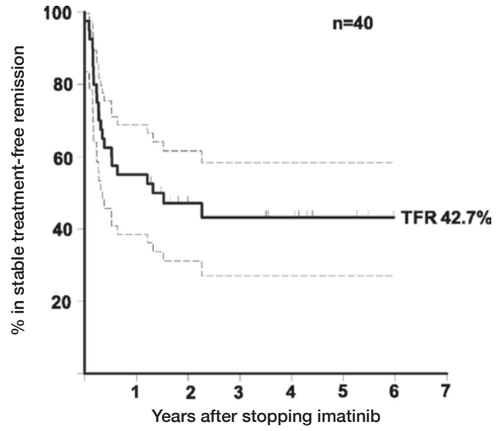
Research in The Melissa White Memorial Laboratory strives to understand the underlying biological principles of resistance to therapy, to evaluate the usefulness and clinical relevance of novel targeted therapies and to develop tests to identify poor responders at diagnosis, so that therapy can be altered accordingly.

Chronic myeloid leukaemia (CML) is characterised by the Philadelphia chromosome that results from a reciprocal translocation between the long arms of chromosome 9 and 22. This translocation results in a fusion of the *BCR* and *ABL1* genes, and this fusion gene encodes a constitutively active tyrosine kinase Bcr-Abl which results in excess proliferation and reduced death of white blood cells. If left untreated, the disease progresses from the chronic phase (CP) into blast crisis, which resembles an acute leukaemia and is invariably fatal. The development of first, second and third generation tyrosine kinase inhibitors (TKIs: imatinib, nilotinib, dasatinib and most recently ponatinib) has revolutionised targeted therapy and markedly improved treatment outcomes for CP-CML patients. However, there are a group of patients who respond poorly, and intolerance, development of TKI resistance and progression to blast crisis remain of major concern. Even in patients who show good clinical responses to first line drugs, the disease is rarely fully eradicated, thus patients currently expect to be on TKI therapy for life.

Outcomes for the Community

While TKI therapy has revolutionized the treatment of CML, an important focus of our laboratory is to identify patients at risk of responding poorly to therapy due to TKI resistance, so that at diagnosis therapy can be tailored for the best possible clinical outcome. Coupled with our world-class clinical trials and translational research, our laboratory heads pioneered training programs that see at least 6 international haematologists trained in the latest techniques for management and monitoring of leukaemia. Taken together the work from our laboratory produces seminal findings in leukaemia research and contributes to the always changing clinical management of adult and childhood leukaemia.

Key discoveries 2013



Rate of treatment-free remission (TFR) in 40 CML patients
Actuarial estimate of the rate of TFR. The 95% CI is indicated by dashed lines.
Ross D M *et al*, Blood 2013; 122: 515-522

Safety and efficacy of imatinib cessation for CML patients with stable undetectable minimal residual disease: results from the TWISTER study

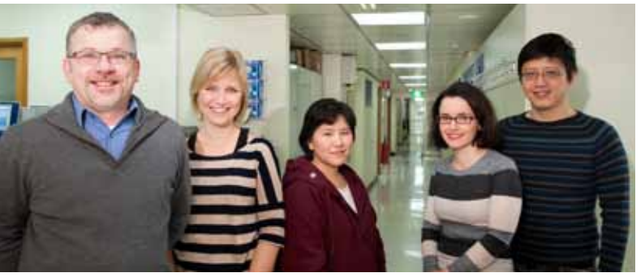
Most patients with chronic myeloid leukemia (CML) treated with imatinib will relapse if treatment is withdrawn. We conducted a prospective clinical trial of imatinib withdrawal in 40 chronic-phase CML patients who had sustained undetectable minimal residual disease (UMRD) by conventional quantitative polymerase chain reaction (PCR) on imatinib for at least two years. Patients stopped imatinib and were monitored frequently for molecular relapse. At 24 months, the actuarial estimate of stable treatment-free remission was 47.1%. Most relapses occurred within four months of stopping imatinib, and no relapses beyond 27 months were seen.

In the 21 patients treated with interferon before imatinib, a shorter duration of interferon treatment before imatinib was significantly associated with relapse risk, as was slower achievement of UMRD after switching to imatinib. Highly sensitive patient-specific BCR-ABL DNA PCR showed persistence of the original CML clone in all patients with stable UMRD, even several years after imatinib withdrawal. No patients with molecular relapse after discontinuation have progressed or developed BCR-ABL mutations (median follow-up, 42 months). All patients who relapsed remained sensitive to imatinib re-treatment.

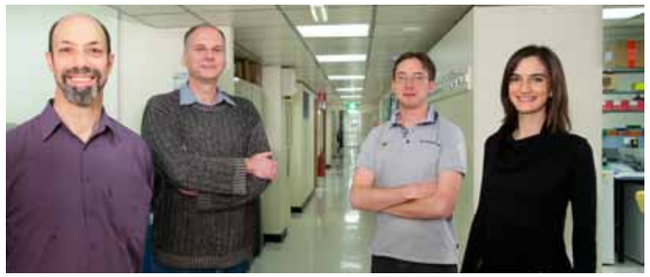
These results confirm the safety and efficacy of a trial of imatinib withdrawal in stable UMRD with frequent, sensitive molecular monitoring and early rescue of molecular relapse. (Blood. 2013; 122(4): 515-522)

Monoclonal antibody targeting of IL-3 receptor á with CSL362 effectively depletes CML progenitor and stem cells

Despite the remarkable efficacy of tyrosine kinase inhibitors (TKIs) in eliminating differentiated chronic myeloid leukaemia (CML) cells, recent evidence suggests that leukemic stem and progenitor cells (LSPCs) persist long-term, which may be partly due to cytokine-mediated resistance. We evaluated the expression of the IL-3 receptor α subunit (CD123), an established marker of acute myeloid leukaemia (AML) stem cells, on CML LPSCs and the potential of targeting those cells with the humanized anti-CD123 monoclonal antibody CSL362. Compared to normal donors CD123 expression was higher in $CD34^+/CD38^+$ cells of both chronic phase and blast crisis CML patients, with levels increasing upon disease progression. CSL362 effectively targeted CML LPSCs by selective antibody-dependent cell-mediated cytotoxicity (ADCC)-facilitated lysis of $CD123^+$ cells and reduced leukemic engraftment in mice. Importantly, not only health donor allogeneic natural killer (NK) cells were able to mount an effective CSL362-mediated ADCC response, but also CML patients' autologous NK cells. In addition, CSL362 also neutralized IL-3-mediated rescue of TKI-induced cell death. Notably, combination of TKI and CSL362-induced ADCC caused even greater reduction of CML progenitors and further augmented their preferential elimination over normal haematopoietic stem and progenitor cells. Thus, our data supports the further evaluation of CSL362 therapy in CML.



Hamish Scott | Bergithe Oftedal | Young Lee | Lucia Gagliardi | Chan-Eng Chong



Chris Hann | Peter Brautigan | Bradley Chereda | Alicia Byrne

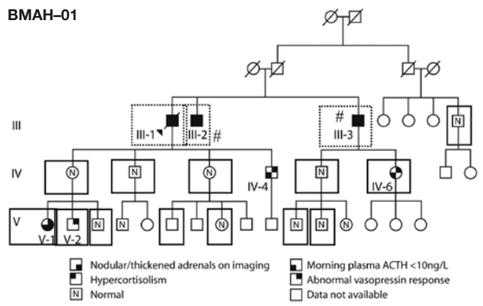
Molecular Pathology Research Laboratory

Professor Hamish S Scott PhD FFSc (RCPA)

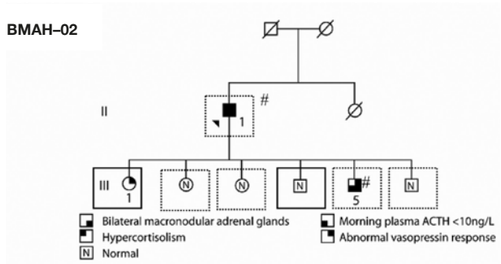
Many disease processes in humans have a genetic component. This can be either inherited (familial and germline), or acquired by somatic mutation during cell division. The identification of genes and mutations that cause or predispose families to diseases, or mutations in genes acquired during disease progression are important as diagnostic and prognostic markers, as well as providing direct targets and biological pathways for therapeutic intervention.

Our research program spans basic to applied genetic research. It takes advantage of existing and emerging technologies, and resources unique to our research team and collaborators, such as patient collections and mouse models. We are interested in how and why genetic mutations occur, how these changes cause diseases or disease predisposition such as cancer and autoimmunity, and ways of better treating and monitoring these diseases. Our 'model' diseases are typically blood cell diseases such as leukaemias, lymphomas and autoimmunity (eg arthritis). These diseases are mechanistically linked, being caused by excessive clonal expansion of a specific blood cell type, and often occur together. We also work on rare, or orphan, diseases with unmet clinical need, such as genetic diagnoses for family planning.

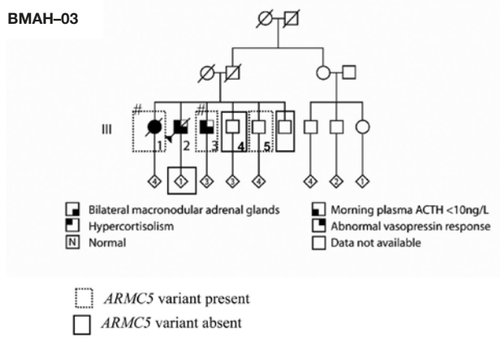
BMAH–01



BMAH–02



BMAH–03



Segregation analysis of the ARMC5 variant in kindreds BMAH-01, BMAH-02 and BMAH-03
Within kindreds, the variant segregated with the disease phenotype as defined by a diagnosis of Cushing's syndrome or the presence of adrenal nodules. In BMAH-03: III-1: One of four offspring carries the variant III-3 and III-4: One offspring from each individual was tested and negative for the variant III-5: Two offspring were tested and negative for the variant
SNV–single nucleotide variant

# indicates individuals who were exome sequenced
► indicates the proband
◇ indicates the number of offspring – gender not specified

Key discoveries 2013

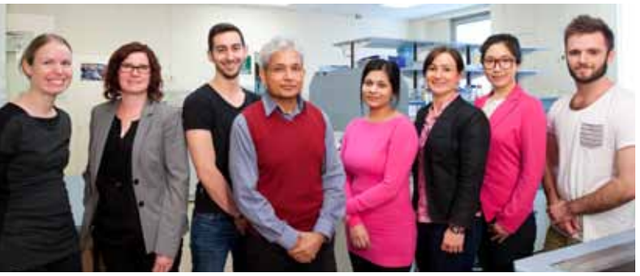
Familial PAX5 mutations confers susceptibility to pre-B cell acute lymphoblastic leukemia
Somatic alterations of the lymphoid transcription factor gene PAX5 (also known as BSAP) are a hallmark of B cell precursor acute lymphoblastic leukemia (B-ALL), but inherited mutations of PAX5 have not previously been described. Here we report a new heterozygous germline variant, c.547G>A (p.Gly183Ser), affecting the octapeptide domain of PAX5 that was found to segregate with disease in two unrelated kindreds with autosomal dominant B-ALL. Leukemic cells from all affected individuals in both families exhibited 9p deletion, with loss of heterozygosity and retention of the mutant PAX5 allele at 9p13. Two additional sporadic ALL cases with 9p loss harbored somatic PAX5 substitutions affecting Gly183. Functional and gene expression analysis of the PAX5 mutation demonstrated that it had significantly reduced transcriptional activity. These data extend the role of PAX5 alterations in the pathogenesis of pre-B cell ALL and implicate PAX5 in a new syndrome of susceptibility to pre-B cell neoplasia.

Genetic studies of Familial Bilateral Macronodular Adrenal Hyperplasia
Bilateral macronodular adrenal hyperplasia (BMAH) is a rare cause of Cushing's syndrome, a disease characterised by the tissue effects of long-term cortisol excess. These include: insulin resistance and diabetes, hypertension, visceral obesity, osteoporosis and fragility fractures and a predisposition to venous thromboembolism. Early diagnosis is paramount in reducing disease morbidity. Whilst previously considered to occur sporadically, we and others have reported on families affected by BMAH. The onset of Cushing's in BMAH is typically insidious, making early diagnosis difficult and until recently, potentially affected individuals from BMAH kindreds could only be identified by repeated clinical, biochemical and radiological screening.We undertook genetic studies to identify the inherited basis of familial BMAH in three kindreds we have previously phenotyped. Whole exome capture and sequencing of two affected individuals from each of three BMAH kindreds identified a single gene (ARMC5) harbouring novel variants in all exome samples. Others have reported ARMC5 mutations occurring in approximately 55% of patients with 'sporadic' forms of BMAH.

Aire dependent Thymic Deletion and Regulatory T Cells Prevent Anti-myeloperoxidase Glomerulonephritis (GN)
Loss of tolerance to neutrophil myeloperoxidase (MPO) underlies the development of ANCA-associated vasculitis and GN, but the mechanisms underlying this loss of tolerance are poorly understood. Here, we assessed the role of the thymus in deletion of autoreactive anti-MPO T cells and the importance of peripheral regulatory T cells in maintaining tolerance to MPO and protecting from GN. Thymic expression of MPO mRNA predominantly localized to medullary thymic epithelial cells. To assess the role of MPO in forming the T cell repertoire and the role of the autoimmune regulator Aire in thymic MPO expression, we compared the effects of immunizing Mpo2/2 mice, Aire-/- mice, and control littermates with MPO. Immunized Mpo-/- and Aire-/- mice developed significantly more proinflammatory cytokine-producing anti-MPO T cells and higher ANCA titers than control mice. When we triggered GN with a subnephritogenic dose of anti-glomerular basement membrane antibody, Aire-/- mice had more severe renal disease than Aire+/+ mice, consistent with a role for Aire-dependent central deletion in establishing tolerance to MPO. Furthermore, depleting peripheral regulatory T cells in wild-type mice also led to more anti-MPO T cells, higher ANCA titers, and more severe GN after immunization with MPO. Taken together, these results suggest that Aire-dependent central deletion and regulatory T cell–mediated peripheral tolerance both play major roles in establishing and maintaining tolerance to MPO, thereby protecting against the development of anti-MPO GN.

Outcomes for the Community

Our discoveries imply that what were previously regarded as predominantly sporadic diseases can in fact be due to germline mutations in many affected patients. Furthermore, the discovery of the germline basis of BMAH has enabled the development of a diagnostic genetic test at SA Pathology for ARMC5 mutations. This will be of benefit to BMAH families because genetic testing will identify mutation carriers, who would benefit from periodic clinical screening and testing, whilst sparing those who do not carry the mutation from unnecessary investigations.



Loretta Dorstyn | Donna Denton | Joey Puccini | Sharad Kumar | Swati Dawar
Claire Wilson | Cindy Xu | Andrej Nikolic

Pranay Goel | Ian Nicholson | Kimberly Mackenzie | Jantina Manning
Omri Alfassy | Sonia Shalini | Alyshea Collaco | Natasha Boase | Shannon Nicolson

Molecular Regulation Laboratory

Professor Sharad Kumar MSc PhD FAA

Our broad research focus is on cellular and molecular basis of disease, with an emphasis on cancer biology. Our two major interests are: (1) the study of programmed cell death and its role in cancer, and (2) understanding the regulation of cellular homeostasis by ubiquitination.

Millions of cells in the human body die every minute as part of normal homeostasis by a special process termed apoptosis. Apoptotic cell death plays a fundamental role in cell and tissue homeostasis and too little or too much of it can lead to many human diseases including cancer. Given the essential role of cell death in normal functioning of the human body, deciphering the mechanisms of apoptosis is essential for understanding disease processes and to design effective treatment strategies for diseases which arise due to inappropriate apoptosis. We study the mechanisms and regulation of cell death in normal homeostasis and during animal development, with a particular emphasis on the roles of the cell death and survival machinery in cancer.

Ubiquitination (attachment of ubiquitin to a target protein) is a common type of protein modification that is involved in the regulation of protein stability, degradation, localisation and trafficking. Ubiquitination is a major regulator of many ion channels, receptors and transporters. We are studying the functions of a group of ubiquitin-protein ligating enzymes (Nedd4 family of ubiquitin ligases), which are implicated in the ubiquitination of a number of proteins. We use a variety of molecular, cellular and gene knockout approaches to study the physiological functions of these enzymes and establish their roles in human diseases.

Outcomes
for the Community

Our research will provide a better understanding of disease mechanisms and the functioning of the human body. For example, we have identified Nedd4-2 as a regulator of ion channels in the central nervous system, which are involved in pain and epilepsy. We are also deciphering the mechanism of key genes involved in cell death, aging and tumour progression, including Caspase-2 and UTX. These findings provide the potential to discover new disease markers and novel therapeutic targets.

Key discoveries 2013

Nedd4-2 controls voltage-gated sodium channels in primary cortical neurons

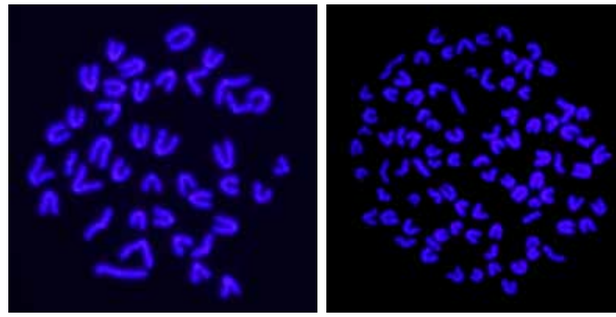
Nedd4-2 is a ubiquitin protein ligase that has been implicated in regulating several ion channels, including voltage-gated sodium channels (Na_vs). However, the conditions under which Nedd4-2 mediates native Na_v regulation has remained uncharacterised. In a recent publication (Biochem J. 457(1): 27-31), using Nedd4-2 deficient mice, we provide the first physiological evidence that Nedd4-2 has an essential function in regulating Na_vs in the central nervous system. We demonstrated that Nedd4-2 is involved in the activation-induced down-regulation of Na_vs in response to increased intracellular sodium, and that this occurs in embryonic cortical neurons but not in dorsal root ganglion neurons. We also found that Nedd4-2 is not involved in the regulation of steady-state levels of Na_v channels on the plasma membrane of either embryonic dorsal root ganglion or cortical neurons. The significance of these results is highlighted by the involvement of Na_v channels in neuropathic pain, and diseases such as epilepsy, so elucidating the mechanism of their regulation has important clinical implications.

Caspase-2 is a tumour suppressor and is required for maintaining genome stability

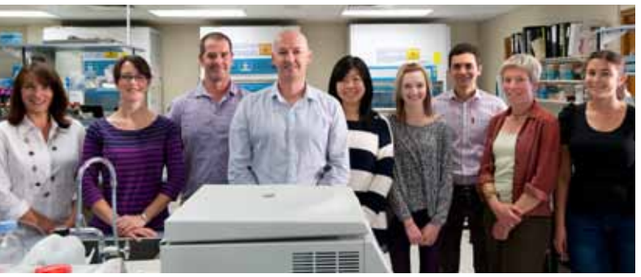
Caspases are cysteine proteases that function as critical regulators of apoptosis and inflammation. Previous work from our laboratory had uncovered that loss of caspase-2 enhances oncogene-induced cell transformation and augments lymphomagenesis in the Eμ-Myc mouse tumour model. We have recently extended upon our previous findings that demonstrate that caspase-2-deficient (*Casp2*$^{-/-}$) cells display defective DNA damage signalling and genomic instability (Cell Death Differ 19: 1288-98). In our most recent work, we found that caspase-2-deficiency enhances lymphomagenesis in *Atm*$^{-/-}$ mice and tumours derived from *Atm*$^{-/-}$*Casp2*$^{-/-}$ mice display increased oxidative damage and enhanced aneuploidy (Proc Natl Acad Sci USA 110, 19920-5). Thus, our work provides additional evidence supporting a role for caspase-2 in tumour suppression and that this function may be linked to its ability in maintaining genome stability and redox homeostasis.

UTX coordinates steroid hormone-mediated autophagy and cell death

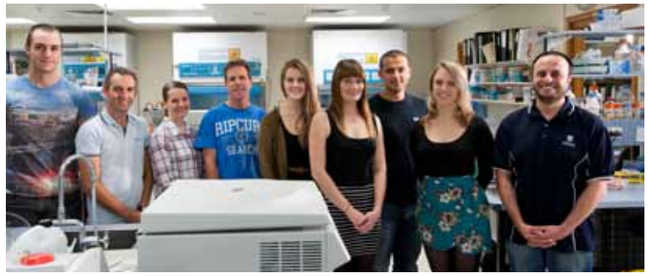
Correct spatial and temporal induction of numerous genes during development requires regulated removal of the repressive histone H3 lysine 27 trimethylation (H3K27me3) modification. Recently, we have identified the histone demethylase gene, UTX, as an 'epigetic modifier' that is necessary to maintain high levels of expression of a number of genes that are required for deleting a specific tissue at a precise time during the development of the fly (Nature Communications 4: 2916). We found that Drosophila UTX binds to the nuclear steroid hormone receptor Ecdysone receptor, and is recruited to the promoters of key apoptosis and autophagy genes to carry out its gene regulatory function. Indeed, salivary gland cell death is delayed in dUTX mutants, and requires UTX catalytic activity. Our findings highlight the importance of UTX activity in regulating hormone-dependent cell death. Interestingly, the conserved human gene is often mutated in many cancer types, and steroid hormones are important in many human cancers, including breast and prostate cancer. Thus this work may provide new insight into the understanding of origins and mechanisms that underlie some types of cancers.



Caspase-2 deficiency leads to chromosomal instability and aneuploidy, as evident in chromosome spreads from lymphomas obtained from Atm-deficient mice (left) and Caspase-2/Atm double deficient mice (right).



Lorena Davies | Melissa Pitman | Jason Powell | Stuart Pitson | Wenying Zhu
Jess Heatlie | Craig Wallington-Beddoe | Jo Woodcock | Elferaan Quatermass



Alexander Lewis | Carl Coolen | Briony Gliddon | Paul Moretti | Courtney Moore
Heidi Neubauer | Mohammed Alahamdi | Earanee Neidzwieki | Maurizio Costabile

Molecular Signalling Laboratory

Professor Stuart Pitson PhD

The Molecular Signalling Laboratory examines sphingolipid-mediated cell signalling pathways, and how they contribute to cancer and other diseases. The primary focus of our work is the enzyme sphingosine kinase, that controls the cellular levels of the important signalling molecules, ceramide, sphingosine and sphingosine 1-phosphate.

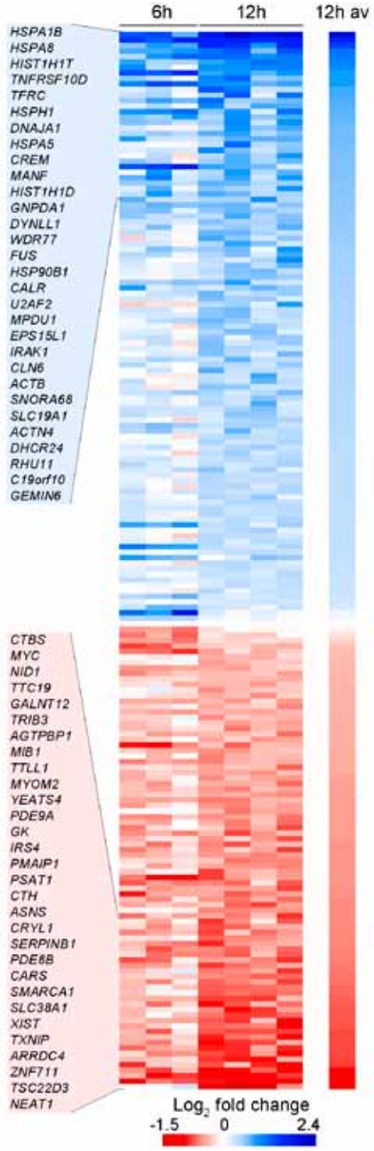
Ceramide, sphingosine and sphingosine 1-phosphate regulate a diverse range of cellular processes by acting as intracellular second messengers, while sphingosine 1-phosphate also acts as a ligand for a family of sphingosine 1-phosphate-specific cell surface receptors. Of greatest interest to our laboratory are findings that elevated cellular sphingosine kinase prevents programmed cell death (apoptosis), enhances cell proliferation, and leads to neoplastic cell transformation. This indicates an oncogenic role for sphingosine kinase, which is further supported by recent data from us and others showing elevated sphingosine kinase in a variety of human cancer cells, and inhibition of tumour growth *in vivo* by genetic or chemical suppression of sphingosine kinase.

In addition to this role in tumourigenesis, sphingosine kinase and sphingosine 1-phosphate appear central players in many other cellular processes, including regulation of leukocyte migration, enhancing blood vessel formation, and enhancing constriction of airway smooth muscle cells. Thus, sphingosine kinase is also a potential target for therapeutic intervention in inflammation, atherosclerosis, hypertension and asthma.

Recent work in the Molecular Signalling Laboratory has concentrated on identifying the mechanisms regulating sphingosine kinase, the cellular functions controlled by this enzyme, and in developing small molecule inhibitors as anti-cancer agents. In particular we have made several major breakthroughs in understanding how this enzyme in activated, relocalised to the plasma membrane, and deactivated, which have provided novel therapeutic targets to control cancer and other diseases. We have also identified that the substrate of sphingosine kinase, sphingosine, is a key regulator of the pro-survival 14-3-3 proteins. Indeed, our work suggests that inactivation of 14-3-3 by sphingosine is a key control mechanism that if deregulated can enhance tumourigenesis. Thus, this pathway also represents a novel therapeutic target that may be exploited to control cancer.

Outcomes
for the **Community**

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



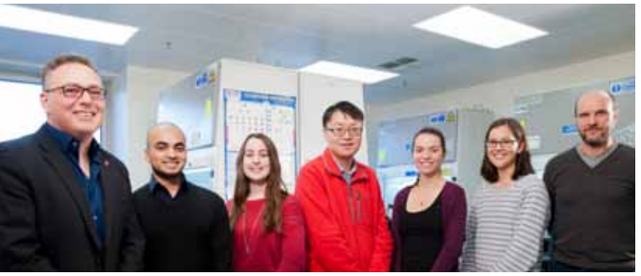
Sphingosine kinase contributes to cancer progression through transferrin receptor 1

Sphingosine kinase shows considerable promise as a target for anti-cancer therapy in a diverse range of solid tumours and leukaemias. To date, however, the mechanisms whereby sphingosine kinase enhances cancer progression have been not well understood. Using a gene expression array approach, we have demonstrated a novel mechanism whereby sphingosine kinase regulates cell survival, proliferation and neoplastic transformation through enhancing expression of transferrin receptor 1. Importantly, these findings, published in Oncogene, identify a novel means of targeting the oncogenic signalling of sphingosine kinase via blocking transferrin receptor 1 function.

Dengue virus inhibition of sphingosine kinase contributes to pathogenesis

In collaborative work with Dr Jillian Carr of Flinders University published in the Journal of General Virology, we have shown that dengue virus infection results in a significant reduction in cellular sphingosine kinase activity, which contributes to elevated virus-induced cell death and pathogenesis associated with this infection. We have also determined the mechanism whereby dengue virus reduces sphingosine kinase activity by showing that the viral RNA hijacks host cell eEF1A, a direct activator of sphingosine kinase, and thereby blocks its stimulatory effects on this enzyme. Importantly, this provides valuable information in understanding of the pathogenesis of this mosquito-borne virus that may enable future therapeutics to be developed to combat this disease.

Increased sphingosine kinase 1 expression results in altered expression of a number of genes
The 30 genes with the greatest up- (blue) or down- (red) fold changes are shown.



Andrew Zannettino | Ankit Duta | Natalia Martin | Stanley Cheung | Kimberley Evans
Sally Martin | Stephen Fitter | Absent Melissa Cantley and Sophia Moraitis

Krzysztof Mrozik | Jacqueline Noll | Kate Vandyke | Mary Matthews
Sharon Paton | Chee Man Cheong | Duncan Hewett | Vicki Wilczek

Myeloma Research Laboratory

Professor Andrew Zannettino PhD

The Myeloma Research Laboratory studies the molecular and cellular basis for the development of the bone marrow cancer, multiple myeloma. Myeloma is characterised by the clonal proliferation of malignant plasma cells (an immune cell type that normally protects us against infection).

Myeloma is the second most common blood cancer affecting humans, with over 1,500 Australians diagnosed each year. Despite recent advances in treatment, myeloma remains almost universally fatal with a 10-year survival rate of approximately 17%. The main clinical manifestations of myeloma are the development of osteolytic bone lesions, bone pain, hypercalcaemia, renal insufficiency, suppressed immunoglobulin production and increased BM angiogenesis (blood vessel formation). It is now widely accepted that most, if not all, cases of myeloma are preceded by a premalignant (asymptomatic) monoclonal gammopathy of uncertain significance (MGUS) stage. However, the genetic factors which trigger the progression from this asymptomatic stage of the disease to overt malignant myeloma remains to be determined. Moreover, recent studies suggest that the bone marrow microenvironment plays a central role in disease progression. Our laboratory's research is focussed on identifying the key genes that are responsible for disease progression and the role played by the bone microenvironment in disease pathogenesis. We believe that these approaches will enable us to identify new molecular markers of disease risk and to design drugs against novel therapeutic targets.

Current projects are focused on:

- Identification of genetic factors that trigger the progression from asymptomatic MGUS to overt malignant MM.
- Defining the role of the bone marrow microenvironment in the development of MM.
- Determining the effects of myeloma plasma cells on mesenchymal stem cell (MSC) differentiation.
- Identifying the role of the mTOR pathway in mesenchymal stem cell biology and bone formation.

Outcomes for the Community

Contribution to the Australian Myeloma Foundation Medical and Scientific Advisory Group amyloidosis guidelines to assist general practitioners and haematologists-oncologists in the detection and treatment of amyloidosis.

Key discoveries 2013

Demonstrated that N-cadherin protein and gene expression is abnormally increased in trephine biopsies and plasma cells from myeloma patients, when compared with those of normal donors.
In addition, we demonstrated for the first time that the levels of circulating N-cadherin were elevated in a subset of patients with myeloma, relative to age-matched controls. Notably, we demonstrated that patients with abnormally high levels of N-cadherin had decreased progression-free survival and overall survival when compared with patients with normal N-cadherin levels. Furthermore, multivariate analyses revealed that the combination of N-cadherin levels and International Staging System (ISS) was a more powerful prognostic indicator than using ISS alone. Collectively, our studies demonstrate that circulating N-cadherin levels are a viable prognostic marker for high-risk myeloma patients.

Increase in trabecular bone volume and trabecular thickness after imatinib treatment is associated with a significant decrease in osteoclast numbers, accompanied by a significant decrease in serum levels of a marker of osteoclast activity.
Imatinib is a tyrosine kinase inhibitor that has been successfully used to treat Philadelphia chromosome-positive chronic myeloid leukemia (CML) and Kit(+) gastrointestinal stromal tumors. We have previously shown that imatinib therapy is associated with an increase in trabecular bone volume. In the present study, we performed a prospective analysis of bone indices in imatinib-treated CML patients to determine the mechanism responsible for this altered bone remodeling. Our studies show that the increase in trabecular bone volume and trabecular thickness after imatinib treatment was associated with a significant decrease in osteoclast numbers, accompanied by a significant decrease in serum levels of a marker of osteoclast activity. In contrast, osteoblast numbers were not altered by up to 24 months of imatinib treatment. Notably, we also found that imatinib caused a site-specific decrease in BMD at the femoral neck. These data suggest that imatinib therapy dysregulates bone remodeling, causing a generalized decrease in osteoclast number and activity that is not counterbalanced by a decrease in osteoblast activity, leading to increased trabecular bone volume. Further long-term investigations are required to determine the causes and consequences of the site-specific decrease in BMD at the femoral neck.

Using flow cytometry, we demonstrated myeloma plasma cell infiltration into the bone marrow leads to an increase in mesenchymal stromal cells and a concomitant decrease in alkaline phophatase osteoblasts in patients with multiple myeloma.
Notably, this increase in mesenchymal stromal cell numbers correlated closely with plasma cell burden at the time of diagnosis. In addition, in comparison with the osteoblast population, the mesenchymal stromal cell population was found to express higher levels of plasma cell- and osteoclast-activating factors, including RANKL and IL-6, providing a mechanism by which an increase in mesenchymal stromal cells may promote and aid the progression of myeloma. Importantly, these findings were faithfully replicated in the C57BL/KaLwRij murine model of myeloma, suggesting that this model may present a unique and clinically relevant system in which to identify and therapeutically modulate the bone microenvironment and, in turn, alter the progression of myeloma disease.

Bone marrow trephine biopsy from a myeloma patient stained with an antibody to CD138 to highlight the malignant plasma cells

Quenten Schwarz | Rachael Lumb | Xiangjun Xu | Absent: Samuela Kabbara

Zarina Greenberg | Eiman Saleh | Sophie Wiszniak | Peter McCarthy

Neurovascular Research Laboratory

Dr Quenten Schwarz PhD

Understanding development and integration of the neuronal and vascular systems at the molecular level presents a major challenge to developmental biologists. Recent advances, including our own, conclusively show that similar molecules are recruited by both systems to coordinate their development.

Our laboratory is particularly interested in understanding the signaling pathways controlling neural stem cell development with the aim of idenitifying molecular defects underlying neurodevelopmental disorders including neuronal tumours, neurocristopathies and neuropsychiatric illness. Together, these disorders affect over 5% of the population and arise from aberrant neuronal development.

Coronal section of an embryonic mouse head stained for cartilage (blue), neural crest stem cells (green) and neurons (red)

Key discoveries 2013

Our group had several seminal findings that lead to breakthrough publications in 2013:

We provided the first evidence that ubiquitination and targeted protein degradation play an essential role in neural crest cell development.
Neural crest cells are a transient population of embryonic stem cells that give rise to much of the cranial skeleton, all cell type of the peripheral nervous system and melanocytes. Understanding the mechanisms controlling their development therefore holds the key to identifying the origins of diseases arising in this cell type, such as neuroblastoma, melanoma and cranofacial disorders. Our laboratory found that the E3 ubiquitin ligase Nedd4 plays an essential role in promoting the identity and survival of neural crest stem cells. Mice lacking this gene had aberrant neural crest cell death and according defects in the cranial skeleton. Our current work is aimed at understanding the role of this ubiquitin ligase in setm cell maintenance in general.

Found an essential role for the protein 14-3-3zeta in dopaminergic signalling, the key pathway that is perturned in mental disorders such as schizophrenia and autism.
Together, these neurodevelopmental disorders affect over 3% of the population and represent one of Australia's major medical issues. We showed that 14-3-3zeta modulates activity of the dopamine transporter DAT that is a major site of drug therapy. Our current work is unravelling the mechanisms through which 14-3-3ζ controls DAT function.

Outcomes for the Community

Our findings provide novel insight to the aetiology of a large number of neuronal and craniofacial disorders. Aberrant stem cell functions sit at the centre of many disorders. Our finding that an E3 ubiquitin ligase is essential for stem cell survival identifies new targets for the innovation of therapies to modify stem cell functions and survival. Our finding that 14-3-3ζ modulates DAT also has dramatic implications toward therapies for a wide range of psychiatric illnesses and drug addiction. DAT is the major site of recreational drug activity and also a major target of all antipsychotic drugs. By understanding the mechanisms through which DAT functions we aim to provide clues to new therapies for drug addiction and psychosis.

Michael Brown

Alex Staudacher | Tessa Gargett

Translational Oncology Laboratory

Professor Michael P Brown MBBS, PhD, FRACP, FRCPA

The Translational Oncology Laboratory is associated with the Royal Adelaide Hospital Cancer Clinical Trials Unit, which has a tumour subtype focus of melanoma and lung cancer.

Accordingly, melanoma projects include a NHMRC-funded phase 1 clinical trial of autologous chimeric antigen receptor (CAR) gene modified T cells in patients with advanced melanoma. The CAR is directed toward the glycolipid, GD2, which is expressed in most metastatic melanoma samples and which may be associated with a resistant, invasive, mesenchymal phenotype of melanoma. In up to a half of advanced melanoma cases, BRAF inhibitor therapy provides short to medium term tumour control. However, this therapy eventually fails in most cases because of mutational and non-mutational mechanisms. We are investigating genotype/phenotype correlations of BRAF inhibitor-resistant melanoma in collaboration with Associate Professor. Stuart Pitson, Associate Professor Claudine Bonder, and Dr Lisa Ebert (CCB). The molecular mechanisms of resistance in melanoma cell lines are being studied as well as the role of vasculogenic mimicry in the phenotype of BRAF inhibitor-resistant melanoma cells. The findings are likely to be of direct therapeutic relevance.

First-line therapy for lung cancer typically involves cytotoxic chemotherapy, which is DNA-damaging and causes cancer cell death. We have preclinical proof of concept for a novel method of detecting cancer cell death based on the APOMAB® monoclonal antibody that is specific for a ribonucleoprotein overexpressed in malignancy. Non-invasive methods for the detection of cancer cell death are useful both for prognostication (where necrotic tumours have a worse prognosis) and prediction of therapeutic response (where increased rates of tumour apoptosis and necrosis are associated with improved patient outcomes).

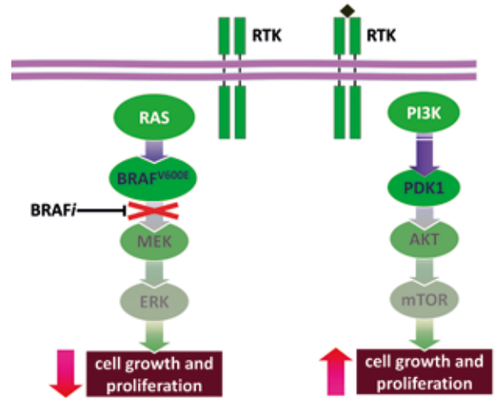
Using the long-lived positron emitter, Zirconium-89, APOMAB will be adapted for immuno-positron emission tomography (immunoPET). In an extension of this project, we shall also investigate the therapeutic potential of APOMAB antibody-drug conjugates (ADCs). ADCs are an emerging class of cancer with two recent US FDA approvals in Hodgkin lymphoma and HER2-positive breast cancer. We are studying the anti-tumour activity of APOMAB-ADCs in pre-clinical lung tumour models and have shown that the activity depends solely on bystander killing effects.

New targeted therapies are shrinking and stabilising cancers of the lung and other organs mainly by blocking kinase-mediated signal transduction. A remaining challenge is how best to translate this therapeutic potential clinically so that more patients can be matched efficiently with the right treatment. Hence, in collaboration with Professor Hamish Scott, Dr Karin Kassahn, and Professor Angel Lopez (CCB and ACRF Genomics Facility, SA Pathology), we are studying the application of various genomic technologies to samples of patient blood and tumour tissue to enable 'reflex' tumour genotyping. Of particular interest is detection of activating and primary resistance mutations in the epidermal growth factor receptor gene in non-small cell lung cancer.

Key discoveries 2013

Epidermal growth factor receptor (EGFR) targeting via radioimmunotherapy and in conjunction with standard cytotoxic chemotherapy and PARP inhibition resulted in eradication of patient-derived xenografts of triple-negative breast cancer. EGFR binding resulted in non-canonical signalling that interfered with tumour repair of double-strand DNA breaks thus further contributing to tumour cell death and anti-effects *in vivo* (Al-Ejeh *et al*, J Nucl Med 2013; highest ranked journal in field of Nuclear Medicine).

BRAF inhibitor therapy using dabrafenib has made a dramatic impact on tumour control in patients with advanced melanoma. However, drug resistance is virtually inevitable and occurs via MEK-dependent and independent mechanisms. This paper shows in comparing genomic analyses of baseline and on-treatment tumour biopsies that deletion or mutation of PTEN, increased copy number of CCND1, and reduced copy number of CDKN2A, were all associated with shorter progression free survival of advanced melanoma patients who are treated with dabrafenib (Nathanson *et al*, Cancer Res 2013; ranking 11 out of 196 journals in the category 'Oncology').



BRAF inhibitor resistance in melanoma may result from 'oncogene bypass' and promote phenotypic alterations including vasculogenic mimicry

Outcomes for the Community

Melanoma and lung cancer are two common types of cancer that require new therapies to improve patient outcomes. We are testing genetic modification of the patient's own T cells as a new way of fighting melanoma in the body. We are also developing a new way of targeting lung cancer based on a technology called antibody drug conjugates.

Michael Samuel | Jasreen Kular | Natasha Pyne

Kaitlin Scheer | Anthony Pollard

Tumour Microenvironment Laboratory

Dr Michael Samuel PhD

The biophysical and biochemical properties of the tumour microenvironment strongly influence the progression of cancers and determine key elements of the prognosis. Increasingly, normalisation of the microenvironment is an important goal of cancer therapy. Our laboratory works to understand how the microenvironment is remodelled at both the biophysical and biochemical levels during tumour initiation and progression, aiming to identify new targets that would be useful as novel cancer therapies.

The Rho signalling pathway is well-known to promote cell motility by its ability to regulate the synthesis and contractility of the cellular actomyosin cytoskeleton. Less well-understood is its role in remodelling the normal tissue microenvironment. Our laboratory uses murine models in which the Rho signalling pathway can be conditionally activated, to determine the mechanisms by which this pathway modifies the ECM and the cellular component of the mivroenvironment. Using one of these models, we have previously demonstrated that activation of the Rho-signalling pathway within the skin causes an increase in the deposition of collagen, a major ECM protein of the dermis. The resulting increase in the stiffness and density of the ECM, disrupted normal tissue homeostasis, promoted tumourigenesis, increased the number and size of lesions and the rate of conversion to malignant carcinoma in a model of cutaneous papillomagenesis and squamous cell carcinoma (SCC) (Cancer Cell 19:776–91). More recently we have established that ROCK, the major effector protein of RhoA/C is highly activated within fibroblasts, macrophages and mast cells populating the tumour microenvironment. We are now working on determining how signalling through the Rho pathway remodels the ECM and modifies the cellular component of the tumour microenvironment during tumour progression.

The 14-3-3 family of phospho-serine binding proteins have diverse functions in cellular processes. They have been implicated as modulators of the Rho signalling cascade, which contains several proteins that are regulated by serine phosphorylation. Our laboratory uses mice deficient in 14-3-3ζ to determine the role of this protein in regulating Rho signalling, tissue homeostasis, tumourigenesis and tumour progression. More recently, we have been working on how 14-3-3ζ regulates the Rho signalling pathway during wound healing.

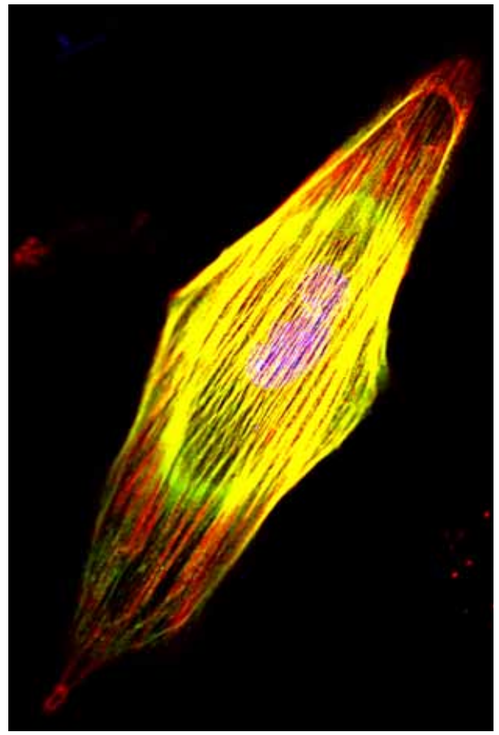
Key discoveries 2013

The function of the Rho signalling pathway in the tumour microenvironment

In collaboration with the Mast Cell Laboratory at the Centre for Cancer biology, we have demonstrated in murine models of skin and intestinal cancer, that tumour associated fibroblasts, macrophages and mast cells exhibit increased signalling through the Rho pathway (Ibbetson *et al*, 2013 and unpublished). Activation of the Rho signalling pathway within these cell types correlates with tumour progression and is not observed in the corresponding normal tissue types. We are currently working on establishing the function of Rho pathway activation in fibroblasts and mast cells within the tumour microenvironment, with the goal of identifying whether normalising Rho signalling within these cell types may be used therapeutically as an approach to targeting the microenvironment.

Regulation of the Rho signalling pathway in wound healing

Using a strain of mice in which 14-3-3ζ expression has been abolished, we have established a novel role for this 14-3-3 isoform in the regulation of Rho signalling during wound healing. The Rho signalling pathway is known to be upregulated at wound margins to permit the establishment of an actomyosin ring that facilitates wound closure. We have established for the first time that Rho signalling at wound margins is also crucial for the production and remodelling of the ECM components that make up the new dermal tissue at the site. We have also shown that 14-3-3ζ acts to restrain Rho signalling at this location, providing temporal control on the production and remodelling of the ECM and through this the speed of re-epithelialisation, enhancing the quality of the resulting healed skin. Slow healing wounds such as those exhibited by diabetics, frequently exhibit high levels of 14-3-3ζ expression. Our observations suggest that the slow wound healing observed may be related to increased inhibition of the Rho signalling pathway in patients.



A skin cell deficient in 14-3-3ζ exhibits enhanced Rho pathway activation as determined by the formation of actin stress fibres (visualised using red fluorescent phalloidin) and the colocalisation of a phosphorylated form of the regulatory myosin light chain (visualised by green immunofluorescence) to the stress fibres

Outcomes for the Community

Epithelial tumours and chronic wounds exhibit altered microenvironments associated with aberrant signalling via the Rho pathway. We are working to identify approaches by which normalising this pathway could lead to novel therapeutic approaches to treating both conditions.

Lisa Ebert | Natasha Pyne | David Dimasi | Emma Thompson | Claudine Bonder

Prithibha Sachi | Lih Tan | Minky Cockshell | Kate Parham | Kiwi Sun

Vascular Biology and Cell Trafficking Laboratory

Associate Professor Claudine Bonder PhD

With a focus on human disease we study the intricate network of blood vessels that carry white blood cells throughout the body. Blood vessels contribute to life threatening diseases such as cancer and heart disease but are also essential for fighting infection and wound repair.

Endothelial cells (ECs) line the lumen of all blood vessels and thus play a pivotal role in maintaining vascular homeostasis. This dynamic interface services an enormous array of functions including the regulation of inflammation, coagulation, vascular tone, permeability, and vessel growth.

A major focus of our group is to (i) investigate blood vasculature in normal and disease states and (ii) better define blood vessel progenitor cells for clinical application. Our work may provide new opportunities to (i) treat debilitating diseases such as allergy, (ii) assist blood vessel repair in patients with cardiovascular disease and (iii) block blood vessel development in cancer patients. More specifically, leukocyte recruitment to sites of inflammation is tightly regulated by ECs which, when activated, express several types of adhesion molecules. Controlling these adhesion molecules is critical to combating diseases such as allergy, cancer and heart disease.

Outcomes
for the **Community**

With a focus on health and well-being we study the intricate network of blood vessels that carry white blood cells throughout our body. Blood vessels contribute to life threatening diseases but are also essential for tissue regeneration and repair. Associate Professor Bonder's work may provide new opportunities to enhance blood vessel development following organ transplantation and control their levels of activation during allerguc inflammation. A better understanding of blood vessels in disease will prviode new treatment options for many debilitating diseases.

Key discoveries 2013

Blood vessels are critical for pancreatic islet function

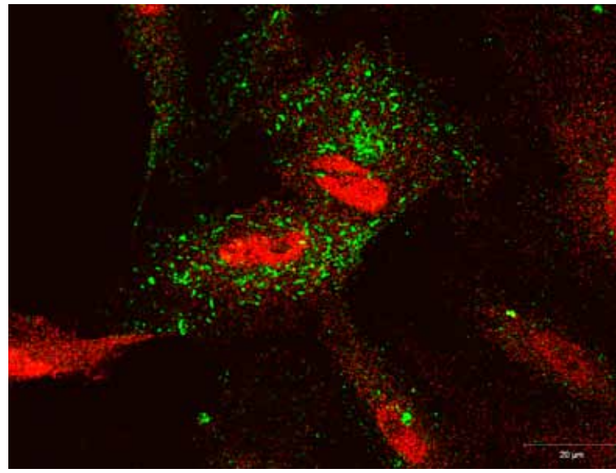
Pancreatic islet transplantation is an emerging cure for Type 1 Diabetes but success is limited by death of insulin producing beta cells post transplantation. Vasculogenic endothelial progenitor cells (EPCs) have the potential to improve islet engraftment, and may also improve islet graft function. In collaboration with Dr Claire Jessup and Associate Professor Toby Coates we have combined EPC and islets into functional mosaic clusters *in vitro* and assessed the interactions between islets and EPC *in vitro* and *in vivo* in a diabetic mouse model of islet transplantation. To date we have shown that mosaic islet:EPC clusters can form successfully and glucose stimulation index function was superior to clusters comprised of islet cells only (Penko Islets 3:1, 2011). More importantly, in 2013 we demonstrated that co-transplantation of islets and EPCs into diabetic mice significantly increased the cure rate when compared to islets alone (Penko D et al Cell Transplantation, 2013). This work has formed a leading project in the six year $59M Cell Therapy Manufacturing CRC wherein smart surface biomaterials will be generated to bind both islets and EPCs for therapeutic application.

Identification of a new target to treat allergic inflammation

Rapid recruitment of neutrophils to a site of inflammation is associated with allergic diseases, such as asthma and anaphylaxis. Although anti-histamines and steroids are the mainstay of treatment for symptomatic relief, their effectiveness is varied; thus, a better understanding of acute allergic reactions is required. We have examined the role of sphingosine kinase (SK) mediated P-selectin expression on ECs for the rapid recruitment of neutrophils. SK is a highly conserved lipid kinase that catalyses the phosphorylation of sphingosine to form sphingosine-1-phosphate. We recently identified that (i) histamine-induced P-selectin expression on human umbilical vein ECs is sphingosine kinase (SK)-1 dependent and (ii) histamine-induced neutrophil rolling along the vasculature *in vitro* and *in vivo* is SK-1 dependent (Sun W *et al* Am J Pathol, 2012). In 2013 we revealed that administration of Fingolimod (approved pro-drug for treatment of multiple sclerosis) attenuates histamine-induced neutrophil recruitment in multiple animal models of allergic inflammation and have initiated human clinical trials to investigate this additional indication for Fingolimod.

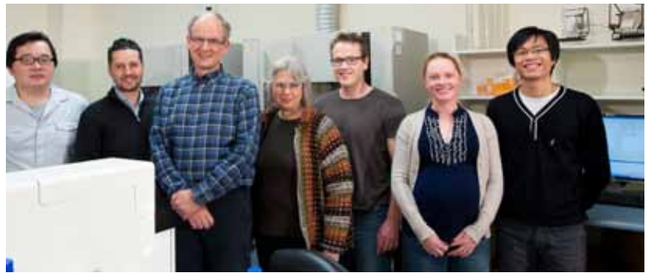
Development of EPCs for therapeutic use:

We recently identified a new population of immature, non-adherent endothelial progenitor cells (naEPCs) (Appleby S *et al* PLoS ONE 2012). These cells are distinct from 'currently used' EPCs by their non-adherence and immature phenotype which will support vascular repair and development across vascular lineages and thus vascular beds. Moreover, naEPCs likely represent the 'true' circulating EPCs which constantly survey the vasculature, ready to respond to vascular injury for repair with novel biomarkers (Patent application PCT/AU2011/001415). Our new protocols provide novel expansion methods to generate ~10^9 naEPCs in a serum free medium which provides better therapeutic opportunities for vascular repair and we have executed *in vivo* models to validate their application.



Human endothelial cells which line blood vessels respond to an allergic stimulus with increased surface expression of p-selectin (green) and production of sphingosine kinase (red)

Mark van der Hoek | Joel Geoghegan | Rosalie Kenyon | Ming Lin



Paul Wang | John Toubia | Andreas Schreiber
Anna Tsykin | David Lawrence | Katherine Pillman | Frank Feng

The Australian Cancer Research Foundation Cancer Genomics Facility

Professor Greg Goodall Director Professor Hamish Scott Director
Joel Geoghegan Bsc, MSc Facility Manager Dr Andreas Schreiber PhD Head of Bioinformatics

Since it's opening in October 2012 the ACRF Cancer Genomics Facilty has become integral to the cutting edge genomics research of CCB researchers.

The facility is the result of a number of generous grants including $3.5 million from the ACRF supported by others from the State Government of South Australia, Therapeutics Innovation Australia (TIA), Superscience Fund, MedVet Laboratories, Cancer Council of South Australia, Co-operative Research Centre for Biomarker Translation, The James and Diana Ramsay Foundation and through a partnership of SA Pathology and the University of Adelaide. 2013 saw the installation of another next generation sequencer, an Illumina Miseq, adding to an already impressive suite of equipment including Ion Proton and Illumina Hiseq sequencers, Fluidigm systems for the analysis of single cells and two microarray platforms. As next generation sequencing technology continues to become more affordable, it's uptake and translation from research environments to clinical utility has been making real progress. Promising in-house trials of microarrays for cytogenetic testing will see their implementation within SA Pathology in the near future. The facility staff work closely with both research and local diagnostic groups to help ensure the facility technology is harnessed to it's full potential.

The wider Adelaide research community has also enjoyed convenient access to facility services with a range of projects undertaken including the study of ancient DNA, agricultural crop, bacterial and viral genomes. The exchange of knowledge from this networking of researchers through the facility has been of great benefit to all users across their different fields.

Bioinformatics

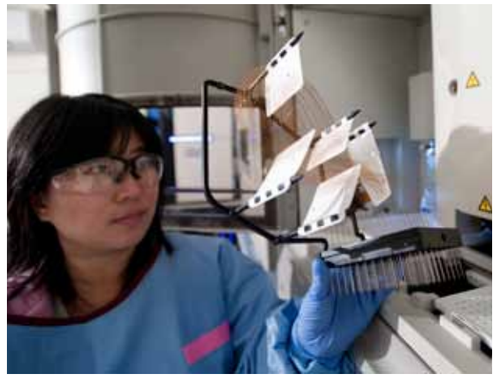
Together with the ACRF Cancer Genomics Facility, the CCB established a dedicated bioinformatics group. Initially, this consisted of a core of three staff funded through the facility to process and analyze the prodigious amounts of data produced by the facility's sequencers. By the end of 2013 the group has expanded through the addition of another four researchers dedicated, and largely funded through, individual research groups of the CCB as well as the University of Adelaide. During the year the group further hosted two junior staff working together with the Leukaemia Unit and the Molecular Pathology Research Laboratory, respectively.

High end bioinformatics requires state-of-the-art computing infrastructure. The Genomics Facility owns a 48 core/256 RB RAM server and shares access to three more high performance servers. All are hosted by eResearch SA, who provide supercomputing to South Australia's research community. The facility is networked to these servers via a fast 1Gb/s high-throughput connection facilitated through our partners at the University of Adelaide. A data storage and backup capability of around 25TB on eResearch SA's Dell Compellent system and a metadata capture platform funded through a grant from the Australian National Data Service (ANDS) has enabled streamlined data-sharing with the Facility's users, obviating risk of data corruption and loss through exchange of portable hard drives. 2013 also saw a successful application for an initial allocation of 50TB of data storage through the federally funded Research Data Storage Infrastructure (RDSI) scheme and an allocation of 64 cores on the National eResearch Collaboration Tools and Resources (NeCTAR) project's compute cloud, ensuring adequate computing resources for the coming year.

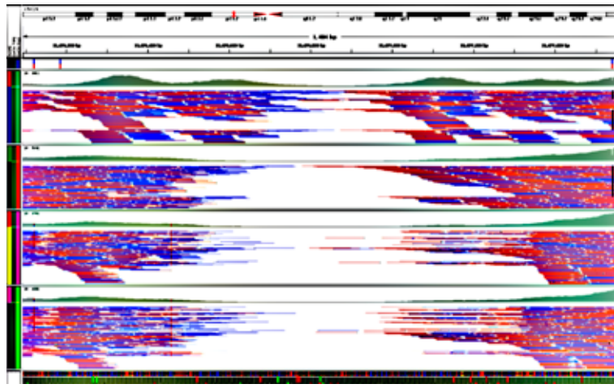
Key discoveries 2013

Our first full year of operations saw the establishment of numerous computing and analysis pipelines. These are required for the initial processing of raw sequencing data that subsequently gets used in downstream higher-level project-specific bioinformatic analyses. They include numerous pipelines for gene and splice variant expression analysis using RNA-Seq, scripts for determination and quantification of transcription factor binding sites in ChIP-Seq experiments, pipelines for mutation detection from whole exome and gene panel sequencing data as well as a variety of scripts for annotating diverse types of sequence data. Follow-up higher level analysis was carried out for dozens of projects detailed elsewhere in this annual report.

The bioinformatics group was pleased to be able to help out with and organize a number of bioinformatics training activities throughout 2013. This included talks and hands-on sessions for Genetics and Molecular Pathology staff, organized by its Technology Advancement Unit, to prepare for increasing uptake of next generation sequencing technologies into SA Health's diagnostic service. The group further assisted the University of Adelaide in running the Australian Mathematical Society's popular BioInfoSummer schools for Dec. 2012 and 2013, which attracted a record number of participants from around Australia and beyond. We were particularly pleased that a small team of our bioinformaticians won the meeting's strongly contested programming competition prize for the second year running. The group is also continuing to provide ongoing weekly hands-on introductory Linux computing sessions for interested CCB staff.



Capillary array from a Sanger Sequencing machine being inspected by Ming Lin



Next generation sequencing data from two pairs of kindreds diagnosed with a rare form of adrenal Cushing's syndrome
Two mutations (top right and bottom left) in the gene ARMC5, identical within the kindred but differing between kindreds, were identified via bioinformatic analysis of whole exome data (L Gagliardi *et al*, J Clin Endocrinol Metab 2014)

Outcomes for the Community

We continue to work closely with researchers and clinicians in basic science (CCB), clinical translational research (eg genetic diagnoses and molecular oncology, CCB and SA Pathology) as well as working towards implementation of our new technologies into standard health care (CCB, SA Pathology and SA Health).

As well as facilitating both basic and clinical research, the genomics facility is already impacting directly on the health care of South Australians. The Genetics and Molecular Pathology Directorate of SA Pathology, with expertise, instruments and personnel from the CCB and the genomics facility, has already implemented several new standard of care tests. This includes a cheaper, more informative test for personalized medicine of South Australian Cancer patients. This will give some patients alternative therapeutic options if conventional therapies fail. We have discovered the gene for a rare familial form of adrenal tumours which we can now accurately diagnose and effectively treat (see diagram). We have also helped identify mutations in several rare genetic diseases, which as well as discovering new biology, importantly helps families understand and plan their next reproductive choices.

Publications

Ahmed F, Choudhury NR, Dutta NK, Zannettino A, Knott R. Near superhydrophobic fibrous scaffold for endothelialization: fabrication, characterization and cellular activities. *Biomacromolecules* 14: 3850-3860, 2013

Al-Ejeh F, Shi W, Miranda M, Simpson PT, Vargas AC, Song S, Wiegmans AP, Swarbrick A, Welm AL, Brown MP, Chenevix-Trench G, Lakhani SR, Khanna KK. Treatment of triple-negative breast cancer using anti-EGFR-directed radioimmunotherapy combined with radiosensitizing chemotherapy and PARP inhibitor. *J Nucl Med* 54: 913-921, 2013

Aloia AL, Duffy L, Pak V, Lee KE, Sanchez-Martinez S, Derse D, Heidecker G, Cornetta K, Rein A. A reporter system for replication-competent gammaretroviruses: the in Gluc-MLV-DERSE assay. *Gene Ther* 20: 169-176, 2013

Angelini S, Soverini S, Ravegnini G, Barnett M, Turrini E, Thornquist M, Pane F, Hughes TP, White DL, Radich J, Kim DW, Saglio G, Cilloni D, Iacobucci I, Perini G, Woodman R, Cantelli-Forti G, Baccarani M, Hrelia P, Martinelli G. Association between imatinib transporters and metabolizing enzymes genotype and response in newly diagnosed chronic myeloid leukemia patients receiving imatinib therapy. *Haematologica* 98: 193-200, 2013

Arthur A, Panagopoulos RA, Cooper L, Menicanin D, Parkinson IH, Codrington JD, Vandyke K, Zannettino AC, Koblar SA, Sims NA, Matsuo K, Gronthos S. EphB4 enhances the process of endochondral ossification and inhibits remodeling during bone fracture repair. *J Bone Miner Res* 28: 926-935, 2013

Attema JL, Bert AG, Lim YY, Kolesnikoff N, Lawrence DM, Pillman KA, Smith E, Drew PA, Khew-Goodall Y, Shannon F, Goodall GJ. Identification of an enhancer that increases miR-200b~200a~429 gene expression in breast cancer cells. *PLoS One* 8: e75517, 2013

Baccarani M, Deininger MW, Rosti G, Hochhaus A, Soverini S, Apperley JF, Cervantes F, Clark RE, Cortes JE, Guilhot F, Hjorth-Hansen H, Hughes TP, Kantarjian HM, Kim DW, Larson RA, Lipton JH, Mahon FX, Martinelli G, Mayer J, Muller MC, Niederwieser D, Pane F, Radich JP, Rousselot P, Saglio G, Saussele S, Schiffer C, Silver R, Simonsson B, Steegmann JL, Goldman JM, Hehlmann R. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood* 122: 872-884, 2013

Bachanova V, Marks DI, Zhang MJ, Wang H, de Lima M, Aljurf MD, Arellano M, Artz AS, Bacher U, Cahn JY, Chen YB, Copelan EA, Drobyski WR, Gale RP, Greer JP, Gupta V, Hale GA, Kebriaei P, Lazarus HM, Lewis ID, Lewis VA, Liesveld JL, Litzow MR, Loren AW, Miller AM, Norkin M, Oran B, Pidala J, Rowe JM, Savani BN, Saber W, Vij R, Waller EK, Wiernik PH, Weisdorf DJ. Ph+ ALL patients in first complete remission have similar survival after reduced intensity and myeloablative allogeneic transplantation: impact of tyrosine kinase inhibitor and minimal residual disease. *Leukemia* 28: 658-665, 2014 (e-pub 2013)

Bonder CS, Ebert LM. Fos-icking for control of angiogenesis: increasing the longevity of peritoneal dialysis. *Kidney Int* 84: 1065-1067, 2013

Bowles J, Secker G, Nguyen C, Kazenwadel J, Truong V, Frampton E, Curtis C, Skoczylas R, Davidson TL, Miura N, Hong YK, Koopman P, Harvey NL, Francois M. Control of retinoid levels by CYP26B1 is important for lymphatic vascular development in the mouse embryo. *Dev Biol* 386: 25-33, 2014 (e-pub 2013)

Branford S, Yeung DT, Ross DM, Prime JA, Field CR, Altamura HK, Yeoman AL, Georgievski J, Jamison BA, Phillis S, Sullivan B, Briggs NE, Hertzberg M, Seymour JF, Reynolds J, Hughes TP. Early molecular response and female sex strongly predict stable undetectable BCR-ABL1, the criteria for imatinib discontinuation in patients with CML. *Blood* 121: 3818-3824, 2013

Brierley GV, Priebe IK, Purins L, Fung KY, Tabor B, Lockett T, Nice E, Gibbs P, Tie J, McMurrick P, Moore J, Ruszkiewicz A, Burgess A, Cosgrove LJ. Serum concentrations of brain-derived neurotrophic factor (BDNF) are decreased in colorectal cancer patients. *Cancer Biomark* 13: 67-73, 2013

Brown MP, Burdett MP. Targeted therapies, aspects of pharmaceutical and oncological management. *Cancer Forum* 37: 70-80, 2013

Brumatti G, Salmanidis M, Kok CH, Bilardi RA, Sandow JJ, Silke N, Mason K, Visser J, Jabbour AM, Glaser SP, Okamoto T, Bouillet P, D'Andrea RJ, Ekert PG. HoxA9 regulated Bcl-2 expression mediates survival of myeloid progenitors and the severity of HoxA9-dependent leukemia. *Oncotarget* 4: 1933-1947, 2013

Carella AM, Branford S, Deininger M, Mahon FX, Saglio G, Eiring A, Khorashad J, O'Hare T, Goldman JM. What challenges remain in chronic myeloid leukemia research? *Haematologica* 98: 1168-1172, 2013

Carr JM, Kua T, Clarke JN, Calvert JK, Zebol JR, Beard MR, Pitson SM. Reduced sphingosine kinase 1 activity in dengue virus type-2 infected cells can be mediated by the 3' untranslated region of dengue virus type-2 RNA. *J Gen Virol* 94: 2437-2448, 2013

Carr JM, Mahalingam S, Bonder CS, Pitson SM. Sphingosine kinase 1 in viral infections. *Rev Med Virol* 23: 73-84, 2013

Chan H, Pitson SM. Post-translational regulation of sphingosine kinases. *Biochim Biophys Acta* 1831: 147-156, 2013

Chandrasegaram MD, Chiam SC, Nguyen NQ, Ruszkiewicz A, Chung A, Neo EL, Chen JW, Worthley CS, Brooke-Smith ME. A case of pancreatic cancer in the setting of autoimmune pancreatitis with nondiagnostic serum markers. *Case Rep Surg* 2013: 809023, 2013

Chow AW, Lee CH, Hiwase DK, To LB, Horvath N. Relapsed multiple myeloma: who benefits from salvage autografts? *Intern Med J* 43: 156-161, 2013

Christie M, Jorissen RN, Mouradov D, Sakthianandeswaren A, Li S, Day F, Tsui C, Lipton L, Desai J, Jones IT, McLaughlin S, Ward RL, Hawkins NJ, Ruszkiewicz AR, Moore J, Burgess AW, Busam D, Zhao Q, Strausberg RL, Simpson AJ, Tomlinson IP, Gibbs P, Sieber OM. Different APC genotypes in proximal and distal sporadic colorectal cancers suggest distinct WNT/beta-catenin signalling thresholds for tumourigenesis. *Oncogene* 32: 4675-4682, 2013

Cortes JE, Kim DW, Pinilla-Ibarz J, le Coutre P, Paquette R, Chuah C, Nicolini FE, Apperley JF, Khoury HJ, Talpaz M, DiPersio J, DeAngelo DJ, Abruzzese E, Rea D, Baccarani M, Muller MC, Gambacorti-Passerini C, Wong S, Lustgarten S, Rivera VM, Clackson T, Turner CD, Haluska FG, Guilhot F, Deininger MW, Hochhaus A, Hughes T, Goldman JM, Shah NP, Kantarjian H, Investigators P. A phase 2 trial of ponatinib in Philadelphia chromosome-positive leukemias. *N Engl J Med* 369: 1783-1796, 2013

Day FL, Jorissen RN, Lipton L, Mouradov D, Sakthianandeswaren A, Christie M, Li S, Tsui C, Tie J, Desai J, Xu ZZ, Molloy P, Whitehall V, Leggett BA, Jones IT, McLaughlin S, Ward RL, Hawkins NJ, Ruszkiewicz AR, Moore J, Busam D, Zhao Q, Strausberg RL, Gibbs P, Sieber OM. PIK3CA and PTEN gene and exon mutation-specific clinicopathologic and molecular associations in colorectal cancer. *Clin Cancer Res* 19: 3285-3296, 2013

Denton D, Aung-Htut MT, Kumar S. Developmentally programmed cell death in Drosophila. *Biochim Biophys Acta* 1833: 3499-3506, 2013

Denton D, Aung-Htut MT, Lorensuhewa N, Nicolson S, Zhu W, Mills K, Cakouros D, Bergmann A, Kumar S. UTX coordinates steroid hormone-mediated autophagy and cell death. *Nat Commun* 4: 2916, 2013

Diakiw SM, D'Andrea RJ, Brown AL. The double life of KLF5: Opposing roles in regulation of gene-expression, cellular function, and transformation. *IUBMB Life* 65: 999-1011, 2013

Diakiw SM, Perugini M, Kok CH, Engler GA, Cummings N, To LB, Wei AH, Lewis ID, Brown AL, D'Andrea RJ. Methylation of KLF5 contributes to reduced expression in acute myeloid leukaemia and is associated with poor overall survival. *Br J Haematol* 161: 884-888, 2013

Dimasi D, Sun WY, Bonder CS. Neutrophil interactions with the vascular endothelium. *Int Immunopharmacol* 17: 1167-1175, 2013

Dorstyn L, Kumar, S. Insect Caspases. *Handbook of Proteolytic Enzymes*. Rawlings NDS, G. Elsevier. 2286-2295, 2013

Duncan EM, Rodgers SE, McRae SJ. Diagnostic testing for mild hemophilia a in patients with discrepant one-stage, two-stage, and chromogenic factor VIII:C assays. *Semin Thromb Hemost* 39: 272-282, 2013

Eadie LN, Hughes TP, White DL. Interaction of the efflux transporters ABCB1 and ABCG2 with imatinib, nilotinib, and dasatinib. *Clin Pharmacol Ther* 95: 294-306, 2014 (e-pub 2013)

Eadie LN, Saunders VA, Hughes TP, White DL. Degree of kinase inhibition achieved in vitro by imatinib and nilotinib is decreased by high levels of ABCB1 but not ABCG2. *Leuk Lymphoma* 54: 569-578, 2013

Eberhardt WE, Mitchell P, Schiller JH, Brown MP, Thomas M, Mills G, Jehl V, Urva SR, De Leo JJ, Gogov S, Papadimitrakopoulou V. Feasibility of adding everolimus to carboplatin and paclitaxel, with or without bevacizumab, for treatment-naive, advanced non-small cell lung cancer. *Invest New Drugs* 32: 123-134, 2014 (e-pub 2013)

Eckhardt CL, van Velzen AS, Peters M, Astermark J, Brons PP, Castaman G, Cnossen MH, Dors N, Escuriola-Ettingshausen C, Hamulyak K, Hart DP, Hay CR, Haya S, van Heerde WL, Hermans C, Holmstrom M, Jimenez-Yuste V, Keenan RD, Klamroth R, Laros-van Gorkom BA, Leebeek FW, Liesner R, Makipernaa A, Male C, Mauser-Bunschoten E, Mazzucconi MG, McRae S, Meijer K, Mitchell M, Morfini M, Nijziel M, Oldenburg J, Peerlinck K, Petrini P, Platokouki H, Reitter-Pfoertner SE, Santagostino E, Schinco P, Smiers FJ, Siegmund B, Tagliaferri A, Yee TT, Kamphuisen PW, van der Bom JG, Fijnvandraat K, Group IS. Factor VIII gene (F8) mutation and risk of inhibitor development in nonsevere hemophilia A. *Blood* 122: 1954-1962, 2013

Ekberg JA, Boase NA, Rychkov G, Manning J, Poronnik P, Kumar S. Nedd4-2 (NEDD4L) controls intracellular Na(+)-mediated activity of voltage-gated sodium channels in primary cortical neurons. Biochem J 457: 27-31, 2014 (e-pub 2013)

Experts in Chronic Myeloid L. The price of drugs for chronic myeloid leukemia (CML) is a reflection of the unsustainable prices of cancer drugs: from the perspective of a large group of CML experts. *Blood* 121: 4439-4442, 2013

Fleming NI, Jorissen RN, Mouradov D, Christie M, Sakthianandeswaren A, Palmieri M, Day F, Li S, Tsui C, Lipton L, Desai J, Jones IT, McLaughlin S, Ward RL, Hawkins NJ, Ruszkiewicz AR, Moore J, Zhu HJ, Mariadason JM, Burgess AW, Busam D, Zhao Q, Strausberg RL, Gibbs P, Sieber OM. SMAD2, SMAD3 and SMAD4 mutations in colorectal cancer. *Cancer Res* 73: 725-735, 2013

Frith JE, Cameron AR, Menzies DJ, Ghosh P, Whitehead DL, Gronthos S, Zannettino AC, Cooper-White JJ. An injectable hydrogel incorporating mesenchymal precursor cells and pentosan polysulphate for intervertebral disc regeneration. *Biomaterials* 34: 9430-9440, 2013

Frith JE, Menzies DJ, Cameron AR, Ghosh P, Whitehead DL, Gronthos S, Zannettino AC, Cooper-White JJ. Effects of bound versus soluble pentosan polysulphate in PEG/HA-based hydrogels tailored for intervertebral disc regeneration. *Biomaterials* 35: 1150-1162, 2014 (e-pub 2013)

Fung KY, Priebe I, Purins L, Tabor B, Brierley GV, Lockett T, Nice E, Gibbs P, Tie J, McMurrick P, Moore J, Ruszkiewicz A, Burgess A, Cosgrove LJ. Performance of serum lipocalin 2 as a diagnostic marker for colorectal cancer. *Cancer Biomark* 13: 75-79, 2013

Gagliardi L, Schreiber AW, Hahn CN, Feng J, Cranston T, Boon H, Hotu C, Oftedal BE, Cutfield R, Adelson DL, Braund WJ, Gordon RD, Rees DA, Grossman AB, Torpy DJ, Scott HS. ARMC5 Mutations are common in familial bilateral macronodular adrenal hyperplasia. *J Clin Endocrinol Metab* jc20141265 (E-pub 2013)

Gallipoli P, Stobo J, Heaney N, Nicolini FE, Clark R, Wilson G, Tighe J, McLintock L, Hughes T, Michor F, Paul J, Drummond M, Holyoake TL. Safety and efficacy of pulsed imatinib with or without G-CSF versus continuous imatinib in chronic phase chronic myeloid leukaemia patients at 5 years follow-up. *Br J Haematol* 163: 674-676, 2013

Giles FJ, le Coutre PD, Pinilla-Ibarz J, Larson RA, Gattermann N, Ottmann OG, Hochhaus A, Radich JP, Saglio G, Hughes TP, Martinelli G, Kim DW, Novick S, Gillis K, Fan X, Cortes J, Baccarani M, Kantarjian HM. Nilotinib in imatinib-resistant or imatinib-intolerant patients with chronic myeloid leukemia in chronic phase: 48-month follow-up results of a phase II study. *Leukemia* 27: 107-112, 2013

Giles KM, Kalinowski FC, Candy PA, Epis MR, Zhang PM, Redfern AD, Stuart LM, Goodall GJ, Leedman PJ. Axl mediates acquired resistance of head and neck cancer cells to the epidermal growth factor receptor inhibitor erlotinib. *Mol Cancer Ther* 12: 2541-2558, 2013

Goldschlager T, Oehme D, Ghosh P, Zannettino A, Rosenfeld JV, Jenkin G. Current and future applications for stem cell therapies in spine surgery. *Curr Stem Cell Res Ther* 8: 381-393, 2013

Grinfeld J, Gerrard G, Alikian M, Alonso-Dominguez J, Ale S, Valganon M, Nteliopoulos G, White D, Marin D, Hedgley C, O'Brien S, Clark R, Goldman JM, Milojkovic D, Apperley JF, Foroni L. A common novel splice variant of SLC22A1 (OCT1) is associated with impaired responses to imatinib in patients with chronic myeloid leukaemia. *Br J Haematol* 163: 631-639, 2013

Helbig KJ, Carr JM, Calvert JK, Wati S, Clarke JN, Eyre NS, Narayana SK, Fiches GN, McCartney EM, Beard MR. Viperin is induced following dengue virus type-2 (DENV-2) infection and has anti-viral actions requiring the C-terminal end of viperin. *PLoS Negl Trop Dis* 7: e2178, 2013

Hercus TR, Barry EF, Dottore M, McClure BJ, Webb AI, Lopez AF, Young IG, Murphy JM. High yield production of a soluble human interleukin-3 variant from E. coli with wild-type bioactivity and improved radiolabeling properties. *PLoS One* 8: e74376, 2013

Hercus TR, Dhagat U, Kan WLT, Broughton SE, Nero TL, Perugini M, Sandow JJ, D'Andrea RJ, Ekert PG, Hughes T, Parker MW, Lopez AF. Signalling by the beta c family of cytokines. *Cytokine Growth Factor Rev* 24: 189-201, 2013

Hiwase DK, Saunders VA, Nievergall E, Ross DD, White DL, Hughes TP. Dasatinib targets chronic myeloid leukemia-CD34+ progenitors as effectively as it targets mature cells. *Haematologica* 98: 896-900, 2013

Hochhaus A, Saglio G, Larson RA, Kim DW, Etienne G, Rosti G, De Souza C, Kurokawa M, Kalaycio ME, Hoenekopp A, Fan X, Shou Y, Kantarjian HM, Hughes TP. Nilotinib is associated with a reduced incidence of BCR-ABL mutations vs imatinib in patients with newly diagnosed chronic myeloid leukemia in chronic phase. *Blood* 121: 3703-3708, 2013

Holmfeldt L, Wei L, Diaz-Flores E, Walsh M, Zhang J, Ding L, Payne-Turner D, Churchman M, Andersson A, Chen SC, McCastlain K, Becksfort J, Ma J, Wu G, Patel SN, Heatley SL, Phillips LA, Song G, Easton J, Parker M, Chen X, Rusch M, Boggs K, Vadodaria B, Hedlund E, Drenberg C, Baker S, Pei D, Cheng C, Huether R, Lu C, Fulton RS, Fulton LL, Tabib Y, Dooling DJ, Ochoa K, Minden M, Lewis ID, To LB, Marlton P, Roberts AW, Raca G, Stock W, Neale G, Drexler HG, Dickins RA, Ellison DW, Shurtleff SA, Pui CH, Ribeiro RC, Devidas M, Carroll AJ, Heerema NA, Wood B, Borowitz MJ, Gastier-Foster JM, Raimondi SC, Mardis ER, Wilson RK, Downing JR, Hunger SP, Loh ML, Mullighan CG. The genomic landscape of hypodiploid acute lymphoblastic leukemia. *Nat Genet* 45: 242-252, 2013

Hughes TP, White, D.L. Which TKI? An embarrassment of riches for CML patients. *ASH Education Book*. American Society of Hematology. 168-175, 2013

Ibbetson SJ, Pyne NT, Pollard AN, Olson MF, Samuel MS. Mechanotransduction pathways promoting tumor progression are

activated in invasive human squamous cell carcinoma. *Am J Pathol* 183: 930-937, 2013

Jabbour E, le Coutre PD, Cortes J, Giles F, Bhalla KN, Pinilla-Ibarz J, Larson RA, Gattermann N, Ottmann OG, Hochhaus A, Hughes TP, Saglio G, Radich JP, Kim DW, Martinelli G, Reynolds J, Woodman RC, Baccarani M, Kantarjian HM. Prediction of outcomes in patients with Ph+ chronic myeloid leukemia in chronic phase treated with nilotinib after imatinib resistance/ intolerance. *Leukemia* 27: 907-913, 2013

Jabbour EJ, Hughes TP, Cortes JE, Kantarjian HM, Hochhaus A. Potential mechanisms of disease progression and management of advanced-phase chronic myeloid leukemia. *Leuk Lymphoma* 2013 (e-pub 2013)

Khalafallah AA, Snarski A, Heng R, Hughes R, Renu S, Arm J, Dutchke R, Robertson IK, To LB. Assessment of whole body MRI and sestamibi technetium-99m bone marrow scan in prediction of multiple myeloma disease progression and outcome: a prospective comparative study. *BMJ Open* 3: 2013

Kim S, Karasuyama H, Lopez AF, Ouyang W, Li X, Le Gros G, Min B. IL-4 Derived from Non-T Cells Induces Basophil- and IL-3-independent Th2 Immune Responses. *Immune Netw* 13: 249-256, 2013

Klein O, Ebert LM, Zanker D, Woods K, Tan BS, Fucikova J, Behren A, Davis ID, Maraskovsky E, Chen W, Cebon J. Flt3 ligand expands CD4+ FoxP3+ regulatory T cells in human subjects. *Eur J Immunol* 43: 533-539, 2013

Kok CH, Brown AL, Perugini M, Iarossi DG, Lewis ID, D'Andrea RJ. The preferential occurrence of FLT3-TKD mutations in inv(16) AML and impact on survival outcome: a combined analysis of 1053 core-binding factor AML patients. *Br J Haematol* 160: 557-559, 2013

Kok CH, Watkins DB, Leclercq T, D'Andrea RJ, Hughes TP, White DL. Low GFI1 expression in white blood cells of CP-CML patients at diagnosis is strongly associated with subsequent blastic transformation. *Leukemia* 27: 1427-1430, 2013

Koltowska K, Betterman KL, Harvey NL, Hogan BM. Getting out and about: the emergence and morphogenesis of the vertebrate lymphatic vasculature. *Development* 140: 1857-1870, 2013

Le TD, Liu L, Liu B, Tsykin A, Goodall GJ, Satou K, Li J. Inferring microRNA and transcription factor regulatory networks in heterogeneous data. *BMC Bioinformatics* 14: 92, 2013

Le TD, Liu L, Tsykin A, Goodall GJ, Liu B, Sun BY, Li J. Inferring microRNA-mRNA causal regulatory relationships from expression data. *Bioinformatics* 29: 765-771, 2013

Lees JG, Ching YW, Adams DH, Bach CT, Samuel MS, Kee AJ, Hardeman EC, Gunning P, Cowin AJ, O'Neill GM. Tropomyosin regulates cell migration during skin wound healing. *J Invest Dermatol* 133: 1330-1339, 2013

Li S, Garrett-Bakelman FE, Akalin A, Zumbo P, Levine R, To BL, Lewis ID, Brown AL, D'Andrea RJ, Melnick A, Mason CE. An optimized algorithm for detecting and annotating regional differential methylation. *BMC Bioinformatics* 14 Suppl 5: S10, 2013

Li X, Roslan S, Johnstone CN, Wright JA, Bracken CP, Anderson M, Bert AG, Selth LA, Anderson RL, Goodall GJ, Gregory PA, Khew-Goodall Y. MiR-200 can repress breast cancer metastasis through ZEB1-independent but moesin-dependent pathways. *Oncogene* 2013 (e-pub 2013)

Lim YY, Wright JA, Attema JL, Gregory PA, Bert AG, Smith E, Thomas D, Lopez AF, Drew PA, Khew-Goodall Y, Goodall GJ. Epigenetic modulation of the miR-200 family is associated with transition to a breast cancer stem-cell-like state. *J Cell Sci* 126: 2256-2266, 2013

Limaye VS, Bonder CS, Sun WY, Lester S, Roberts-Thomson PJ, Blumbergs P. Levels of soluble adhesion molecules and their associations in inflammatory myositis. *Int J Rheum Dis* 16: 99-101, 2013

Liu B, Liu L, Tsykin A, Goodall GJ, Cairns MJ, Li J. Discovering functional microRNA-mRNA regulatory modules in heterogeneous data. *Adv Exp Med Biol* 774: 267-290, 2013

Liu PY, Xu N, Malyukova A, Scarlett CJ, Sun YT, Zhang XD, Ling D, Su SP, Nelson C, Chang DK, Koach J, Tee AE, Haber M, Norris MD, Toon C, Rooman I, Xue C, Cheung BB, Kumar S, Marshall GM, Biankin AV, Liu T. The histone deacetylase SIRT2 stabilizes Myc oncoproteins. *Cell Death Differ* 20: 503-514, 2013

Lonic A, Powell JA, Kong Y, Thomas D, Holien JK, Truong N, Parker MW, Guthridge MA. Phosphorylation of serine 779 in fibroblast growth factor receptor 1 and 2 by protein kinase C(epsilon) regulates Ras/ mitogen-activated protein kinase signaling and neuronal differentiation. *J Biol Chem* 288: 14874-14885, 2013

McCartney EM, Helbig KJ, Narayana SK, Eyre NS, Aloia AL, Beard MR. Signal transducer and activator of transcription 3 is a proviral host factor for hepatitis C virus. *Hepatology* 58: 1558-1568, 2013

McRae S. Overweight and obese middle-aged women have increased risk of venous thromboembolism, particularly following surgery. *Evid Based Nurs* 16: 38-39, 2013

Mellor JD, Brown MP, Irving HR, Zalcberg JR, Dobrovic A. A critical review of the role of Fc gamma receptor polymorphisms in the response to monoclonal antibodies in cancer. *J Hematol Oncol* 6: 1, 2013

Michaelis LC, Saad A, Zhong X, Le-Rademacher J, Freytes CO, Marks DI, Lazarus HM, Bird JM, Holmberg L, Kamble RT, Kumar S, Lill M, Meehan KR, Saber W, Schriber J, Tay J, Vogl DT, Wirk B, Savani BN, Gale RP, Vesole DH, Schiller GJ, Abidi M, Anderson KC, Nishihori T, Kalaycio ME, Vose JM, Moreb JS, Drobyski W, Munker R, Roy V, Ghobadi A, Holland HK, Nath R, To LB, Maiolino A, Kassim AA, Giralt SA, Landau H, Schouten HC, Maziarz RT, Mikhael J, Kindwall-Keller T, Stiff PJ, Gibson J, Lonial S, Krishnan A, Dispenzieri A, Hari P, Plasma Cell Disorders Working Committee of the Center for International B, Marrow Transplant R. Salvage second hematopoietic cell transplantation in myeloma. *Biol Blood Marrow Transplant* 19: 760-766, 2013

Molina L, Fasquelle L, Nouvian R, Salvetat N, Scott HS, Guipponi M, Molina F, Puel JL, Delprat B. Tmprss3 loss of function impairs cochlear inner hair cell Kcnma1 channel membrane expression. *Hum Mol Genet* 22: 1289-1299, 2013

Moriconi F, Beard MR, Yuen LK. Bioinformatics methods for the analysis of hepatitis viruses. *Antivir Ther* 18: 531-539, 2013

Nathanson KL, Martin AM, Wubbenhorst B, Greshock J, Letrero R, D'Andrea K, O'Day S, Infante JR, Falchook GS, Arkenau HT, Millward M, Brown MP, Pavlick A, Davies MA, Ma B, Gagnon R, Curtis M, Lebowitz PF, Kefford R, Long GV. Tumor genetic analyses of patients with metastatic melanoma treated with the BRAF inhibitor dabrafenib (GSK2118436). *Clin Cancer Res* 19: 4868-4878, 2013

Neilsen PM, Noll JE, Mattiske S, Bracken CP, Gregory PA, Schulz RB, Lim SP, Kumar R, Suetani RJ, Goodall GJ, Callen DF. Mutant p53 drives invasion in breast tumors through up-regulation of miR-155. *Oncogene* 32: 2992-3000, 2013

Neubauer HA, Pitson SM. Roles, regulation and inhibitors of sphingosine kinase 2. *FEBS J* 280: 5317-5336, 2013

Ng RL, Scott NM, Strickland DH, Gorman S, Grimbaldeston MA, Norval M, Waithman J, Hart PH. Altered immunity and dendritic cell activity in the periphery of mice after long-term engraftment with bone marrow from ultraviolet-irradiated mice. *J Immunol* 190: 5471-5484, 2013

Nguyen NQ, Schoeman MN, Ruszkiewicz A. Clinical utility of EUS before cholangioscopy in the evaluation of difficult biliary strictures. *Gastrointest Endosc* 78: 868-874, 2013

Noll JE, Williams SA, Tong CM, Wang H, Quach JM, Purton LE, Pilkington K, To LB, Evdokiou A, Gronthos S, Zannettino AC. Myeloma plasma cells alter the bone marrow microenvironment by stimulating the proliferation of mesenchymal stromal cells. Haematologica 99: 163-171, 2014

Paltridge JL, Belle L, Khew-Goodall Y. The secretome in cancer progression. *Biochim Biophys Acta* 1834: 2233-2241, 2013

Parker WT, Yeoman AL, Jamison BA, Yeung DT, Scott HS, Hughes TP, Branford S. BCR-ABL1 kinase domain mutations may persist at very low levels for many years and lead to subsequent TKI resistance. *Br J Cancer* 109: 1593-1598, 2013

Paterson EL, Schindler M, Goodall GJ. MicroRNAs and the Progression of Colorectal Cancer. *Landes Biosciences* In: Metastatic Cancer: Integrated Organ System and Biological Approach. Ed: R Jandial and K Hunter, Landes Biosciences. ISBN: 978-1-58706-659-7, 2013

Paterson EL, Kazenwadel J, Bert AG, Khew-Goodall Y, Ruszkiewicz A, Goodall GJ. Down-regulation of the miRNA-200 family at the invasive front of colorectal cancers with degraded basement membrane indicates EMT is involved in cancer progression. *Neoplasia* 15: 180-191, 2013

Peng SL, Thomas M, Ruszkiewicz A, Hunter A, Lawrence M, Moore J. Conventional adverse features do not predict response to adjuvant chemotherapy in stage II colon cancer. *ANZ J Surg* 2013 (e-pub 2013)

Penko D, Rojas Canales D, Mohanasundaram D, Peiris HS, Sun WY, Drogemuller CJ, Keating DJ, Coates PT, Bonder CS, Jessup CF. Endothelial progenitor cells enhance islet engraftment, influence beta cell function and modulate islet connexin 36 expression. *Cell Transplant* 2013 (e-pub 2013)

Perugini M, Iarossi DG, Kok CH, Cummings N, Diakiw SM, Brown AL, Danner S, Bardy P, Bik To L, Wei AH, Lewis ID, D'Andrea RJ. GADD45A methylation predicts poor overall survival in acute myeloid leukemia and is associated with IDH1/2 and DNMT3A mutations. *Leukemia* 27: 1588-1592, 2013

Pettengell R, Schmitz N, Gisselbrecht C, Smith G, Patton WN, Metzner B, Caballero D, Tilly H, Walewski JA, Bence-Bruckler I, To B, Geisler CH, Schots R, Kimby E, Taverna CJ, Kozak T, Dreger P, Uddin R, Ruiz de Elvira C, Goldstone AH. Rituximab purging and/or maintenance in patients undergoing autologous transplantation for relapsed follicular lymphoma: a prospective randomized trial from the lymphoma working party of the European group for blood and marrow transplantation. *J Clin Oncol* 31: 1624-1630, 2013

Pham DH, Powell JA, Gliddon BL, Moretti PA, Tsykin A, Van der Hoek M, Kenyon R, Goodall GJ, Pitson SM. Enhanced expression of transferrin receptor 1 contributes to oncogenic signalling by sphingosine kinase 1. *Oncogene* 2013 (e-pub 2013)

Pishas KI, Neuhaus SJ, Clayer MT, Adwal A, Brown MP, Evdokiou A, Callen DF, Neilsen PM. Pre-activation of the p53 pathway through Nutlin-3a sensitises sarcomas to drozitumab therapy. *Oncol Rep* 30: 471-477, 2013

Pitman MR, Jarman KE, Leclercq TM, Pham DH, Pitson SM. Sphingosine kinases: biochemistry, regulation and role. *Lysophospholipid Receptors: Signaling and Biochemistry.* Chun J John Wiley & Sons. 153-183, 2013

Puccini J, Dorstyn L, Kumar S. Caspase-2 as a tumour suppressor. *Cell Death Differ* 20: 1133-1139, 2013

Puccini J, Dorstyn L, Kumar S. Genetic background and tumour susceptibility in mouse models. *Cell Death Differ* 20: 964, 2013

Puccini J, Shalini S, Voss AK, Gatei M, Wilson CH, Hiwase DK, Lavin MF, Dorstyn L, Kumar S. Loss of caspase-2 augments lymphomagenesis and enhances genomic instability in Atm-deficient mice. *Proc Natl Acad Sci USA* 110: 19920-19925, 2013

Ramshaw H, Xu X, Jaehne EJ, McCarthy P, Greenberg Z, Saleh E, McClure B, Woodcock J, Kabbara S, Wiszniak S, Wang TY, Parish C, van den Buuse M, Baune BT, Lopez A, Schwarz Q. Locomotor hyperactivity in 14-3-3zeta KO mice is associated with dopamine transporter dysfunction. *Transl Psychiatry* 3: e327, 2013

Richardson JD, Bertaso AG, Frost L, Psaltis PJ, Carbone A, Koschade B, Wong DT, Nelson AJ, Paton S, Williams K, Azarisman S, Worthley MI, Teo KS, Gronthos S, Zannettino AC, Worthley SG. Cardiac magnetic resonance, transthoracic and transoesophageal echocardiography: a comparison of *in vivo* assessment of ventricular function in rats. *Lab Anim* 47: 291-300, 2013

Richardson JD, Bertaso AG, Psaltis PJ, Frost L, Carbone A, Paton S, Nelson AJ, Wong DT, Worthley MI, Gronthos S, Zannettino AC, Worthley SG. Impact of timing and dose of mesenchymal stromal cell therapy in a preclinical model of acute myocardial infarction. *J Card Fail* 19: 342-353, 2013

Richardson JD, Nelson AJ, Zannettino AC, Gronthos S, Worthley SG, Psaltis PJ. Optimization of the cardiovascular therapeutic properties of mesenchymal stromal/stem cells–taking the next step. *Stem Cell Rev* 9: 281-302, 2013

Richardson JD, Psaltis PJ, Frost L, Paton S, Carbone A, Bertaso AG, Nelson AJ, Wong DT, Worthley MI, Gronthos S, Zannettino AC, Worthley SG. Incremental benefits of repeated mesenchymal stromal cell administration compared with solitary intervention after myocardial infarction. *Cytotherapy* 16: 460-470, 2014

Roberts ND, Kortschak RD, Parker WT, Schreiber AW, Branford S, Scott HS, Glonek G, Adelson DL. A comparative analysis of algorithms for somatic SNV detection in cancer. *Bioinformatics* 29: 2223-2230, 2013

Roediger B, Kyle R, Yip KH, Sumaria N, Guy TV, Kim BS, Mitchell AJ, Tay SS, Jain R, Forbes-Blom E, Chen X, Tong PL, Bolton HA, Artis D, Paul WE, Fazekas de St Groth B, Grimbaldeston MA, Le Gros G, Weninger W. Cutaneous immunosurveillance and regulation of inflammation by group 2 innate lymphoid cells. *Nat Immunol* 14: 564-573, 2013

Ronzaud C, Loffing-Cueni D, Hausel P, Debonneville A, Malsure SR, Fowler-Jaeger N, Boase NA, Perrier R, Maillard M, Yang B, Stokes JB, Koesters R, Kumar S, Hummler E, Loffing J, Staub O. Renal tubular NEDD4-2 deficiency causes NCC-mediated salt-dependent hypertension. *J Clin Invest* 123: 657-665, 2013

Ross DM, Branford S, Seymour JF, Schwarer AP, Arthur C, Yeung DT, Dang P, Goyne JM, Slader C, Filshie RJ, Mills AK, Melo JV, White DL, Grigg AP, Hughes TP. Safety and efficacy of imatinib cessation for CML patients with stable undetectable minimal residual disease: results from the TWISTER study. *Blood* 122: 515-522, 2013

Ross DM, O'Hely M, Bartley PA, Dang P, Score J, Goyne JM, Sobrinho-Simoes M, Cross NC, Melo JV, Speed TP, Hughes TP, Morley AA. Distribution of genomic breakpoints in chronic myeloid leukemia: analysis of 308 patients. *Leukemia* 27: 2105-2107, 2013

Roy SS, Gonugunta VK, Bandyopadhyay A, Rao MK, Goodall GJ, Sun LZ, Tekmal RR, Vadlamudi RK. Significance of PELP1/ HDAC2/miR-200 regulatory network in EMT and metastasis of breast cancer. *Oncogene* 2013 (e-pub 2013)

Salmanidis M, Brumatti G, Narayan N, Green BD, van den Bergen JA, Sandow JJ, Bert AG, Silke N, Sladic R, Puthalakath H, Rohrbeck L, Okamoto T, Bouillet P, Herold MJ, Goodall GJ, Jabbour AM, Ekert PG. Hoxb8 regulates expression of microRNAs to control cell death and differentiation. *Cell Death Differ* 20: 1370-1380, 2013

Schafranek L, Leclercq TM, White DL, Hughes TP. Clarithromycin enhances dasatinib-induced cell death in chronic myeloid leukemia cells, by inhibition of late stage autophagy. Leuk *Lymphoma* 54: 198-201, 2013

Scott HS. Human 'monogenic' disease gene discovery: when models of inheritance go wrong. *Hum Mutat* 34:v: 2013

Selth LA, Townley SL, Bert AG, Stricker PD, Sutherland PD, Horvath LG, Goodall GJ, Butler LM, Tilley WD. Circulating microRNAs predict biochemical recurrence in prostate cancer patients. *Br J Cancer* 109: 641-650, 2013

Shah S, Schrader KA, Waanders E, Timms AE, Vijai J, Miething C, Wechsler J, Yang J, Hayes J, Klein RJ, Zhang J, Wei L, Wu G, Rusch M, Nagahawatte P, Ma J, Chen SC, Song G, Cheng J, Meyers P, Bhojwani D, Jhanwar S, Maslak P, Fleisher M, Littman J, Offit L, Rau-Murthy R, Fleischut MH,

Publications continued

Corines M, Murali R, Gao X, Manschreck C, Kitzing T, Murty VV, Raimondi SC, Kuiper RP, Simons A, Schiffman JD, Onel K, Plon SE, Wheeler DA, Ritter D, Ziegler DS, Tucker K, Sutton R, Chenevix-Trench G, Li J, Huntsman DG, Hansford S, Senz J, Walsh T, Lee M, Hahn CN, Roberts KG, King MC, Lo SM, Levine RL, Viale A, Socci ND, Nathanson KL, Scott HS, Daly M, Lipkin SM, Lowe SW, Downing JR, Altshuler D, Sandlund JT, Horwitz MS, Mullighan CG, Offit K. A recurrent germline PAX5 mutation confers susceptibility to pre-B cell acute lymphoblastic leukemia. *Nat Genet* 45: 1226-1231, 2013

Singh R, Jayanna M, Navadgi S, Ruszkiewicz A, Saito Y, Uedo N. Narrow-band imaging with dual focus magnification in differentiating colorectal neoplasia. *Dig Endosc* 25 Suppl 2: 16-20, 2013

Singh R, Mei SL, Jayanna M, Ruszkiewicz A. Education and imaging: Gastrointestinal: Patchy distribution of coeliac disease diagnosed with narrow band imaging and optical magnification. *J Gastroenterol Hepatol* 28: 584, 2013

Singh R, Shahzad MA, Tam W, Goda K, Yu LH, Fujishiro M, Uedo N, Ruszkiewicz A. Preliminary feasibility study using a novel narrow-band imaging system with dual focus magnification capability in Barrett's esophagus: is the time ripe to abandon random biopsies? *Dig Endosc* 25 Suppl 2: 151-156, 2013

Sleep JA, Schreiber AW, Baumann U. Sequencing error correction without a reference genome. *BMC Bioinformatics* 14: 367, 2013

Stein AM, Martinelli G, Hughes TP, Muller MC, Beppu L, Gottardi E, Branford S, Soverini S, Woodman RC, Hochhaus A, Kim DW, Saglio G, Radich JP. Rapid initial decline in BCR-ABL1 is associated with superior responses to second-line nilotinib in patients with chronic-phase chronic myeloid leukemia. *BMC Cancer* 13: 173, 2013

Stevens NE, Fraser CK, Alsharifi M, Brown MP, Diener KR, Hayball JD. An empirical approach towards the efficient and optimal production of influenza-neutralizing ovine polyclonal antibodies demonstrates that the novel adjuvant CoVaccine HT is functionally superior to Freund's adjuvant. *PLoS One* 8: e68895, 2013

Tan B, Anaka M, Deb S, Freyer C, Ebert LM, Chueh AC, Al-Obaidi S, Behren A, Jayachandran A, Cebon J, Chen W, Mariadason JM. FOXP3 over-expression inhibits melanoma tumorigenesis via effects on proliferation and apoptosis. *Oncotarget* 5: 264-276, 2014

Tan DS, Gan PY, O'Sullivan KM, Hammett MV, Summers SA, Ooi JD, Lundgren BA, Boyd RL, Scott HS, Kitching AR, Chidgey AP, Holdsworth SR. Thymic deletion and regulatory T cells prevent antimyeloperoxidase GN. *J Am Soc Nephrol* 24: 573-585, 2013

Tan P, Wei A, Mithraprabhu S, Cummings N, Liu HB, Perugini M, Reed K, Avery S, Patil S, Walker P, Mollee P, Grigg A, D'Andrea R, Dear A, Spencer A. Dual epigenetic targeting with panobinostat and azacitidine in acute myeloid leukemia and high-risk myelodysplastic syndrome. *Blood Cancer J* 4: e170, 2014 (e-pub 2013)

Tettamanti S, Marin V, Pizzitola I, Magnani CF, Giordano Attianese GM, Cribioli E, Maltese F, Galimberti S, Lopez AF, Biondi A, Bonnet D, Biagi E. Targeting of acute myeloid leukaemia by cytokine-induced killer cells redirected with a novel CD123-specific chimeric antigen receptor. *Br J Haematol* 161: 389-401, 2013

Thomas D, Powell JA, Green BD, Barry EF, Ma Y, Woodcock J, Fitter S, Zannettino AC, Pitson SM, Hughes TP, Lopez AF, Shepherd PR, Wei AH, Ekert PG, Guthridge MA. Protein kinase activity of phosphoinositide 3-kinase regulates cytokine-dependent cell survival. *PLoS Biol* 11: e1001515, 2013

Thomas D, Powell JA, Vergez F, Segal DH, Nguyen NY, Baker A, Teh TC, Barry EF, Sarry JE, Lee EM, Nero TL, Jabbour AM, Pomilio G, Green BD, Manenti S, Glaser SP, Parker MW, Lopez AF, Ekert PG, Lock RB, Huang DC, Nilsson SK, Recher C, Wei AH, Guthridge MA. Targeting acute myeloid leukemia by dual inhibition of PI3K signaling and Cdk9-mediated Mcl-1 transcription. *Blood* 122: 738-748, 2013

Thomson DW, Bracken CP, Szubert JM, Goodall GJ. On measuring miRNAs after transient transfection of mimics or antisense inhibitors. *PLoS One* 8: e55214, 2013

Vandyke K, Zannettino, ACW. *Effects of Tyrosine Kinase Inhibitors on Growth in Paediatric Patients. Imatinib: Chemical Structure, Pharmacology and Adverse Effects.* Akhtari M. Nova Publishers. 2013

Vandyke K, Chow AW, Williams SA, To LB, Zannettino AC. Circulating N-cadherin levels are a negative prognostic indicator in patients with multiple myeloma. *Br J Haematol* 161: 499-507, 2013

Vandyke K, Fitter S, Drew J, Fukumoto S, Schultz CG, Sims NA, Yeung DT, Hughes TP, Zannettino AC. Prospective histo-morphometric and DXA evaluation of bone remodeling in imatinib-treated CML patients: evidence for site-specific skeletal effects. *J Clin Endocrinol Metab* 98: 67-76, 2013

Wang Y, Thomson CA, Allan LL, Jackson LM, Olson M, Hercus TR, Nero TL, Turner A, Parker MW, Lopez AL, Waddell TK, Anderson GP, Hamilton JA, Schrader JW. Characterization of pathogenic human monoclonal autoantibodies against GM-CSF. *Proc Natl Acad Sci USA* 110: 7832-7837, 2013

Ward C, Conner G, Donnan G, Gallus A, McRae S. Practical management of patients on apixaban: a consensus guide. *Thromb J* 11: 27, 2013

Watkins DB, Hughes TP, White DL, D'Andrea RJ. NPM1 mutations occur rarely or not at all in chronic myeloid leukaemia patients in chronic phase or blast crisis. *Leukemia* 27: 489-490, 2013

White DL, Eadie LN, Saunders VA, Hiwase DK, Hughes TP. Proton pump inhibitors significantly increase the intracellular concentration of nilotinib, but not imatinib in target CML cells. *Leukemia* 27: 1201-1204, 2013

White HE, Hedges J, Bendit I, Branford S, Colomer D, Hochhaus A, Hughes T, Kamel-Reid S, Kim DW, Modur V, Muller MC, Pagnano KB, Pane F, Radich J, Cross NC, Labourier E. Establishment and validation of analytical reference panels for the standardization of quantitative BCR-ABL1 measurements on the international scale. *Clin Chem* 59: 938-948, 2013

Wiszniak S, Kabbara S, Lumb R, Scherer M, Secker G, Harvey N, Kumar S, Schwarz Q. The ubiquitin ligase Nedd4 regulates craniofacial development by promoting cranial neural crest cell survival and stem-cell like properties. *Dev Biol* 383: 186-200, 2013

Wiszniak S, Lumb R, Kabbara S, Scherer M, Schwarz Q. Li-gazing at the crest: modulation of the neural crest by the ubiquitin pathway. *Int J Biochem Cell Biol* 45: 1087-1091, 2013

Yip KH, Kolesnikoff N, Yu C, Hauschild N, Taing H, Biggs L, Goltzman D, Gregory PA, Anderson PH, Samuel MS, Galli SJ, Lopez AF, Grimbaldeston MA. Mechanisms of vitamin D(3) metabolite repression of IgE-dependent mast cell activation. *J Allergy Clin Immunol* 133: 1356-1364, 2014 (e-pub 2013)

Young JA, Ting KK, Li J, Moller T, Dunn L, Lu Y, Moses J, Prado-Lourenco L, Khachigian LM, Ng M, Gregory PA, Goodall GJ, Tsykin A, Lichtenstein I, Hahn CN, Tran N, Shackel N, Kench JG, McCaughan G, Vadas MA, Gamble JR. Regulation of vascular leak and recovery from ischemic injury by general and VE-cadherin-restricted miRNA antagonists of miR-27. *Blood* 122: 2911-2919, 2013

Zannettino ACW, Martin SK, Gronthos S, To LB, Peet D. *The role of the chemokine CXCL 12 in the pathogenesis of multiple myeloma (MM). Chemokine Research Frontiers.* Colombus F. Nova Publishers, 2013

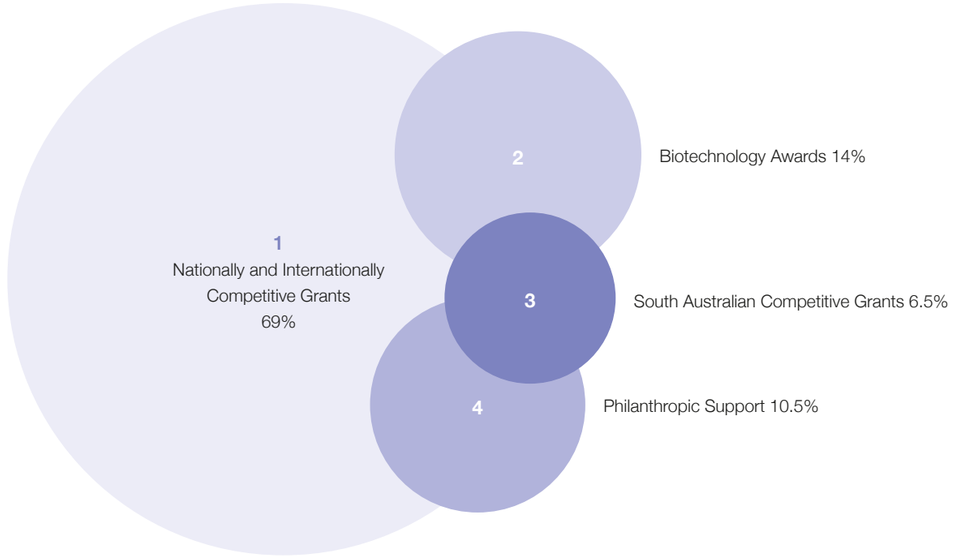
Zola H, Thomas, D, Lopez, AF Monoclonal Antibodies: Therapeutic Uses. eLS. 2013

Financial Highlights

Research Income 2012

1	Nationally and Internationally Competitive Grants		10,843,856
2	Biotechnology Awards		2,165,487
3	South Australian Competitive Grants		1,029,707
4	Philanthropic Support		1,622,000
	Total	AUD	15,661,050

All amounts shown are in Australian currency



New Grants and Fellowships

Investigator	Title	Granting Body
Beard MR	Hepatitis C infection: epidemiology pathogenesis and treatment	National Health and Medical Research Council
Bonder C, Lopez A	Cell Therapy Manufacturing	CRC: Government and Industry
Bracken C	Florey Fellowship	RAH Research Foundation
Bray SC	Gene expression analysis in a cell model of Diamond Blackfan Anaemia	Australian Hotel Association (AHA Hotel Care)
Bray SC	Travel support to present at the European Hematology Association Annual Meeting	University of Adelaide Discipline of Medicine Travel Grant
Cantley M	Early Career Fellowship	National Health and Medical Research Council
Carr J, Abraham AM, Pitson SM, Bonder CS	Endothelial progenitor cells and sphingosine-1-phosphate as immunomodulators and immunotherapeutic targets during DENV infection	Australia-India Strategic Research Fund
D'Andrea R, Lane S, Ross D, Bardy P	Targeting the EGFR and C-MET Tyrosine Kinase Receptors in Myeloproliferative Neoplasms	National Health and Medical Research Council
D'Andrea R, To LB	Diamond Blackfan Anaemia and associated bone marrow failure syndromes	Captain Courageous Foundation
Dorstyn L, Kumar S	Deciphering the mechanisms of a caspase-mediated tumour suppressor pathway	International Association of Cancer Research (AICR)
Eyre N, Aloia A	Hepatitis C virus NS5A protein phosphorylation as a target of antiviral drug development	Australian Centre for HIV and Hepatitis Virology
Gargett T, Brown MP, Hercus T, Lopez AF	Investigating in vitro effects of GM-CSF signalling blockade on differentiation and function of tumour-promoting Myeloid Derived Suppressor Cells (MDSC)	Royal Adelaide Hospital
Goodall GJ, Khew-Goodall Y	Control of the actin cytoskeleton by miR-200 family microRNAs in neuroblastoma and neural crest-derived cells	The Kids' Cancer Project
Grimbaldeston MA, Samuel MS, Gebhardt T	Mast cells are key negative regulators of skin tumourigenesis	National Health and Medical Research Council
Harvey N	The transcriptional control of lymphatic vessel development	ARC Future Fellowship
Harvey N, Scott H	Defining the role of GATA2 in the construction of lymphatic vessels	National Health and Medical Research Council
Haynes D, Cantley M	Targeting histone deacetylases 1 and 5 to reduce inflammation and bone loss in periodontitis	National Health and Medical Research Council
Helbig K	Improving treatment outcomes in individuals with chronic HCV and steatosis.	Australian Centre for HIV and Hepatitis Virology
Helbig K	Early pathogen recognition pathways in the crocodile and the role of viperin in pathogen defence	Charles Darwin University
Hughes T, White D, Branford S, Mullighan C, Yong A	Studies Directed at Maximising Achievement of Treatment Free Remission in CML	National Health and Medical Research Council
Jans DA, Bogoyevitch MA, Goodall GJ	Transcription factor nuclear residency as a driver of gene expression	Australian Research Council
Kok C	Mary Overton Early Career Fellowship	RAH Research Foundation
Kumar S	Novel ways of regulating membrane proteins in cell physiology and disease	National Health and Medical Research Council
Lewis I, D'Andrea R, Brown A	Identification of mutations in genes encoding mitochondrial complex subunits in AML	RAH Contributing Haematologists' Committee funding
Lewis I, D'Andrea R, Wang S, Brown A	Establishment of xenograft models for the testing of new therapeutics	RAH Contributing Haematologists' Committee funding
Lewis I, D'Andrea R, Brown A	Investigation of mutation and altered expression of Fanconi Anaemia genes in Acute Myeloid Leukaemia	RAH Contributing Haematologists' Committee funding
Lopez A, Parker M, Hughes T	Aberrant Signalling in Leukaemia: Program Grant	National Health and Medical Research Council
Parker W, Yeung D	Development of novel methods to examine drug resistance in chronic myeloid leukaemia	Leukaemia Foundation of Australia
Pitson SM	Characterising a highly oncogenic variant of sphingosine kinase 1	Cancer Council SA/ SAHMRI Beat Cancer Project Grant
Pitson SM	Targeting sphingosine kinase 1c degradation to enhance cancer chemotherapeutic sensitivity	Royal Adelaide Hospital
Powell JA	Sphingosine kinase as a therapeutic target in acute myeloid leukaemia	Royal Adelaide Hospital
Puccini J	Travel Grant	Cancer Council
Puccini J	Travel Grant	Discipline of Medicine, University of Adelaide
Schwarz Q	Analysing the role of VEGF in craniofacial development	National Health and Medical Research Council
To LB, Hughes T, Lopez A, Zannettino A, Scott F, D'Andrea R, Kuss B, Lewis I, Cambareri T, White D	South Australian Blood Cancer Tumour Bank	SA Cancer Research Collaborative (Beat Cancer) and Medvet
Wallington-Beddoe CT	Early Career Fellowship	National Health and Medical Research Council
White D	Innovative Cancer Imaging and Therapeutics Facility	Australian Cancer Research Foundation
Wilson C	Early Career Fellowship	National Health and Medical Research Council
Woodcock J, Lopez A, Hughes T	Targeting dimeric 14-3-3 protein as therapy for Ph+ Leukaemia	Royal Adelaide Hospital
Yeung D, Parker W, Ross D, Hughes T, Branford S	The use of digital PCR to increase sensitivity of MRD detection in Ph+ leukaemia	Contributing Haematologists' Committee, RAH
Zannettino A, Gronthos S, Fitter S	Characterisation of the molecular target of the monoclonal antibody STRO-1, in mesenchymal stem cell mediated tissue repair and immune modulation	Adelaide Research Innovation Commercialization Grant
Zannettino A, Morgan G, Mullighan C, To LB	Understanding clonal evolution in multiple myeloma	National Health and Medical Research Council
Zannettino A, Morgan G, Mullighan C, To LB	Molecular determination of the evolution of myeloma	Ray and Shirl Norman Trust
Zannettino A, Purton L, To LB	Does modifying the bone marrow stromal microenvironment alter the disease course of multiple myeloma?	Cancer Council
Zannettino A, LB To	Is elevated N-cadherin a prognostic indicator in multiple myeloma patients?	Cancer Australia/Leukaemia Foundation

Seminar Program

Dr Kieran Harvey
Group Leader, Cell Growth and Proliferation,
Peter MacCallum Cancer Centre, Melbourne
Organ size control and the Hippo pathway 07/03/13

Prof David Tremethick
Head of Genome Biology Dept, John Curtin School
of Medical Research, Australian National University, Canberra
Linking chromatin structure with cell fate 14/03/13

Associate Professor Claudine Bonder
Head, Vascular Biology and Cell
Trafficking Laboratory, Centre for Cancer Biology, Adelaide
Control the vasculature, for goodness sake 04/04/13

Dr Antje Blumenthal
Balzan Research Fellow, Epithelial Cancer Division,
University of Qld, Diamantina Institute, Brisbane
Regulators of host responses to bacterial infection 11/04/13

Dr Jeff Babon
Laboratory Head, Structural Biology Division, Walter and Eliza
Hall Institute, Melbourne *Control of Cytokine Signalling* 18/04/13

Prof Charles Mackay
Centre for Immunology and Inflammation, Monash University
Clayton, Vic *Diet and the gut microbiota as a basis for western lifestyle inflammatory diseases* 02/05/13

Assoc Prof Matthias Ernst Laboratory Head, Cell Signalling
and Cell Death, Walter and Eliza Hall Institute, Melbourne
Therapeutically exploiting Stat3 signalling in gastrointestinal tumourigenesis 09/05/13

Prof Paul Thomas
Pfizer Australia Research Fellow, School of Molecular
and Biomedical Science, University of Adelaide *Identifying mechanisms of brain and gonad disorders using Sox3 transgenic mice* 16/05/13

Dr Peter Czabotar Structural Biology Division, Walter
and Eliza Hall Institute, Melbourne *Crystal structures of Bax reveal molecular events initiating apoptosis* 23/05/13

Dr Alice Pébay
Senior Research Fellow, Neuroregeneration Research
Unit, Centre for Eye Research Australia, Department of
Ophthalmology, University of Melbourne *Modulation of neural stem/progenitor cell biology by Lysophosphatidic acid. Potential implication for neurotrauma* 30/05/13

Dr Mathias Francois
Group Leader, NHMRC CDA Fellow, Institute for Molecular
Bioscience, University of Qld, Brisbane *SOXF transcription factors: from developmental biology to drug discovery* 06/06/13

Dr Pritinder Kaur
NHMRC Senior Research Fellow; Group Leader, Epithelial
Stem Cell Biology Laboratory, Peter MacCallum Cancer Centre,
Melbourne *Pericytes/perivascular cells: an aggressive tumour microenvironmental cell type capable of promoting ovarian cancer growth and metastasis* 13/06/13

CCB Annual General Meeting
20/06/13

Dr Douglas Fairlie
Laboratory Head, Structural Biology Division,
Walter and Eliza Hall Institute, Melbourne
Apoptosis regulation and therapeutic targeting 04/07/13

Assoc Prof Geraldine O'Neill Group Leader, Children's
Cancer Research Unit, Children's Hospital at Westmead, Sydney
Interior decoration: Tropomyosin in actin dynamics and cell migration 11/07/13

Prof Paul Gleeson
Head, Dept of Biochemistry and Molecular Biology, University
of Melbourne, Bio21 Institute, Melbourne
Membrane transport and recycling of internalised membrane proteins: relevance to development, disease and therapeutics 18/07/13

Dr Andrew Webb
Division of Systems Biology and Personalised Medicine,
Walter and Eliza Hall Institute, Melbourne
Quantitative proteomic techniques in biological and medical research 24/07/13

Prof John O'Leary
Chair of Pathology, Trinity College Dublin, Ireland
New insights into the cancer metastatic cascade 24/07/13

Prof Richard Simpson
La Trobe Institute for Molecular Science (LIMS),
La Trobe University, Melbourne
Exosomes: proteome insights and diagnostic potential 25/07/13

Dr Siok Tey
Bone Marrow Transplantation Laboratory, Queensland Institute
of Medical Research, Brisbane
Cellular therapy for graft-versus-host disease 01/08/13

Assoc Prof David Tarlinton
Division of Immunology, Walter and Eliza Hall Institute, Melbourne
Plasma cells from beginning to end 08/08/13

Dr Kaylene Simpson
Head, Victorian Centre for Functional Genomics,
Peter MacCallum Cancer Centre, Melbourne
Functional genomics strategies for gene discovery 15/08/13

Assoc Prof Joan Heath
Division of Chemical Biology, Walter and Eliza Hall Institute,
Melbourne
Zebrafish mutants provide insights into mRNA splicing, autophagy and colon cancer 22/08/13

Assoc Prof Leanne Dibbens
Head, Epilepsy Research Program, School of Pharmacy
and Medical Sciences, University of South Australia
New Genes and Pathways in Epilepsy and its Co-morbidities including Intellectual Disability and Psychiatric Features 29/08/13

Dr Linda Wakim
Postdoctoral Fellow, Microbiology and Immunology,
University of Melbourne
IFITM3–rendering tissue resident memory T cells resistant to virus infection 05/09/13

Assoc Prof Simone Schoenwaelder
Australian Centre for Blood Diseases, and Department
of Clinical Haematology, Monash University
14-3-3zeta regulation of the dying platelet 09/09/13

Dr Elizabeth Forbes-Blom
Senior Research Fellow, Allergic and Parasitic
Diseases Laboratory, Malaghan Institute, New Zealand
IL-25 regulates intestinal homeostasis 12/09/13

Prof Stephen Clarke
Director of Translational Research,
Royal North Shore Hospital, University of Sydney
The impact of cancer associated inflammation on outcomes of cancer treatment 19/09/13

Prof Allison Cowin
Centre for Regenerative Medicine, Mawson Institute, Adelaide
Cancer: the wound that never heals? Similarities between the role of the cytoskeletal protein Flii in wound repair and cancer 26/09/13

Prof Mark Febbraio
Head, Cellular and Molecular Metabolism Laboratory,
Baker IDI Heart and Diabetes Institute, Melbourne
Targeting gp130 to prevent inflammation and promote insulin action 03/10/13

Prof Alpha Yap
Head, Division of Molecular Cell Biology, Institute
for Molecular Bioscience, University of Qld, Brisbane
Tension in the minority: the junctional cytoskeleton and oncogenic extrusion 10/10/13

Prof Heddy Zola
SA Pathology, *Core Facilities and Central Research Services Feedback* 17/10/13

Dr James Wells
Epithelial Cancer Group, University of Qld Diamantina
Institute, Brisbane
Activating T-cells in the skin to treat skin cancer 24/10/13

Dr Lisa Ebert
Florey Fellow, Vascular Biology and Cell Trafficking Laboratory,
Centre for Cancer Biology, Adelaide *Waging war on melanoma by targeting the immune and vascular systems* 31/10/13

Prof Dirk Schadendorf
University Hospital Essen, Germany
Evolving Treatment Landscape in Melanoma 12/11/13

Dr Samir Taoudi
Division of Molecular Medicine, Walter and Eliza Hall Institute
of Medical Research, Melbourne
Haematopoiesis during embryonic development 14/11/13

Barossa Meeting 20–23 November 2013

Assoc Prof Rohan Teasdale
Laboratory Head, Molecular Cell Biology Division,
Institute for Molecular Bioscience, University of Qld, Brisbane
The Role of Retromer Mediated Sorting of Cargo in Parkinson's Disease and Insulin-Stimulated Trafficking in Adipocytes 28/11/13

Invited Presentations

Acute Leukaemia Laboratory

Professor Richard D'Andrea

Invited Speaker

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Lowy Cancer Symposium: Discovering Cancer Therapeutics. Sydney, Australia. May

Associate Professor Ian Lewis

Invited Speaker

19th Annual Meeting of the International Society of Cellular Therapy. Auckland, New Zealand. April

10th Malaysian National Haematology Scientific Meeting. Penang, Malaysia. April

Dr Anna Brown

Invited Speaker

Blood and Bone Symposium: 11th One-Day Symposium of the Human Genetics Society of Australasia – South Australian Branch. Adelaide, Australia. September

Cell Signalling Laboratory

Associate Professor Yeesim Khew-Goodall

Invited Speaker/Chair/Co-Chair

6th International EMT Meeting. Alicante, Spain. November

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

4thAustralia-China Biomedical Research Conference. Hangzhou, China. October

ComBio 2013. Perth, Australia. September

Conference Organising Committee

6th International EMT Meeting. Alicante, Spain. November

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the OMICS era Adelaide, Australia. November

Dr Ana Lonic

Invited Speaker

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the OMICS era Adelaide, Australia. November

Cytokine Receptor Laboratory

Professor Angel Lopez

Invited Speaker

Inaugural Meeting of the International Cytokine and Interferon Society (ICIS). San Francisco, USA. September

International Cell Death Society Meeting. Fuengirola, Spain. June

Lowy Cancer Research Centre Seminar Series. Sydney, Australia. September

Invited Session Chair

15th International Congress of Immunology. Milan, Italy. August

38th Lorne Conference on Protein Structure and Function. Lorne, Australia. February

Co-Convenor

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Dr Tim Hercus

Invited Speaker

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

38th Lorne Conference on Protein Structure and Function: Lorne, Australia, February

Gene Regulation Laboratory

Professor Greg Goodall

Selected Speaker

6th International EMT Meeting. Alicante, Spain. November

Invited Speaker

72nd Meeting of the Japanese Cancer Association. Yokohama, Japan. October

Invited Plenary Speaker

4th Australia-China Biomedical Research Conference. Hangzhou, China. October

Haematology Clinical Research Laboratory

Professor Luen Bik To

Invited Speaker

'Art of Haematology' Meeting. Kuala Lumpur, Malaysia. November

Associate Professor Ian Lewis

Invited Speaker

10th Malaysian National Haematology Scientific Meeting. Penang, Malaysia. April

Dr Simon McRae

Invited Speaker

HAA Meeting. Gold Coast, Australia. October

East Asia Haemophilia Forum. Seoul, Korea South. July

Hepatitis C Virus Research Laboratory

Associate Professor Michael Beard

Convenor

20th International Symposium of Hepatitis C Virus and Related Viruses. Melbourne, Australia. October

Invited Speaker

8th Australasian Conference on Viral Hepatitis. Auckland, NZ. September

Keynote Presentation

Royal Golden Jubilee (RGJ) Research Congress. Thailand. April

Dr Karla Helbig

Invited Session Chair

20th International Symposium of Hepatitis C Virus and Related Viruses. Melbourne, Australia. October

Organising Committee

Australian Centre for HIV and Hepatitis Research Workshop 2013. Melbourne, Australia. October

Dr Nick Eyre

Invited Speaker

20th International Symposium on Hepatitis C Virus and Related Viruses. Melbourne, Australia. October

Dr Amanda Aloia

Session Chair

Australian Centre for HIV and Hepatitis Virology Research 2013 Annual Scientific Workshop. Melbourne, Australia. October

Leukaemia Unit, Genetics and Molecular Pathology

Associate Professor Susan Branford

Session Chair and Abstract Reviewer

American Society of Hematology Conference. New Orleans, USA. December

Session Chair

European School of Haematology: 15th International Conference on CML: Biology and Therapy. Estoril, Portugal. September

Invited speaker

1st Indian Cancer Congress, Monitoring CML Therapy: Delhi, India. November

2013 Haematology Lead Meetings: Sydney, Melbourne, Perth, Adelaide, Darwin, Liverpool.May, July, August, October

Seminar in Best Practices in Molecular Monitoring of CML. Kota Bahru, Malaysia. September

2nd Haematology Updates 2013. The goal of CML therapy in 2013 and Beyond. Kuala Lumpur, Malaysia. September

Journal Club Meetings

Peter MacCallum Cancer Centre, Royal Melbourne Hospital and Austin Hospital. Melbourne, Australia. September

GET Haematology Weekend meeting, Future directions in molecular monitoring. Sydney, Australia. June

Australasian Leukaemia and Lymphoma Group (ALLG) Haematology Educational Day for data managers and research nurses. Adelaide, Australia. May

Singapore Society of Haematology Annual Scientific Meeting. Singapore. April

Integrated Clinical Oncology Network. Lecture and post lecture discussion. Brisbane, Australia. April

CML Tour Taiwan/India: The Goal of CML Therapy and the Importance of Achieving Early Response in CML India and Taiwan. March

International update on CML. K.G's Medical University. Lucknow, India. March

CML Global Opinion Leaders Summit (GOLS) 2013: Helsinki, Finland. February

Lymphatic Development Laboratory

Associate Professor Natasha Harvey

Invited Speaker and/or Session Chair

2nd Meeting of the Australian Network of Cardiac and Vascular Developmental Biologists. Gold Coast, Australia. October

ComBio 2013. Perth, Australia. September.

Flinders University. Adelaide, Australia. May

St Vincent's Institute of Medical Research. Melbourne, Australia. April

Co-Convenor

Australian Vascular Biology Society - Australia New Zealand Microcirculation Society Joint Meeting. Barossa Valley, Australia, September

3rd Adelaide Cell and Developmental Biology Meeting. Adelaide, Australia, November

Mast Cell Laboratory

Associate Professor Michele Grimbaldeston

Invited Speaker and Symposium Chair

6th Asia and Oceania Congress on Photobiology. Sydney, Australia. November

Session Chair and Short Talk

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Symposium Chair and Plenary Speaker (Lafferty Debate) 43rd Annual Scientific Meeting of the Australasian Society for Immunology. New Zealand, December

Invited Speaker

Newcastle University Immunology Seminar Program. Newcastle, Australia. July

Adelaide University Immunology Seminar Program. Adelaide, Australia. June

Keynote Speaker

Australasian Society of Clinical Immunology: SA Branch. Adelaide, Australia. June

Invited Speaker

Bio21 and CSL Ltd Speaker Program. Melbourne, Australia. February

Melissa White Memorial Laboratory

Professor Timothy Hughes

Chair and Invited Speaker

ASH CML Education Talk. New Orleans, USA. December

Co-Chair and Invited Speaker

ESH/iCMLf CML Meeting. Estoril, Portugal. September

CML Global Opinion Leader Meeting (GOLS). Helsinki, Finland. March

Plenary Speaker and Organiser

Society of Haematologic Oncology (SOHO) Meeting Houston, USA. September

Invited Speaker

The Haematology Annual Meeting. Gold Coast, Australia. October

AP Summit, Japan. July

Novartis Symposia: European Haematology Association (EHA). Stockholm, Sweden. June

1st Arab World Congress on Public Health. Dubai. April

Professor Deborah White

Invited Speaker

11th Australasian Biospecimen Network (ABNA) Annual Meeting. Melbourne, Australia. December

CML Monitoring Advisory Board. Adelaide, Australia. December

2013 Haematology: New Frontiers in Therapeutic Options. Gold Coast, Australia. October

iCMLf Meeting, Portugal. September

Walter and Eliza Hall Institute Translational Research Symposium. Melbourne, Australia. July

Invited Speaker for Journal Clubs

Royal North Shore Hospital, Westmead Hospital, Royal Prince Alfred Hospital, Millennium Research Institute, and Centenary Institute. Sydney, Australia.

Molecular Pathology Research Laboratory

Professor Hamish Scott

Keynote Speaker

HGSA SA Branch, 2013 Annual Meeting. Adelaide, Australia. October

Invited Speaker / Conference Committee / Session Chair

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Conference Committee

The 5th National Epigenetics Meeting. Shoal Bay, Australia. November

Molecular Regulation Laboratory

Professor Sharad Kumar

Invited Speaker

Institute of Molecular and Cell Biology: A * Star. Singapore. December

Bio21, University of Melbourne. Melbourne, Australia. October

University of Rome Tor Vergata. Rome, Italy. October

Monash Institute of Medical Research. Clayton, Australia. September

International Cell Death Society Meeting. Malaga, Spain. June

Institute of Biochemistry II, Goethe University School of Medicine. Frankfurt, Germany. June

University of Technology Sydney. Sydney, Australia. May

Cold Spring Harbor Asia Conference: Suzhou, China. April

2013 Hunter Cell Biology Meeting. Pokolbin, Australia. March

EMBO Workshop. Obergurgl, Austria. January

New Fellow's Talk

Science at the Shine Dome, Australian Academy of Science, Canberra, Australia. May

Invited Symposium Chair, Chair of a Plenary Session

ComBio 2013. Perth, Australia. September

Plenary Lecture

Lemberg Lecture, ComBio 2013. Perth, Australia. September

23rd Federation of Asian and Oceanian Biochemists and Molecular Biologists (FAOBMB) Conference. Singapore. December

Dr Donna Denton

Invited speaker

2013 Hunter Cell Biology Meeting. Pokolbin, Australia. March

Mr Joey Puccini

Invited Speaker

Cell Growth and Proliferation Gordon Research Seminar. Vermont, USA. June

Invited Presentations continued

Molecular Signalling Laboratory

Professor Stuart Pitson

Co-Convenor

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Invited Speaker

Monash Institute for Pharamaceutical Sciences. Melbourne, Australia. November

Dr Melissa Pitman

Invited Speaker

Adelaide Protein Group Early Career Researcher Awards. Adelaide, Australia. October

Dr Jason Powell

Invited Speaker

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Dr Joanna Woodcock

Invited Speaker

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Myeloma Research Laboratory

Professor Andrew Zannettino

Invited Speaker

School of Aeorospace, Mechanical and Mechatronic Engineering, University of Sydney. Sydney, Australia. October

ANZBMS Annual Scientific Meeting. Melbourne, Australia. September

Neurovascular Research Laboratory

Dr Quenten Schwarz

Invited Speaker

EMBL Australia, Monash University. Melbourne, Australia. December

CSCR Seminar and Networking Forum, Robinson Centre, University of Adelaide. Adelaide, Australia. December

Department of Medicine, Melbourne University. Melbourne, Australia. December

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

SAHMRI Mind and Brain Mini Symposium, The Science Exchange, Adelaide, Australia. November

2nd Meeting of the Australian Network of Cardiac and Vascular. Gold Coast, Australia. November

2nd Translational Psychiatry Symposium. Adelaide, Australia. October

Neural Crest in Stem Cells, Development and Disease Meeting. Weisman Institute, Rehovot, Israel. October

Case Western Reserve University, Department of Genetics and Genome. Cleveland, Ohio, USA. September

McGill University, Montreal Neuroscience Institute. Montreal, Canada. September

3rd Neuroscience Seminar 2013 / NeuroFair 2013, University Putra Malaysia. August

Translational Oncology Laboratory

Professor Michael P Brown

Co-Chair

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide SA. November

Invited Speaker

International Society for Cell Therapy Annual Scientific Meeting. Auckland, New Zealand. April

Novartis Melanoma Investigator Forum 2013. Singapore. May

Dr Alex Staudacher

Invited Speaker

European Association of Nuclear Medicine 2013 Congress. Lyon, France. October

Tumour Microenvironment Laboratory

Dr Michael Samuel

Selected Speaker

Beatson International Cancer Conference: Targeting the Tumour Stroma. Glasgow, UK. July

Invited Speaker

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

University of Adelaide Biochemistry Research Reports. Adelaide, Australia. May

6th Imaging Workshop, 13th Hunter Meeting, Hunter Valley, Australia. March

Keynote Speaker

University of Adelaide Postgraduate Research Symposium. Adelaide, Australia. July

Conference Organiser/Session Chair

6th Barossa Science Amongst the Vines Scientific Meeting: Cell Signalling in the Omics era Adelaide, Australia. November

Vascular Biology and Cell Trafficking Laboratory

Associate Professor Claudine Bonder

Co-Chair

Barossa Cell Signalling Meeting, Adelaide, Australia. November

Australian Vascular Biology Society. Adelaide, Australia. September

Australian Society for Medical Research. Adelaide, Australia. June

Invited Speaker

Centre for Stem Cell Research, University of Adelaide. Adelaide, Australia. December

6th Barossa Science Amongst the Vines Scientific Meeting: Adelaide, Australia. November

Queen Elizabeth Hospital, Cardiology Seminar Series. Adelaide, Australia. October

Flinders University, Neuroscience Seminar Series. Adelaide, Australia. September

Dr Lisa Ebert

Invited Speaker

Melbourne Immunotherapy Group Symposium. Melbourne, Australia. October

Australasian Society for Immunology (ASI) Adelaide Immunology Retreat. Murray Bridge, Australia. August

Awards

Acute Leukaemia Laboratory

Dr Sarah Bray

European Hematology Association Travel Grant

Cytokine Receptor Laboratory

Ms Nicole Christie

Best PhD Presentation at the Australian Society of Medical Research Annual Scientific Meeting 2013

Runner-up Best Poster for the University of South Australia's Division of Health Sciences Research Policy Committee Poster Competition 2013

Haematology Clinical Research Laboratory

Mr Rick Tocchetti and **Ms Merrilee Clarke** (BloodMove)

SA Health Award: Excellence in Non-clinical Services

Australasian College of Health Services Management 2013 Excellence and Innovation Award

Hepatitis C Virus Research Laboratory

Mr Guillaume Fiches

HCV2013 International Symposium on Hepatitis C Virus and Related Viruses Travel Award (Melbourne)

Leukaemia Unit, Genetics and Molecular Pathology

Associate Professor Susan Branford

Australian Society of Medical Research SA Leading Lights Award 2013

Centre for Cancer Biology Best Primary Research Publication for 2012

Dr Wendy Parker

South Australian Young Woman of the Year Award 2013 from the South Australian Women of Year Reunion Group

Simpson Prize, Best Published Paper (Early Career)

Lymphatic Development Laboratory

Associate Professor Natasha Harvey

ARC Future Fellowship

ANZSCDB Young Investigator Award

Dr Genevieve Secker

Best Postdoctoral Oral Presentation, 3rd Adelaide Cell and Developmental Biology Meeting

Mast Cell Laboratory

Mr Nicholas Hauschild

Best Presentation by a Research Assistant, Australasian Society for Immunology SA/NT State Branch Adelaide Immunology Retreat

Ms Alicia Chenoweth

Best Presentation by an Honours Student, Australasian Society for Immunology SA/NT State Branch Adelaide Immunology Retreat

First Class Honours Degree

Ms Viera Stanekova

High Achiever Vacation Research Scholarship, University of South Australia

Chancellor's Letter of Commendation, University of South Australia

University of South Australia Medal 2013

Melissa White Memorial Laboratory

Ms Lisa Schafranek

American Hematology Society Abstract Excellence Award, American Society of Hematology Annual Conference, New Orleans, USA

Florey Medical Research Poster Presentation Prize (FHS conference), Faculty of Health Sciences Postgraduate Research Conference, National Wine Centre, Adelaide, SA

Finalist/Runner-up Medical Staff Society Prize, Royal Adelaide Hospital Medical Staff Society, Adelaide, SA

Faculty Finalist 3 minute thesis competition, School of Medicine, University of Adelaide, Adelaide, SA

Mr Dale Watkins

SAHMRI Best Poster Prize, University of Adelaide Faculty of Health Sciences Postgraduate Research Conference, Adelaide, SA

Molecular Regulation Laboratory

Professor Sharad Kumar

Elected a Fellow of the Australian Academy of Science

2013 Lemberg Medal, the highest honour bestowed by the Australian Society for Biochemistry and Molecular Biology (ASBMB)

2013 Federation of Asian and Oceanian Biochemists and Molecular Biologists (FAOBMB) Award for Research Excellence, the highest honour bestowed by the FAOBMB

Dr Claire Wilson

NHMRC Early Career Research Fellowship Poster Prize, ANZSCDB, Adelaide

Mr Pranay Goel

Student Poster Prize, ANZSCDB, Adelaide

Mr Joey Puccini

Student Oral Presentation, ANZSCDB, Adelaide

Molecular Signalling Laboratory

Dr Melissa Pitman

Runner-up, Adelaide Protein Group Early Career Researcher Awards, Adelaide, SA

Ms Heidi Neubauer

University of Adelaide School of Molecular and Biomedical Science Best Poster Award, Adelaide, SA

Barossa 2013: Cell Signalling in the Omics Era meeting Student Poster Award, Barossa Valley, SA

Myeloma Research Laboratory

Dr Melissa Cantley

(NHMRC Peter Doherty Early Career Fellow)

Selected to attend the Nobel Laureates meeting in June 2014.

Neurovascular Research Laboratory

Dr Sophie Wiszniak

Best Presentation, 3rd ANZSCDB State Meeting, Adelaide, SA

Ms Eiman Saleh

Best Presentation, Adelaide Protein Group Meeting 2013, Adelaide, SA

Poster Award Combio 2013

Poster Award University of Adelaide Medical School Open Day

Ms Rachael Lumb

Poster Award University of Adelaide Medical School Open Day

Best Poster award Robinson Stem Cell Centre Annual Retreat

Translational Oncology Laboratory

Dr Tessa Gargett

PhD (University of Adelaide)

Dr Alexander Staucher

2013 EANM Eckert and Ziegler Abstract Award, Lyon, France

Vascular Biology and Cell Trafficking Laboratory

Associate Professor Claudine Bonder

ASMR Leading Light finalist

Ms Kate Parham

Medical Staff Society Research Prize, SA Pathology, Adelaide, SA

Research Staff and Students

Acute Leukaemia Laboratory
Professor Richard D'Andrea
Associate Professor Ian Lewis
Dr Sarah Bray
Dr Anna Brown
Dr Chung Hoow Kok
Dr Michelle Perugini
Dr Saumya Samaraweera
Mr Grant Engler
Ms Diana Iarossi
Mr Nick Li
Ms Amilia Wee
Students
Nisha Rao (PhD)
Teresa Sadras (PhD)
Nur Hezrin Shahrin (PhD)
Kyaw Ze Ya Maung (PhD)
Mahmoud Bassal (PhD)
Puspita Suci Wulandari (Masters of Biotechnology)
Yu Feng (Hons)
Students who completed their degrees during 2013
Yu Feng (Hons)
Teresa Sadras (PhD)
Puspita Suci Wulandari (Masters of Biotechnology)

Cell Signalling Laboratory
Associate Professor Yeesim Khew-Goodall
Dr Leila Belle
Dr Xiaochun Li
Dr Ana Lonic
Ms Freya Gehling
Students
Mr James Paltridge (PhD)

Cytokine Receptor Laboratory
Professor Angel Lopez
Dr Tim Hercus
Dr Winnie Kan
Dr Hayley Ramshaw
Dr Frank Stomski
Ms Emma Barry
Ms Mara Dottore
Ms Barbara McClure
Ms Melanie Pudney
Ms Anna Sapa
Ms Rebecca Wright
Students
Mr Michael McKendrick (Hons)
Ms Nicole Wittwer (nee Christie) (PhD)
Students who completed their degrees during 2013
Mr Michael McKendrick (1st Class Hons)

Gastroenterology Research Laboratory
Associate Professor Andrew Ruszkiewicz
Dr Maria Caruso
Dr Jing-Song Chen
Dr Melissa Thompson
Ms Teresa Tin

Gene Regulation Laboratory
Professor Greg Goodall
Dr Joanne Attema
Dr Cameron Bracken
Dr Simon Conn
Dr Philip Gregory
Dr Kimi Honma
Dr Katherine Pillman
Dr Marika Salmanidis
Dr Anna Tsykin
Mr Matthew Anderson
Mr Andrew Bert
Ms Suraya Roslan
Ms Rosemary Sladic
Students
Victoria Arnet (PhD)
Francisco Sadras (PhD)
Corine Ting (PhD)
Daniel Thomson (PhD)

Haematology Clinical Research Laboratory
Professor L Bik To
Associate Professor Ian Lewis
Dr Peter Bardy
Dr Pratyush Giri
Dr Devendra Hiwase
Dr Noemi Horvath
Dr Cindy Lee
Dr Simon Mcrae
Dr David Ross
Dr Agnes Yong
Scientific Staff
Ms Deborah Bennetta
Ms Carolyn Butcher
Ms Malgorzata (Gosia) Badowicz
Ms Elizabeth Duncan
Ms Pam Dyson
Ms Narelle Fitzpatrick
Ms Kate Harrison
Mr Peter Harrison
Ms Smita Hiwase
Ms Monica Kutyna
Ms Kerry Munro
Ms Thanh Nguyen
Ms Silvana Niutta
Mr Trevor Rawling
Ms Susan Rodgers
Ms Judy Stevens
Mr Rick Tocchetti
Mr Michael Vo
Students
Ms Elizabeth Duncan (PhD)

Hepatitis C Virus Research Laboratory
Associate Professor Michael Beard
Dr Amanda Aloia
Dr Nick Eyre
Dr Karla Helbig
Dr Erin McCartney
Dr Kylie van der Hoek
Students
Dr Eddie Tse (PhD)
Dr Kate Muller (PhD)
Mr Guillaume Fiches (PhD)
Ms Sumudu Narayana (Hons)
Ms Onruedee Khantisitthiporn (PhD)
Mr Viet Hoang (Masters)
Ms Kathleen Davey (Hons)

Leukaemia Unit, Genetics and Molecular Pathology
Associate Professor Susan Branford
Dr Justine Marum
Dr Wendy Parker
Dr Leanne Purins
Dr Doris Stangl
Dr Paul Wang
Ms Emma Channon
Ms Zoe Donaldson
Ms Chani Field
Ms Jasmina Georgievski
Ms Mary Leong
Mr Stuart Phillis
Ms Nicola Roberts
Mr Brad Sullivan
Students
Dr David Yeung (PhD)
Ms Christina Ivansson (Masters)
Students who completed their degrees during 2013
Ms Christina Ivansson (Masters)

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

Mast Cell Laboratory
Associate Professor Michele Grimbaldeston
Dr Natasha Kolesnikoff
Dr Kwok Ho Yip
Mr Nicholas Hauschild
Ms Svetlana Vassilieva
Students
Alicia Chenoweth (Honours, University of Adelaide)
Viera Stanekova (3rd Year, UniSA)
Houng Taing (PhD, University of Adelaide, 2012-)

Melissa White Memorial Laboratory
Research: Professor Deborah White
Clinical: Professor Timothy Hughes
Dr Sue Heatley
Dr Chung Hoow Kok
Dr Tamara Leclercq
Dr Eva Nievergall
Mrs Phoung Dang
Mrs Amity Frede
Mr Jarrad Goyne
Mrs Jenny Mclean
Ms Verity Saunders
Students
Mrs Oi-Lin Lee (PhD)
Ms Liu Lu (PhD)
Ms Lisa Schafranek (PhD)
Mr Dale Watkins (PhD)
Students who completed their degrees during 2013
Dr Laura Eadie (PhD)
Dr Jackie Wong (PhD)

Molecular Pathology Research Laboratory
Professor Hamish Scott
Dr Chan Eng Chong
Dr Jinghua Feng
Dr Lucia Gagliardi
Dr Christopher N Hahn
Dr Manuela Klingler-Hoffmann
Dr Bergithe E V Oftedal
Ms Milena Babic
Mr Peter Brautigan
Ms Young Lee
Students
Ms Parvathy Venugopal (PhD)
Mr Bradley Chereda (PhD)
Ms Nathalie Nataren (Hons)
Mr Alex Janssan (Hons)
Students who completed their degrees during 2013
Mr Chan Eng Chong (PhD)
Mr Bradley Chereda (PhD)
Ms Nathalie Nataren (Hons)
Mr Alex Janssan (Hons)

Molecular Regulation Laboratory
Professor Sharad Kumar
Dr May Aung-Htut
Dr Natasha Boase
Dr Donna Denton
Dr Loretta Dorstyn
Dr Natalie Foot
Dr Kimberly Mackenzie
Dr Jantina Manning
Dr Ian Nicholson
Dr Sonia Shalini
Dr Claire Wilson
Mrs Alyshea Collaco
Ms Shannon Nicolson
Mr Andrej Nikolic
Students
Ms Swati Dawar (PhD)
Mr Pranay Goel (PhD)
Mr Lukas Peintner (PhD)
Mr Joey Puccini (PhD)
Ms Tianqi (Cindy) Xu (PhD)

Molecular Signalling Laboratory
Professor Stuart Pitson
Dr Briony Gliddon
Dr Melissa Pitman
Dr Jason Powell
Dr Craig Wallington-Beddoe
Dr Joanna Woodcock
Ms Kristy Alexander
Mr Carl Coolen
Ms Lorena Davies
Ms Julia Dobbins
Mr Paul Moretti
Students
Mr Huasheng Chan (PhD)
Ms Heidi Neubauer (PhD)
Ms Wenying Zhu (PhD)
Ms Haiwei Qu (MSc)
Ms Helen Dockrell (Hons)
Students who completed their degrees during 2013
Ms Haiwei Qu (MSc)
Ms Helen Dockrell (Hons)

Myeloma Research Laboratory
Professor Andrew Zannettino
Dr Stanley Cheung
Dr Duncan Hewett
Dr Stephen Fitter
Dr Sally Martin
Dr Jacqueline Noll
Dr Kate Vandyke
Dr Melissa Cantley
PhD Students
Mr Krzysztof Mrozik
Ms Mary Matthews
Mr Ankit Dutta
Ms Chee Man Cheong
Ms Natalia Martin
Technical/Research Assistants
Mrs Vicki Wilczek
Mrs Sharon Paton
Students
Ms Sophia Moraitis (Hons)
Ms Kimberley Evans (Hons)
Students who completed their degrees during 2013
Mr Ankit Dutta (Hons)
Mr Tony Le (Hons)
Ms Rachel Bala (Hons)

Neurovascular Research Laboratory
Dr Quenten Schwarz
Dr Peter McCarthy
Dr Sophie Wiszniak
Ms Samuela Kabbara
Mr Xiangjun Xu
Students
Ms Zarina Greenberg
Ms Rachael Lumb
Ms Eiman Saleh

Translational Oncology Laboratory
Professor Michael P Brown
Dr Tessa Gargett
Dr Alexander Staucher
Ms Rosa Katsikeros
Students
Ms Prithibha Sachi
(Hons; co-supervised with Dr Lisa Ebert)

Tumour Microenvironment Laboratory
Dr Michael Samuel
Dr Tony Pollard
Dr Jasreen Kular
Ms Natasha Pyne
Ms Kaitlin Scheer
Students
Mr Han Yuan (Undergraduate)
Ms Shadi Hosseini (Undergraduate)

Vascular Biology and Cell Trafficking Laboratory
Associate Professor Claudine Bonder
Dr David Dimasi
Dr Lisa Ebert
Dr Lachlan Moldenhauer
Dr Katie Tooley
Ms Michaelia Cockshell
Ms Samantha Escarbe
Ms Natasha Pyne
Ms Lih Tan
Ms Emma Thompson
Students
Ms Kate Parham (PhD)
Ms Wai Yan Sun (PhD)
Ms Prithibha Sacchi (Hons)

ACRF Cancer Genomics Facility
Professor Greg Goodall
Professor Hamish Scott
Facility Manager: Mr Joel Geoghegan
Bioinformatics: Dr Andreas Schreiber
Mr Mark van der Hoek
Ms Rosalie Kenyon
Ms Ming Lin
Mr David Lawrence
Dr Anna Tsykin
Mr Jinghua (Frank) Feng
Dr Katherine Pillman
Mr Paul Wang
Mr John Toubia

Our Supporters

Primary Supporters

SA PATHOLOGY

University of South Australia

Private Benefactors

- Fay Fuller Foundation
- James and Diana Ramsay Foundation
- Matthew Roberts Foundation
- The Shahin Family
- Mr Michael and Mrs Andrea White and extended family

Government of South Australia, SA Health

Australian Government, National Health and Medical Research Council, NHMRC

Australian Cancer Research Foundation

James & Diana Ramsay Foundation

Cancer Council SA

Medvet Laboratories

CRC Biomarker Translation

Australian Executor Trustees

National Breast Cancer Foundation

The University of Adelaide

Royal Adelaide Hospital Research Fund

Leukaemia Foundation, Vision to Cure, Mission to Care

BioSA

Fay Fuller Foundation

The Kids Cancer Project

Leukemia & Lymphoma Society, fighting blood cancers

Australian Government, Cancer Australia

Australian Government, Australian Research Council

Research Australia

The RAH Research Fund Team raises funds for the Centre for Cancer Biology
Vicki Sage | Mark Goldsmith, Fundraising Manager
Alexia Rocha | Mathew Jackson | Julie Dunlap | Michelle Robb

Supporting Our World Class Research

The Centre for Cancer Biology relies on grants awarded to our researchers and the generous support of individuals and organisations to carry out our vital research.

Make a donation

You can make a donation at any time by sending a cheque or money order.
All donations are greatly appreciated and are fully tax deductable.
No administrative fees or overheads are deducted when you donate:
one hundred percent of your donation goes directly to research.

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.
A personalised plaque may be affixed to any equipment bought.

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.

Fellowships

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

Contact

For all support enquiries or donations, please contact us on +61 8 8222 3422, email Anna.Nitschke@health.sa.gov.au

or mail:
Centre for Cancer Biology
SA Pathology
PO Box 14 Rundle Mall
Adelaide South Australia 5000
Australia

or

Mr Mark Goldsmith
Fundraising Manager
RAH Research Fund

+61 8 8222 5281
Mark.Goldsmith@health.sa.gov.au

Sheridan Building
Royal Adelaide Hospital
North Terrace, Adelaide
South Australia 5000
Australia