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2011 Organisational Structure

HEAD OF SCHOOL
Prof Robyn Ward

Resources & Operations
Karen Walker
School Manager
Irena Tomossy
Finance Manager
Ria Riadi
EA to Head of School
Conjoint Coordinator
Dr Rema Oliver
OHS Chairman

Research Groups
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Clinical Pharmacology & Toxicology Group
A/Prof Mike Bennett
Diving & Hyperbaric Medicine Group
Dr Geoff Lambert
Headache Research Group
Prof Minas Coroneo
Ophthalmology Group
Dr Jonathan Erlich
Neuroscience Research Group
A/Prof Matthew Kiernan
Neuroscience Research Group
A/Prof Bettina Meiser
Psychosocial Research Group
A/Prof Paul Thomas
Pulmonary Inflammation Group
Prof Phil Crowe, A/Prof Jia-Lin Yang and Dr Shing Wong
Surgical Oncology Research Group
Prof Bill Walsh
Surgical & Orthopaedic Research Laboratory

Adult Cancer Program
Prof Robyn Ward
Head, Adult Cancer Program

Prof Phil Hogg
Allosteric Disulphides Group

Prof Susan Wilson
Biostatistical Genomics Group

A/Prof Claire Vajdic
Cancer Aetiology and Prevention Group

Prof Robyn Ward & Dr Luke Hesson
Colorectal Cancer Group

Dr Megan Hitchins
Medical Epigenetics Group
Dr Kerrie McDonald
Neuro-Oncology Group
Dr Viola Heinzelmann-Schwarz
Ovarian Cancer Group

Dr Salie-Anne Pearson
Pharmacoepidemiology & Pharmaceutical Policy Group

A/Prof Jia-Lin Yang
Sarcoma Research Group

Dr John Rimanda
Stem Cell Group

Dr Caroline Ford
Wnt Signalling & Metastasis Group

Translational Cancer Research Network

Lena Caruso
Network Research Manager

Postgraduate
A/Prof Claire Vajdic
Postgraduate Coordinator
Dr Jonathan Erlich
Postgraduate Coordinator
Caitlyn Granse
Administrative Assistant

Dr Arvin Dasmodaran
Director, Clinical Teaching Unit
Dr Barbara-Ann Adelstein
Phase 1 Coordinator
Dr Melvin Chin
Phase 2 Coordinator
Dr Shing Wong
Phase 3 Coordinator
Jenny Ryall
Administrative Assistant

Dr Anthony Don
Bioactive Lipid Signalling Group
Dr Jason Wong
Bioinformatics & Protein Mass Spectrometry Group
Prof Phil Hogg & Dr Pierre Dilda
Cancer Drug Development Group
Dr Vivien Chen
Coagulation in Cancer Group

Dr Jake Olivier
Biostatistics Group

Laboratories
Weini Samuel
Laboratory Manager
Anusha Hettiaratchi
Biorepository Manager
I am pleased to present the 2011 annual report of the Prince of Wales Clinical School. The last year represented a further period of growth in both the teaching and research domains. Our partnership with Prince of Wales Hospital and the newly formed Local Health District (SESLHD) have resulted in a number of mutually beneficial new initiatives, planning, consolidation and establishing new partnerships. At year end, POWCS supported 316 undergraduate students of whom, 8 were honours and 38 were independent learning students. In addition, there were 74 postgraduate students undertaking studies across a broad range of areas in Medicine and Surgery.

At year end, 12 postgraduate research students had completed their degrees, 8 PhDs, 2 Masters and 1 MD. Congratulations to Dr Stephen Duma, Dr Ben Cheah, Dr Brian Tse, Ms Melissa Sams, Dr Nicholas Murray, Dr Lee Walsh, Dr Iman Izimi, Dr Maoyi Tian, Dr Con Manganas, Dr Seung Heon ‘Eric’ Han, Dr Rajesh Reddy and Dr Kwok Wai ‘Alfred’ Wong. On behalf of the students and the school I would like to acknowledge the supervisors who have mentored each student through the challenge of completing a higher degree. Special recognition goes to our postgraduate coordinators, Dr Jonathan Erlich and Associate Professor Claire Vajdic, and all of our postgraduate progress review panel members who collectively spend hundreds of hours to ensure students are well supported and have the best chance of successful candidatures.

Thanks go to our Conjointes who dedicate their time and energy to teaching our undergraduate medical students. We welcome the new conjoints: Dr Sze-Yuan Ooi, Dr Hong Chew Chee, Dr Neil Simon, Dr Tim Peltz, Dr Adam Berger, Dr Frank Arena, Dr Sachin Shetty, Dr Sai Htun Naing Win, Dr Michael Hunter, Dr David Broe, Dr Carole Harris, Dr Penny Clohessy, Dr George Wu, Dr Sanjay Warrier, Dr Gordon Flynn, Dr Mark Muhlmann, Dr Anup Desai. We look forward to many years of partnership with you.

The School’s vibrant research program continued to prosper in 2011. In total the research endeavours of the school are represented in 26 groups involved in laboratory, clinical and population health research. These groups work in the Lowy Cancer Research Centre, Neuroscience Research Australia and the Prince of Wales Hospital. They are generously supported by funding bodies such as the National Health and Medical Research Council, the Australian Research Council, Cancer Council Australia and the Cancer Institute NSW.

After over 9 years of dedicated service, Professor Phil Jones stepped down as Head of the undergraduate Clinical Teaching Unit in the School. The good news is that he will still keep close ties with us, continuing as a lecturer, examiner and tutor for the undergraduate medical students. We give him our sincerest thanks for his immeasurable contribution to students and we wish him all the best in his role as Associate Dean (Education) for the Medicine Education Student Office.

Thank you to Dr Johnathan Erlich for his dedicated service as Occupational Health and Safety Chairperson and welcome Dr Rema Oliver to the post. During 2011 no major incidents were reported and workplace inspection, testing and tagging programs were completed, including laboratory audits which achieved high compliance scoring.

In 2012, the Director of Clinical Teaching role will be taken up by a familiar face, Dr Arvin Damodaran, a previous POWCS student and Prince of Wales Hospital staff member. He will be supported by the Phase Coordinators: Dr Barbara-Ann Adelstein (Phase 1), Dr Melvin Chin (Phase 2) and Dr Shing Wong (Phase 3), and the experienced administrative team in the CTU.

On the horizon, new facilities for clinical research are currently being planned. The new clinical research centre (Australian Advanced Treatment Centre, AATC) will accommodate all aspects of clinical research including early phase trials.

Finally, I would like to acknowledge the contribution of the School Manager, Ms Karen Walker, and Irena Tomossy, Finance Manager who provide outstanding support and customer service for the School.

Robyn Ward, Head of School
Prince of Wales Clinical School continued to demonstrate the growth trend in attracting highly competitive external research funding. An important highlight is that the Cancer Institute NSW awarded a $6.5M program grant for 5 years to establish the Translational Cancer Research Network (TCRN). The TCRN is a partnership between the UNSW, the cancer centres of the Prince of Wales Hospital, Royal Hospital for Women, Sutherland Hospitals as well as regional cancer services of NSW.

The school received the following research grants:

• A population-based family study of follicular lymphoma (1.6M)
• Biomarkers of acute renal toxicity in humans (over $1M)
• Determining the transcriptional program of a leukaemogenic transcription factor in normal and leukaemic cells ($650,000)

In addition, the School received other category 1-2 funding including a $2.2M Cancer Council Translational Program Grant for research in the area of brain and pancreatic cancers. There were also significant numbers of other peer-reviewed grants and fellowship awards in external funds, received by members of the School, totalling almost $12M. This brought the total school funds up to $15M.

Our ties with the foundations and philanthropic organisations remain strong with hundreds of thousands of dollars in funding donated towards clinical research and student scholarships.

The School manages diverse and complex funding sources. These include: external, commercial, and philanthropic research, along with the university special-purpose strategic and operational funds.

Irena Tomossy
School Overview

The year was one of continued growth for the Prince of Wales Clinical School with staffing and Conjoint numbers trending upwards, an ongoing emphasis on cross organisational governance and incremental improvements to our working environment.

Prince of Wales Clinical School had 130 staff comprising full time and part time academic, research and support staff. The School had 206 Conjoint appointments. This staffing level represents an increase of 5% and 4% respectively on 2010. The School delivered teaching to 316 undergraduate students and 74 postgraduate students. We farewelled a number of staff who made a substantial contribution as well as welcoming numerous appointments. In particular, we had confirmation of the new Clinical Teaching Unit Director for 2012, Dr Arvin Damodaran.

People & Performance

We continued to implement performance development programs. These provide a mechanism for supervisors to develop key targets and measures, and allow staff to both realise their potential and be recognised for their achievements.

Communication & Governance

A major initiative of 2011 to improve communication with the community was a new School website, launched in March 2012.

The School oversaw and scheduled the following key committees on a regular basis:
  - OHS School Committee
  - School quarterly meeting
  - The Administration and Resource Committee
  - Adult Cancer Program Team Leader Committee

Additionally, as part of a university wide strategy of focused career pathways for women, I was invited to join the Medical Faculty Women’s Employment Strategy Committee. I also accepted an invitation to join the UNSW Grants Management Office Research Administrators Network which has as its remit the strengthening and improvement of communication flow between the Grants Office and the Faculty of Medicine.

Infrastructure Improvements

Throughout 2011 we continued to focus on improving the physical work environment by upgrading the audio visual facility in the John Dwyer Lecture Theatre, refurbishing the southern foyer of the Edmund Blacket Building, and upgrading the School’s information and technology hardware.

Karen Walker
Adult Cancer Program

The Adult Cancer Program (ACP) which is housed within the Lowy Cancer Research Centre, was formed in 2009 and represents one of the founding research groups of the Lowy Cancer Research Centre. With Professor Robyn Ward at its head, this program brings together internationally recognised teams of basic science, clinical researchers and population health researchers to address the problem of human cancer. One of the distinguishing features of the ACP is the broad skill base of our clinical and basic research team leaders and the strong link between research and patient care.

Under the leadership of Dr Kerrie McDonald, and with the assistance of the Cure for Life Foundation, the Neuro-Oncology research team grew from strength to strength. We established and developed two new research groups: Dr Caroline Ford now heads up the Wnt Signalling Metastasis Group and Dr Vivien Chen is jumpstarting the Coagulation in Cancer Group.

We also had much to celebrate:

- $6.5M was awarded by the Cancer Institute of NSW to undertake translational cancer research
- A/Prof Claire Vajdic’s inclusion in a successful $1.6M NHMRC project grant for Population based family study of follicular lymphoma
- Professor Phil Hogg’s significant $2.2M Cancer Council program grant for Metabolism inhibitors for brain and pancreatic cancers
- Dr John Pimanda’s and Dr Megan Hitchins’ successful grants and publications.

A major strength of the Lowy Cancer Research Centre is its strong relationship with key research and clinical organisations. These include the Children’s Cancer Institute of Australia and the three major teaching hospitals of the adjacent Randwick Campus (Prince of Wales Hospital, Royal Hospital for Women, Sydney Children’s Hospital).
All life forms make proteins that contain strong bonds between pairs of cysteine amino acids called disulphide bonds. Professor Hogg and his team have discovered a new type of functional disulphide bond, one that controls how mature proteins work by breaking or forming in a precise way. They have called these bonds ‘allosteric disulphides’. Their characterisation will lead to a better understanding of not only mammalian biology, but also the biology of viral and bacterial pathogens.

Application of Phil and his team’s basic research has led to the development of a novel class of anti-cancer drugs and a cell death imaging agent that are in clinical development.

Current projects
- Control of von Willebrand Factor haemostatic activity by allosteric disulphide bonds
- Control of proteinase activity by allosteric disulphide bonds
- Control of HIV infection by allosteric disulphide bonds

Progress in 2011

The team has discovered that disulphide bonds are remarkably well conserved throughout the evolution of eukaryotes – organisms whose cells contain complex structures enclosed within membranes. Moreover, there is a positive correlation between the rate of disulphide bond acquisition and organismal complexity. The faster rate of accrual of disulphide bonds in these organisms is in accordance with the greater diversity and sophistication of protein function in these species.

We have characterised the reduction-oxidation properties of the allosteric disulphide bond in Tissue Factor, the protein responsible for initiating blood coagulation. These studies reinforce the role of this disulphide bond in thrombosis, or blood clotting.

The team has shown how the pro-thrombotic protein, von Willebrand factor, self-associates at a molecular level. These observations provide the basis for exploring defects in VWF association in patients with unexplained haemorrhage or thrombosis.

Outlook

We have found that the important human enzymes, mast cell tryptase and aminopeptidase II, appear to be regulated by allosteric disulphide bonds. We will examine this regulation and its role in lung inflammation (tryptase) and cancer (aminopeptidase II).

We will continue our examination of the role of allosteric disulphide bonds in HIV infection. In particular, we will seek to understand how allosteric disulphide bonds in the HIV coat protein, gp120, regulate its function and impact on HIV vaccine design.

**Highlights**

**The more complex the species the faster the evolutionary acquisition of disulphide bonds**

Disulphide bonds play critical roles in protein stability and function. By analysing the conservation of all structurally validated disulphide bonds across 29 completely sequenced eukaryotic genomes, we observe elevated conservation of disulphide-bonded cysteines (half-cystines) compared with unpaired cysteines and other amino acids. Remarkably, half-cystines are even more conserved than tryptophan—the most conserved amino acid. Overall, once disulphide bonds are acquired in proteins, they are rarely lost. Moreover, the acquisition of disulphide bonds shows a strong positive correlation with organismal complexity. The accrual of disulphide bonds is likely to reflect the demand for greater sophistication in protein function in complex species. Our findings suggest that there has been positive selection for disulphide bonds through eukaryotic evolution.

**Molecular mechanism of association of von Willebrand Factor**

von Willebrand Factor (VWF) is a plasma protein that binds platelets to an injured vascular wall during thrombosis. When exposed to the shear forces found in flowing blood, VWF molecules undergo lateral self-association that results in a meshwork of VWF fibres. Fibre formation has been shown to involve thiol/disulphide exchange between VWF molecules. We have identified the disulphide bonds in VWF that mediate lateral self-association of the molecule and have described how these disulphide bonds function. These observations provide the basis for exploring defects in lateral VWF association in patients with unexplained haemorrhage or thrombosis.

**Leader and Team**

**Leader:** Prof Philip Hogg, Director, Lowy Cancer Research Centre and NHMRC Senior Principal Research Fellow

**Team:** Dr Helena Liang, Postdoctoral Research Fellow; Dr Kristina Cook, Postdoctoral Research Fellow; Dr Diego Butera, Postdoctoral Research Fellow; Dr Joyce Chiu, Postdoctoral Research Fellow; Dr Lisa Matthias, Postdoctoral Research Fellow; Dr Andrea Herbert, Postdoctoral Research Fellow; Mr Tim Ganderton, PhD Student; Mr Iman Azimi, PhD Student
We investigate how a group of cellular molecules termed sphingolipids control the proliferation, migration/invasion and survival of cancer cells. In doing so we aim to take a “systems” level, integrated approach to understanding how the synthesis and turn-over of these molecules is spatially and temporally regulated to control cell fate. We also investigate how alterations to sphingolipid composition, both in brain cells and the myelin sheaths that surround neurons, contribute to the pathogenesis of Alzheimer’s Disease.

Current projects

- Sphingolipid metabolic balance in glioblastoma (brain tumour) proliferation, survival, and clinical outcome (collaboration with Dr Kerrie McDonald, Adult Cancer Program)
- Alterations to myelin sphingolipid content in Alzheimer’s Disease (collaboration with Prof Brett Garner, University of Wollongong)
- Development of synthetic sphingosine analogues as anti-cancer agents (collaboration with Dr Nicole Verrills, University of Newcastle and A/Prof Jonathan Morris, School of Chemistry, UNSW)

Progress in 2011

- Comprehensive analysis of sphingolipid metabolites in glioma (see highlights).
- Developed a new fluorescent method for assaying ceramide synthase enzyme activity, to replace the radioactive assay. Despite their crucial role in generating bioactive metabolites that control diverse physiological functions, many of the lipid metabolic enzymes have remained “mysterious” to the broader research community. In our continual effort to develop the toolkit for bioactive lipid research, we have developed a simple fluorescent assay for ceramide synthases. These enzymes are the gatekeepers to the synthesis of the entire sphingolipid family, including the complex glycolipids (gangliosides) that are crucial to the cell surface “signature” of many specialised cell types (e.g. cells of the immune and nervous systems)
- Begun to investigate transcriptional control of the sphingosine kinase 1 gene in glioblastoma cells. Sphingosine kinase 1 is upregulated in many different forms of cancer, including glioblastoma, a cancer in which high sphingosine kinase 1 expression is known to correlate with a poor survival outcome

Outlook

In 2012 we will investigate the prognostic significance of the mentioned changes in terms of treatment outcome and patient survival. Secondly, whilst overall levels of the pro-apoptotic lipid ceramide are greatly reduced in glioblastoma we have identified a metabolic pathway that results in the increased synthesis of a particular ceramide variant in this cancer. This ceramide variant is then metabolically converted to the glycolipid lactosylceramide, which has been shown to promote survival of colon cancer cells. We plan to investigate whether this lactosylceramide is further metabolised to higher order glycolipids called gangliosides, which may enable the cancer cells to metastasise or recruit blood vessels.

Highlights

*Comprehensive analysis of sphingolipid metabolic alterations in glioblastoma*, in collaboration with Dr Kerrie McDonald and PhD Student Dr Hazem Abuhusain.

We published two articles describing new methods for comprehensive analysis of the sphingolipid metabolic pathway in cells or tissues. Applying these new tools to the incurable cancer glioblastoma, we have identified two major changes to sphingolipid metabolism that support the cancer’s therapeutic resistance and malignancy. Firstly, we have shown that glioblastoma is characterised by reduced levels of the pro-apoptotic lipid ceramide and increased levels of the anti-apoptotic and pro-migratory/pro-invasive lipid sphingosine 1-phosphate. This is the first demonstration of the “sphingolipid rheostat” in action, in human cancer tissue.

Leader and Team

*Leader: Dr Anthony Don*, Cancer Institute NSW Fellow
*Team: Mr Eric Qiao, Research Assistant; Mr Chung Gyo Lee, MPhil Student; Ms Mindy Da, Honours Student*
With the proliferation of biological data over the past decade, bioinformatics has become an indispensable tool in understanding biological processes. Our research involves the application of methods in data mining and machine learning to a broad range of problems in proteomics, genomics and molecular evolution of proteins. We are also interested in the use of mass spectrometry for the analysis of proteins and are developing novel analytical methods that will enable the study of sub-proteomes.

Current projects
- Integrative analysis of transcriptomic and proteomics datasets in cancer
- Screening of candidate binding proteins to functional DNA elements in leukemic cell lines
- Identification of newly synthesised proteins during platelet activation
- Mass spectrometry analysis and quantification of allosteric protein disulfide bonds

Progress in 2011
- Identification of universal alterations in DNA methylation and nucleosome positioning in a matched normal/tumor sample
- Developed new approach to analysis targeted metabolomics mass spectrometry datasets
- Identified novel phosphorylated residues in oncogenic protein ERG in leukemic cells
- Characterised the acquisition and evolution of protein disulfide bonds in animals evolution
- Developed approach to monitor the evolution of influenza viruses using mass spectrometry data

Highlights

Identification of universal alterations in DNA methylation and nucleosome positioning in a matched normal/tumor sample

DNA methylation and nucleosome positioning are known to be important in the epigenetic regulation of gene expression. More recently, studies using whole-genome approaches have also suggested that nucleosomes are likely to play an important role in the regulation of alternative splicing. In many tumours, DNA methylation is significantly altered, with the cancer epigenome characterised by global hypomethylation and site-specific hypermethylation.

In collaboration with the Colorectal Cancer Group we have used MethylMiner (Invitrogen) to enrich for methylated DNA and micrococcal nuclease (MNase) digestion to isolate nucleosome-protected DNA, followed by next-generation sequencing, to explore changes in DNA methylation and nucleosome positioning across gene promoters and intragenic regions in an early colorectal adenoma. We determined the level of DNA methylation and nucleosome occupancy at a number of different gene regions including transcription start sites, promoter CpG islands and intron/exons. By aligning respective regions across all genes, we computed the average read coverage per base within and around each region. This enabled us to compare the relative methylation or nucleosome occupancy between normal and tumour samples at a global level. Finally, we performed hierarchical clustering and principal components analysis to identify patterns of DNA methylation and nucleosome occupancy across all genes across the different gene regions analyzed.

Our results show an increase in nucleosome occupancy at methylated promoters and provide interesting insights into the interplay between DNA methylation and nucleosome re-modeling in the epigenetic regulation of DNA function.

Leader and Team

Leader: Dr Jason Wong, Cancer Institute NSW Early Career Development Fellow and UNSW Vice-Chancellor’s Post-Doctoral Fellow

Team: Mr Tim Ganderton, Research Associate; Ms Ranjeeta Menon, Research Associate; Dr Lies Boelen, Research Assistant; Mr John Ng, PhD Student; Mr Dominik Beck, PhD Student (Supervised jointly with Dr John Pimanda); Ms Jackie Huang, Honours Student (Supervised jointly with Dr John Pimanda; Mr Peter Zarzour, Honours Student (Co-supervised with Dr Luke Hesson)
Adult Cancer Program

Biostatistical Genomics Group

What are the major factors underpinning complex genetic diseases like cancer, diabetes, or Crohn’s disease? To answer such questions new biostatistical tools are needed, including software for mining the human genome with interactions between the genome and environment being incorporated. The focus of the Biostatistical Genomics Group is development and evaluation of statistical methods and software tools for analysis of complex genomic disease data. Application of these methods and tools will form the basis of a superior understanding of the overall process leading to disease and hence better predictions with important ramifications for new treatments and health care planning.

Current Projects

- Methods for simultaneous analysis of genomic, gene expression and methylation data
- Biostatistical approaches to inference of genetic regulatory networks
- Design and analysis of large-scale genomic and proteomic experiments

Progress in 2011

- Statistical methodologies for inferring genetic regulatory networks from systems biology data has been further refined
- Current approaches to estimating genomic risk associated with complex disease using SNP data are being explored
- Development of novel methods for analysis of proteomic experimental data to identify and quantify proteins in complex samples is underway

Leader and Team

**Leader: Prof Susan Wilson**

**Team:** Dr Penghao Wang, Postdoctoral Fellow; Dr Sally Galbraith, jointly with School of Mathematics & Statistics; Ms Alex Gillett, PhD Student, jointly with Faculty of Science; Mr Chris Pardy, PhD Student
Adult Cancer Program
Cancer Aetiology and Prevention Group

The Cancer Aetiology and Prevention Group (CAPG) aims to better understand the causes of cancer and factors that influence outcomes after cancer diagnosis. The CAPG employs classical and innovative cancer epidemiological methods and includes large-scale studies of cancer incidence, survival and risk factors in people with immune dysfunction. It also includes studies of two complex, common and poorly understood cancers, lymphoid malignancies and cancer of unknown primary origin. The studies involve national and international collaborations that integrate cancer epidemiology with biostatistics, biological sciences, pharmacoepidemiology and health services research. The research program builds an evidence base for preventative strategies that will reduce the burden of cancer.

Current projects

- The Lymphoma lifestyle, Environment and Family study (the LEAF Study)
- Cancer risk and blood-borne viruses in opioid dependent persons in pharmacotherapy
- Health service utilisation in cancer of unknown primary
- Cancer after heart, lung and liver transplantation in Australia
- The descriptive epidemiology of haematopoietic neoplasms in Australia
- Cutaneous melanoma in kidney transplant recipients: pathology report review and predictors of survival

Progress in 2011

- Commenced recruitment into the LEAF Study in New South Wales and Victoria
- Quantified the risk of cancer in opioid-dependent persons on pharmacotherapy in NSW and identified the relationship with infection by blood-borne viruses
- Completed a pathology report review of cases of cancer of unknown primary diagnosed between 2004 and 2007 in Department of Veteran’s Affairs members
- Quantified the risk of cancer after heart, lung and liver transplantation in Australia and completed the abstraction of clinical data from all Australian liver transplant units

Highlights

The LEAF study

This project, a collaboration with the Cancer Council Victoria, is the largest lymphoma study ever conducted in Australia. More than 1,200 men and women with follicular lymphoma and a member of their family will participate over four years. The study aims to investigate the causes of follicular lymphoma and the factors that influence survival after diagnosis. It will examine genes, lifestyle and environmental factors, and assemble a biobank. In 2011, ethical approval was obtained and the first patients were approached to participate.

Cancer risk and blood-borne viruses in opioid dependent persons in pharmacotherapy

We performed a population-based cohort study of 45,412 opioid-dependent individuals registered for opioid-substitution therapy in New South Wales between 1985 and 2007. Notifications of cancer, death and hepatitis C, hepatitis B and HIV infections were ascertained by record linkage with population-based registers. The risk of cancer was increased for 11 specific cancers, most commonly lung cancer, non-Hodgkin lymphoma and liver cancer. We found that oncogenic blood-borne viruses play a major role in the cancer risk profile in opioid-dependency. The opioid-substitution therapy setting may be utilised for targeted cancer prevention strategies in this marginalised population.

Leader and Team

Leader: A/Prof Claire Vajdic

Team: Dr Marina van Leeuwen, NHMRC Early Career Fellow; Ms Nicki Meagher, Research Manager; Dr Nina Na, PhD Student; Mr Lawrence Er, PhD Student; Mr Alex Swart, Honours Student; Mr Derek Liang, ILP Student; Ms Andrea Schaffer, NSW Health Trainee Biostatistician; Ms Sadaf Marashi Pour, NSW Health Trainee Biostatistician
Tumours metabolise sugar differently than normal tissue. Normal tissue is well supplied by oxygen from the blood and uses this oxygen to metabolise sugar to produce energy. Tumours, in contrast, are usually starved of oxygen because their blood supply is not sufficient to provide the amounts of oxygen needed by a growing tumour. This forces tumours to make energy from sugar without using oxygen. A byproduct of this oxygen-poor metabolism is the production of acid that poisons the surrounding tissue, which facilitates tumour spread and malignancy. We have developed a new class of anti-cancer drugs that target this aberrant tumour metabolism. They inactivate a key protein in energy-producing structures known as mitochondria. The molecules are unique and we are the only group in the world targeting cancer in this way. The first compound, GSAO, is currently being tested in a clinical trial in adults with solid tumours. To date, 32 patients have been treated with GSAO. The compound is well tolerated and there is early evidence of anti-tumour activity. A second generation compound, PENAO, has better anti-tumour efficacy than GSAO. It will enter a clinical trial in patients with advanced solid tumours early in 2012.

Current projects

- New metabolism inhibitors for glioblastoma and pancreatic cancer treatment
- Identification of a predictive marker for cancer treatment
- In vivo imaging of tumours cell death
- Adamantane-type polyarsenical compounds as anti-cancer drugs

Progress in 2011

- Showed how PENAO inhibits migration and triggers proliferation arrest and cell death in drug resistant glioblastoma cell lines and primary glioma tumour-initiating cells
- Discovered that cancer-activated pancreatic stromal cells are responsible for part of GSAO action

Outlook for 2012

- Complete pre-clinical characterisation of PENAO in models of glioblastoma
- Complete characterisation of γ-glutamyl transferase as a predictive marker for GSAO action using human tumour biopsies
- Complete evaluation of a GSAO analogue as a diagnostic for the efficacy of cancer chemotherapy
- Determine the mechanism of action of adamantane-like polyarsenical compounds derived from Arsenicin A on drug resistant cancer cell lines

Highlights

**Targeting glioblastoma metabolism using PENAO**

Over half of brain cancers are glioblastomas and new therapies are urgently required. In terms of years of life lost, the population burden from glioblastoma is the highest of all the malignant cancers. In comparison with standard drugs used in the treatment of glioblastoma, PENAO’s activity is very promising. We have shown that PENAO inhibits metabolism of glucose and triggers the mitochondrial transition pore in glioblastoma cells, which leads to inhibition of cell migration, proliferation arrest and mitochondrial-mediated cell death. All of these cellular effects occur at sub to low micromolar concentrations of PENAO. PENAO was found to cross the intact blood-brain-barrier in mice and administration of PENAO to ten mice bearing subcutaneous glioblastoma tumors resulted in eight partial and two complete tumor responses without signs or symptoms of treatment toxicity. Our aim is to test PENAO in a clinical trial in glioblastoma patients.

Leader and Team

**Leaders:** Dr Pierre Dilda, Senior Research Fellow; Prof Philip Hogg, Director, Lowy Cancer Research Centre and NHMRC Senior Principal Research Fellow

**Team:** Dr Stephanie Decollogne, Postdoctoral Research Fellow; Dr Peter Luk, Postdoctoral Research Fellow; Ms Danielle Park, PhD Student; Ms Emma Ramsay, PhD Student; Mrs Swapna Joshi, Research Assistant; Ms Lisbeth Serum, Research Assistant
Adult Cancer Program
Coagulation in Cancer Group

Thrombosis (or blood clotting) is the most common cause of death in the Western world as a result of stroke, myocardial infarction and venous thromboembolism. Our group is interested in the mechanisms of clot formation, the biology of platelets and coagulation proteins and how manipulation of these can be used to influence disease. We use real time intravital fluorescent microscopy to investigate the processes of platelet accumulation and coagulation initiation in the mouse circulation. Our particular focus is on platelet apoptosis and aging, microparticles and the interaction between the tumour environment and the coagulation system. The goal is to understand the processes that promote abnormal thrombosis, thus to be able to predict, prevent and treat thrombosis in clinical syndromes.

Thromboembolism in cancer:
Thrombosis is the second most common cause of death in cancer patients. There is a complex interaction between cancer being able to activate the coagulation system leading to increase venous embolic disease and a reciprocal mechanism by which increased coagulation increases the risk of cancer progression, tumour metastasis and mortality. Tumours shed microscopic particles that circulate in the blood stream and can be delivered to the platelet clot. We see that extracellular nucleic acids are present at the platelet thrombus and are elucidating the links between the tumour, white cell nucleic acids and clot in the presence of chemotherapy.

Current projects
• Mechanism of thromboembolism in cancer
• Imaging platelet apoptosis and its contribution to thrombus formation in vivo
• Von Willebrand Factor Lateralisation Study lateralisation defects: a potential novel cause for excess bleeding
• Establishment of an intravital thrombotic mouse stroke model using real time confocal microscopy

Progress in 2011
• In the final stages of establishing a facility for image intensified high speed multichannel fluorescence intravital microscopy.
• Commenced recruitment of patients for the VWF study through South Eastern Area Laboratory Services at Prince of Wales Hospital. This aims to elucidate a novel mechanism to explain excess bleeding. It is a locally translational project, taking a protein chemistry project from Professor Hogg’s lab (Ganderton et al Blood 2011) into a clinical population. Professor Hogg identified the amino acids in the von Willebrand Factor (VWF) protein responsible for the ability of the protein to form the meshworks that are required for optimal platelet clot formation. We are screening patients with clinical manifestations of unexplained excessive bleeding for this defect
• Validation of CDI-1 as a marker for platelet apoptosis. We have validated a novel apoptosis marker based on a trivalent arsenical moiety and are ready to put it into mouse models to look at the biology of the apoptotic platelet in thrombus formation in a stroke model and a peripheral vasculature thrombosis model
• In collaboration with Professor Housley at the Translational Neuroscience Facility (UNSW) we have established a mouse model of stroke using confocal microscopy for direct visualisation of thrombus formation in the cerebral vasculature. This allows real time spatial monitoring of stroke formation in the living mouse to investigate mechanisms for neuroprotection in stroke

Outlook for 2012
• Complete recruitment across Sydney and South Australia for the VWF lateralisation trial and publication of results
• We plan to understand contributors to the increase in thromboembolism in cancer using mouse models and validate potential biomarkers for thrombosis in clinical cohorts – initially retrospectively using tumour biobanks, then prospectively
• Entering a new collaboration with the Red Cross Blood Bank Research Division looking at apoptosis in transfusion pack storage
• Establishing the intravital facility for visualising thrombus formation in the mouse which will be open for external use via the UNSW Analytical Centre

Leader and Team
Leader: Dr Vivien Chen, CJ Martin Research Fellow, UNSW and Staff Specialist Haematologist, Prince of Wales Hospital
Team: Dr Minh Hua, PhD Student; Dr Leo Pasalic, PhD Student; Mr Li Gu, summer student
Adult Cancer Program
Colorectal Cancer Group

The Colorectal Cancer Group is at the forefront of epigenetic research with extensive expertise in the genetic and epigenetic analysis of colorectal cancer. A major focus of our group is the study of a type of colorectal neoplasia known as laterally spreading tumours (LSTs). Though very little is known about molecular changes associated with LSTs it is clear that some subtypes show a very high malignant potential. In collaboration with a team of gastroenterologists at Westmead hospital we are currently collecting the most extensive biobank of LST specimens in the world. As part of our research we will comprehensively characterise the molecular changes involved in the formation of LSTs using next generation sequencing technology to provide a high-resolution map of the genome, epigenome and transcriptome.

Another active area of research in our laboratory is the investigation of the molecular events associated with gene silencing. This research aims to reveal insights into the mechanisms by which genes are epigenetically silenced in cancer. Collectively, research within the Molecular and Cellular Oncology Laboratory is geared towards a better understanding of the mechanisms by which genetic and epigenetic changes lead to colorectal cancer.

Current projects
- Genome-wide profiling of Laterally Spreading Tumours (LSTs) of the colorectum
- Investigation of the molecular events associated with gene resilencing following the withdrawal of epigenetic therapies

Progress in 2011

**Colorectal Cancer Project**
- Over 465 specimens and matched normal tissues from 301 patients collected and catalogued within the Lowy Biorepository
- Completion of the molecular analysis of a cohort of 135 specimens and preparation of a manuscript for publication
- Completion of next-generation sequencing of 29 specimens
- Began collaborations that will allow the genome-wide analysis of further specimens

**Cancer Therapy Project**
- Significant progress has been made towards completion of this project. Moving from a gene-centric project to a genome-wide investigation and encompasses a much more comprehensive analysis than previously planned

These projects have contributed to 5 abstracts at the annual American Association for Cancer Research (AACR), Australian Gastroenterology Week (AGW), Australian Health and Medical Research Congress (AHMRC), Research in Computational Molecular Biology (RECOMB) meetings, as well as an invited oral presentation at the 1st International Genomic Medicine Conference in Saudi Arabia.

Leader and Team

*Leaders:* Dr Luke Hesson, Research Fellow; Prof Robyn Ward, Head of POWCS and Head of Adult Cancer Program

*Team:* Dr Mathew Sloane, Research Fellow; Dr Sameer Srivastava, Research Fellow; Mrs Deborah Packham, Research Assistant; Ms Jenny Liu, PhD Student; Ms Vibha Patil, PhD Student; Mr Peter Zarzour, Honours student; Mr Alan Lim, ILP Student
Glioblastoma (GBM) is the most common brain cancer with a median survival of only 15 months. Infiltration, cell migration and resistance to chemotherapy and radiotherapy are characteristic of GBM. As new therapeutic regimes are developed, it is paramount that we work out a strategy for identifying the patients that will show a positive response to treatment. The discovery of new biomarkers with capacity to predict patient response to treatment is a key priority of the Cure For Life Neuro-oncology Group. Understanding the mechanisms of tumour migration and infiltration is another research priority. The group has strong collaboration with clinical professionals including Associate Professor Charlie Teo, Dr Helen Wheeler and Dr Elizabeth Hovey.

Current projects

- Preclinical investigation of the efficacy of PENAO, a novel arsenic compound
- Sphingolipid metabolism in glioblastoma
- MicroRNA combined with chemotherapy
- Understanding the mechanisms of tumour relapse
- Australian Genomics and Clinical Outcomes of Glioma (AGOG)

Progress in 2011

- MGMT promoter methylation testing was developed using pyrosequencing technology. The results of this test will help guide oncologists in their assessment of patient response to alkylating drugs such as temozolomide
- Showed for the first time that a microRNA is capable of regulating tumour migration. This study was recently accepted in the European Journal of Cancer

Leader and Team

**Leader:** Dr Kerrie McDonald, Chair, Cure For Life Neuro-oncology Group

**The Team:** Dr Siska Sumual, Postdoctoral Scientist; Mr Jack Zhou, Postdoctoral Scientist; Ms Sylvia Chung, Research Officer; Ms Sarita Tiwari, Research Assistant; Ms Hatic Sevim, PhD Student; Dr Hazem Abuhusain, PhD Student; Ms Dan Lu, PhD Student; Dr Han Shen, Masters student; Mr Hae Jo, Honours student

### Highlights

Three talented postdoctoral scientists, Dr Siska Sumual, Dr Jack Zhou and Ms Sylvia Chung, lead the way with their respective research programs. Siska has identified a mutation that controls invasion, Jack is working out ways to improve traditional chemotherapy and Sylvia is busy building stem cell models with Professor Teo. These stem cell models will provide us with a testing system which is more representative of neurological tumours.

Another four PhD Students, Dr Hazem Abuhusain, Dr Han Shen, Ms Hatic Sevim and Ms Dan Lu, are also pushing the research boundaries. Hatic recently had a manuscript published in an international journal, *J Cancer Research Clinical Oncology*, which detailed why single genes are ineffective as targets for therapies. Hatic, Hazem and Dan were all awarded Prince of Wales Clinical School Scholarships. The team would not be complete without Ms Sarita Tiwari, Mr Hae Jo and Dr Kyoko Okada.

The group has made significant inroads in improving the treatment and survival rates for patients with brain tumours with tests they have developed becoming routine and new research trials underway. Professor Phil Hogg (Director, Lowy Cancer Research Centre) has developed a new drug called PENAO. PENAO specifically targets and kills cancer cells. We have shown this drug to be highly effective on brain tumour cells. In a recent preclinical study, mice treated with PENAO went into remission from their brain cancer. The preclinical studies are continuing and a clinical trial is being designed.

Another exciting avenue of research for the team is in the area of mutation discovery. Siska has identified a mutation in a key protein involved in tumour cell migration. Unfortunately, the presence of this mutation leads to increased tumour aggressiveness. It is now a target for treatment. Dr Kerrie McDonald, Kyoko, Dan and Sarita have been working on a mutation associated with response to chemotherapy treatment. Final *in vitro* (cell) experiments will help clarify what role this mutation may play in predicting chemotherapy sensitivity.

Tissue banking is an integral part of the laboratory research and Kerrie is the co-director of the Australian Genomics and Clinical Outcomes of Glioma (AGOG) project. Over 200 biospecimens (tissue, matched bloods and clinical data) have been collected and registered for research use. A project using this AGOG resource is underway to help identify patients who will respond to a particular kind of treatment. The Steve and Lynette Waugh Brain Tumour Bank (which collects all brain lesions) is a resource to encourage collaboration.
Adult Cancer Program
Medical Epigenetics

The group focuses on unusual ‘epigenetic’ mechanisms that predispose individuals to young-onset cancer. Most familial cancers occur due to the inheritance of a mutation within the genetic code of a cancer-protection gene. Some patients are mutation-negative, but instead, their gene has been switched off by the accumulation of a repressive chemical at the start of the gene, namely methylation. Termed an ‘epimutation’ this cancer causing mechanism shows unusual patterns of inheritance. In addition, mutations in front of the gene can similarly attract methylation. The aim of this group is to determine the role and inheritance of various types of epimutation in cancer.

Current Projects
- Inheritance and mechanisms underlying different forms of MLH1 epimutation in familial cancer
- Interactions between sequence variation and epigenotype
- Studying how a common promoter-enhancer, SNP in the MGMT gene, predisposes to epigenetic silencing in various types of cancer

Progress in 2011
- Identification and publication of new cases and families with MLH1 epimutations. These have shown involvement in different patterns of inheritance due to distinct underlying mechanisms

- PhD Students, Joice Kuroiwa Trzmielina and Chau-To Kwok are writing their theses full time with the aim to submit in March 2012

Highlights
Our group identified the first dominantly transmitted MLH1 epimutation in an Australian family, and revealed its likely cause as a 5'UTR single nucleotide variant. This represents a novel cause for cancer susceptibility. This finding was published in an article in the high impact journal Cancer Cell and received national media attention.

Leader and Team
Leader: Dr Megan Hitchins, NHMRC Career Development Fellow, UNSW Senior Research Fellow, UNSW Senior Lecturer
The Team: Dr Robert Rapkins, Post-Doctoral Researcher; Dr Sameer Srivastava, Endeavour Post-Doctoral Fellow; Ms Joice Kuroiwa-Trzmielina, PhD Student; Ms Chau-To Kwok, PhD Student
Ovarian cancer is the gynaecological malignancy with the highest mortality worldwide. Seventy-five percent of patients get diagnosed in advanced stage of the disease as symptoms are rare to detect at an early stage. Our research focus is on the detection of ovarian cancer at an early stage using blood-based molecular markers in order to identify more effective methods of early diagnosis. Our group has numerous national and international collaborations, particularly in Russia, USA and Switzerland.

Current Projects
- The role of IgG and IgM anti-glycan antibodies and the immune system in ovarian cancer
- C-Kit expression in vulvar melanomas
- Clinicopathological characteristics of carcinosarcoma of the endometrium and the ovary
- The role of small field radiation in nodal negative high risk stage I cervical cancers

Progress in 2011
- Published 8 papers this year and increased our international biospecimen collection from 4 sites in Switzerland and Australia to more than 1,400 enrolled patients
- We have started collaborations with multiple Australian centres at Ian Wark Institute, Adelaide (Dr Benjamin Thierry), Monash University, Melbourne (Prof Fabienne Mackay), Macquarie University (Prof Nicki Packer), Peter Mac Cullen Research Centre, Melbourne (Prof David Bowtell) and the Walter and Eliza Hall Institute, Melbourne (A/Prof Clare Scott)
- Our international collaborators include Professor Nicolai Bovin (Russian Academy of Science), Associate Professor Margaret Huflejt (New York University) and Professor Ruedi Aebersold (ETH Zürich Switzerland).
Sarcoma Research Group (SRG) is the experimental cancer research team located at the Integrated Cancer Research section of the Adult Cancer Program, Lowy Cancer Research Centre. It is also associated with the Surgical Oncology Research Group (SORG) based at Prince of Wales Hospital. The SRG focuses on basic and translational studies to improve treatment of human sarcomas (or tumours).

Associate Professor Jia Lin Yang, the team leader of SRG, has contributed in research leadership and supervision, biostatistics support, cancer education and administration, as well as serving as Editor-in-Chief for the international journal, World Journal of Cancer Research (www.aspbs.com/wjcr) in 2011.

Current projects
- DNA MMR deficiency and cancer sensitivity to calcium channel blockers
- Investigation of miR34 and its promoter in a panel of cancer cell lines and tissue samples
- Effect and mechanism of concurrent inhibition of EGFR and STAT3 in treatment of soft tissue sarcoma
- Effect of pan-Her inhibitor in human sarcoma
- Significance of inhibition of MEK/ERK signalling in soft tissue sarcoma

Progress in 2011
- STAT3/EGFR targeted therapy in soft tissue sarcoma
- IGF1R targeted therapy enhances chemotherapy in osteosarcoma (bone tumours)
- MEK/ERK signalling and lung metastasis of osteosarcoma
- New gene groups in osteosarcomagenesis
- Adjuvant radiotherapy in the treatment of extremity soft tissue sarcoma
- Retrospective review of inflammatory breast cancer from Prince of Wales Hospital
- Retrospective analysis of desmoids tumours (benign, slow-growing tumours)
- Chemoradiation versus radiotherapy in extremity STS
- Establishment of the STATS-CHOICE e-program
- Establishment of Cancer Sciences course for UNSW

Highlights

Cancer Research
We found that blocking EGFR signalling alone can not inhibit JAK-STAT bypass signalling for sarcoma cell survival. The solution is to concurrently inhibit both EGFR and STAT3, leading to cancer cell death in vitro. This study was awarded the Choong-Dickinson Best Poster Prize at the Australian Sarcoma Group meeting in Melbourne in October 2011.

Cancer Education
A Cancer Sciences (PATH3208) undergraduate course for UNSW was established in 2011 and will be run by the Prince of Wales Clinical School in Session II, 2012. The course outline can be found on the website: http://medicalsciences.med.unsw.edu.au/SOMSWeb.nsf/page/Science+Current+Students.

Leader and Team
Leader: A/Prof Jia-Lin Yang

The Team: Ms Xiaochun Wang, Masters Student; Ms Nuha Ibrahim, ILP Student; Ms Kathleen Batty, ILP Student; Mr Chun-Jek Tan, ILP Student
Adult Cancer Program

Stem Cell Group

The primary focus of our research program is to better understand how genes that drive blood and mesenchymal stem cell development are regulated.

Current Projects

We are investigating the following core areas:

• Transcription factor interactions that drive haematopoietic stem cell (HSC) and mesenchymal stem cells (MSC) development, self-renewal and differentiation

• Interactions between the core transcription factor networks in HSCs and MSCs with cell signalling pathways associated with their development and maintenance

• Links between the transcription factor network in embryonic HSCs and in leukaemic cells

• Pathogenesis of myelodysplasia (MDS) with a view to drug development

Progress in 2011

• Described a role for ERG, an ETS transcription factor in the pathogenesis and maintenance of T-acute lymphoblastic leukaemia (T-ALL) (Thoms et al Blood 2011). Completed a detailed investigation of the ERG locus in acute myeloid leukaemia to show a link between the activity of stem cell enhancers and the establishment of stem cell programs in leukaemic cells (Diffner et al submitted)

• Described a reciprocal relationship between the master regulator of blood stem cell development in the embryo, Runx1 and Smad6, a modulator of Bmp signalling (Knezevic et al Molecular and Cellular Biology 2011). Using this and other known interactions that control Runx1 activity, we have built a mathematical model with Dr Oleg Igoshin that was shown to correctly predict the early emergence of blood stem cells in Runx1 haplo-insufficient embryos (Tiwari et al submitted)

• Advanced the analysis of bone marrow samples collected from patients with Myelodysplasia and Chronic Myelomonocytic Leukaemia during treatment with a DNA demethylating agent with a view to determine the relationship between global epigenetic change, gene expression, clonal evolution and clinical response

• Advanced our investigations into the origins of mesenchymal stem cells, their transcriptional identity and relationship with embryonic haematopoiesis

• Advanced our investigations into the a priori discovery of regulatory complexes that bind stem cell enhancers in leukaemic cells, post-translational modification of oncogenic transcription factors, the impact of oncogenic transcription factors in primary human cord blood stem progenitors and profiling genome-wide binding targets of transcription factors in primary cells

• Completed a ENU mutagenesis screen for recessive haematopoietic defects during embryonic development and commenced characterising the role of identified mutants

• Concluded a number of collaborative research studies with Drs Jason Wong (Beck et al Bioinformatics 2012 in press), Robyn Ward (Liu et al submitted) and Bertie Gottgens (Oram et al submitted)

• Published results from a series of collaborative research studies with Drs Doug Hilton, WEHI (Taoudi et al Genes and Development 2011), Richard Harvey, VCCRI (Chong et al Stem Cell 2011), Andrew Elefanty, Monash (Pereira et al Stem Cell Research 2012 in press) and David Curtis, Monash (Curtis et al Stem Cells 2012 in press)

Leader and Team

Leader: Dr John Pimanda, Senior Lecturer and Consultant Haematologist

Team: Dr Vashe Chandrakanthan, Senior Research Associate; Dr Julie Thoms, Senior Research Associate; Dr Eva Diffner, Research Associate; Dr Ashwin Unnikrishnan, Research Associate; Dr Jair Kwan, Research Associate; Dr Anchit Khanna, Research Associate; Ms Kathy Knezevic, Senior Research Officer; Ms Rabab Nasrallah, PhD Student; Mr Jonathan Marks-Bluth, PhD Student; Ms Melinda Tursky, PhD Student
Our overall aim is to understand the key processes in epithelial to mesenchymal transition (EMT) and metastasis, in order to identify targets for novel cancer therapies. Our group focuses on an important signalling pathway involved in metastasis and EMT, the Wnt signalling pathway. We are particularly interested in investigating the epigenetic regulation of a number of key proteins involved in this pathway, and understanding their role in the context of ovarian, breast and colorectal cancer.

Current Projects

- Modulation of Wnt antagonists in ovarian cancer and effects on EMT
- The role of the non-canonical pathway in ovarian cancer
- Regulation of Wnt receptors in cancer

Progress in 2011

- Continued work based around successful NHMRC project grant awarded from 2010
- Obtained further funding for research projects from Cure Cancer Australia
- Continued strong research collaboration with Dr Viola Heinzelmann-Schwarz for ovarian cancer projects
- Established new research collaborations
- Recruited new students

Outlook for 2012

- One new UNSW PhD Student and 1 ILP Student will start work on Wnt receptors in cancer
- Results from Wnt antagonist study will be presented internationally and published

Highlights

After being established in late 2009, the Wnt Signalling & Metastasis Group grew to 5 members in 2011. A strong collaboration was also established with the Ovarian Cancer Group and we are investigating the role of Wnt signalling in ovarian cancer. Data from this collaboration was published and presented internationally at the 5th International EMT Meeting in Singapore in October, 2011.

Leader and Team

**Leader:** Dr Caroline Ford, Research Fellow

**The Team:** Ms Eve Jary, Research Assistant; Ms Gaya-Punniyamoorthy, PhD Student; Mr Sean Ma, Honours Student; Ms Yan Ni Loh, ILP Student; Ms Laura Baker, 3rd year medical student
As part of the South Asian Clinical Toxicology Research Collaboration (SACTRC) collaboration we have developed a centre of clinical toxicology research excellence in Sri Lanka – largely funded by the NHMRC and Wellcome Trust International Collaborative Research Grant scheme. The main focus of this work is pesticide poisoning, although the collaboration began with trials on snake envenomation and oleander poisoning and continues to be active in researching these areas and in other community based public and mental health projects.

Current Projects

- SACTRC
- Australian Snakebite Project
- Renal biomarker collaboration

Progress in 2011

- Continued work based around four successful project grants:
  - Randomised Control Trial (RCT) of safe storage of pesticides in Sri Lanka
  - RCT of education for primary care doctors in Sri Lanka
  - RCT of FFP in Russell’s viper envenomation
  - Renal biomarkers of acute nephrotoxicity
- Obtained two new grants totalling $1.385 million for "Renal Biomarker equipment and Neurotoxicity following poisoning and envenomation" in collaboration with POWH and SACTRC respectively

Highlights

SACTRC continued to successfully transition to ongoing project grant funding (now guaranteed until 2015) with local leadership. This will take it through to its second decade and hopefully a long and healthy life. It is now funded by 6 large project grants and has over 100 publications. There continues to be many outcomes from this research — outcomes from the research have been incorporated into World Health Organisation and national treatment guidelines, and three pesticides were banned from January 2011.

The Australian Snakebite Project achieved its 12th research publication. This is the only substantive project on human snakebite ever conducted in Australia. This has led to recently updated guidance on antivenoms in Australian Medicines Handbook, Australian Therapeutic Guidelines, Australian Prescriber and TOXINZ.

Leader and Team

Leader: Prof Nick Buckley

Team: Prof Andrew Dawson, Adjunct Professor, Project Director SACTRC; Ms Melissa Pearson, PhD Student; Ms Jacqueline Anderson, PhD Student; Mr Mohamed Fahim, PhD Student; Mr Tim Pianta, PhD Student
Our research group was organised in 2010 with the aim of fostering research in all aspects of both diving and hyperbaric medicine. Diving medicine is concerned with all physiological and medical aspects of immersion and breathing compressed gas under water and is of great interest to both recreational divers, and commercial and military operations. Hyperbaric medicine is involved with all aspects of the treatment of disease by the application of high oxygen partial pressures. The group is particularly focussed on the evidence-basis of these disciplines and is a world leader in the critical appraisal and meta-analysis of the evidence for the application of hyperbaric oxygen in a wide range of disease.

Our research is intimately involved in the delivery of clinical services through the Department of Diving and Hyperbaric Medicine – a state-wide service located at Prince of Wales Hospital.

Current projects
- The Australasian database of Hyperbaric Oxygen Therapy (HBOT) for chronic wounds
- The treatment of idiopathic sudden sensorineural hearing loss with hyperbaric oxygen therapy
- Myopic shift and HBOT

Progress in 2011
- Our group continues to co-ordinate and publish the ongoing results of the Australia/New Zealand outcomes database in the treatment of chronic wounds with HBOT. This remains the most comprehensive data published on the fate of wounds and individuals who are referred to hyperbaric facilities for the treatment of non-healing ulcers of whatever aetiology and is a significant source of data for an ongoing Medicare Services Advisory Committee investigation of the appropriate use of hyperbaric therapy in this area
- Throughout 2011 we continued to recruit patients to the multi-centre randomised controlled trial of HBOT for the treatment of sudden sensorineural hearing loss.

Highlights

Installation of the new hyperbaric chamber

The research group is now the proud possessor of the largest therapeutic compression chamber in the world. This facility takes Prince of Wales Hospital and UNSW into the forefront of clinical hyperbaric and diving therapy.

It houses both our clinical and research facilities including the dedicated research vessel ‘Deeplab’ – suitable for equipment, in vitro and in vivo studies in all animals up to human scale. Our new clinical chamber consists of four internal compartments, all capable of independent compression according to patient and research requirements. One large compartment is designed primarily for our routine ‘walk-in’ patients – where we will be able to treat 10 patients in a single session; another large compartment will be set up as a two bed intensive care area and a smaller chamber area is designed for use at higher pressures for the treatment of diving injuries.

The facility includes a teaching and simulation area to enable our active education program. We are now well advanced on the work of renovating and replacing the clinical and administrative areas.

Hosting the Annual Scientific Meeting (ASM) of the Hyperbaric Technicians and Nurses Association

The group hosted the ASM of the national body representing the non-medical disciplines working in the field. The group participated in the three day ASM with a number of presentations concerning our research efforts here as well as organising and running a one day workshop on the use of deep helium and oxygen tables for the treatment of severe neurological decompression illness. This workshop will set national guidelines for the appropriate safe use of this advanced recompression strategy.

Leader and Team

Leader: A/Prof (Conjoint) Michael Bennett, Research Director, ADHMRG, Academic Head (Anaesthesia) and Supervisor of Training, Department of Diving and Hyperbaric Medicine

Team: Dr Robert Turner, Director of the Department of Diving and Hyperbaric Medicine; Dr Jan Lehm, Co-investigator; Dr Barbara Trytko, Researcher; Ms Samantha Wills, Primary Researcher; Dr Glen Hawkins, Principal Investigator; Dr Nayden Naydenov, Data Collector
The group is engaged on a research project into the causes and mechanisms of headache. The research investigates the neural pathways involved in the perception of head pain and in the control of the craniovascular reactivity. The research also looks into the neurophysiological recording of single neuron activity in vivo, the monitoring of cranial blood flow and use of histological techniques to assess neuronal activity.

Current projects

• Clear demonstration that migraine is not primarily a peripheral vascular pathology
• Identification of somatostatin as a critical neurotransmitter in the transformation of migraine triggers into migraine headache

Progress in 2011

• Validating the existence of the neural pathways involved in the triggering of migraine. This work has been successfully completed and published to considerable acclaim, being seen as a ‘tipping point’ in the search for the cause of migraine
• A strong case has been made that the neurohormone somatostatin is critical to the initiation and perpetuation of migraine. If so, this will be a major breakthrough because it can explain much that was previously inexplicable about migraine

Highlights

We published that migraine must be a central nervous system disorder and not a vascular pathology. This work drew the following comment from the President of the International headache Society, “the study goes some way to balance the long held, and misleading, view that migraine requires a peripheral sensory input”. The work on somatostatin was presented in Washington in June, and a side visit with NASA astronauts freshly off the STS-134 mission was made, to discuss the relevance of this work to so-called ‘space headache’.

Leader and Team

**Leader:** Dr Geoff Lambert, Senior, Research Fellow

**Team:** A/Prof A.S. Zagami, Cocreator of the program; Mr Seyed Ehsan Panahi, Research Assistant
Ischaemia reperfusion (IR) is a leading cause of acute kidney injury and is an unavoidable occurrence in renal transplantation. Our group has previously shown that the tissue factor-thrombin-protease activated receptor (PAR) pathway plays a pivotal role in kidney injury after IR. Our recent work has focused on understanding the complex cell signalling network that is down stream of PAR-1 as we explore ways to manipulate this pathway to prevent IR injury.

**Current projects**
- Investigating the relationship between PAR-1 signalling and Sphingosine-1-phosphate (S1P) signalling
- Exploring whether PAR-1 regulates adenosine signalling as another pathway involving the S1P system

**Recent advances**
We have been investigating the relationship between PAR-1 signalling and Sphingosine-1-phosphate (S1P) signalling. Thrombin via PAR-1 may generate S1P and S1P appears to play a role in IR injury that is dependent on the pattern of receptor expression. Activation of S1P receptor-1 (S1P-r1) improves renal function and deficiency of the receptor leads to more severe injury. S1P receptor-3 (S1P-r3) has also been shown to be an important mediator of inflammation in the kidney. We have shown that inhibition of PAR-1 with a specific antagonist improves renal IR injury and is associated with decreased S1P-r3.

We have also explored whether PAR-1 regulates adenosine signalling as another pathway involving the S1P system. We looked at the expression of the two main enzymes in the adenosine pathway CD39 and CD73. PAR-1 deficiency was not associated with increased expression of either molecule but rather decreased expression of CD39 which is the important first step in the pathway. This suggests PAR-1 inhibition was not resulting in increased adenosine receptor signalling.

To date our data suggests PAR-1 signalling regulates pro inflammatory pathways and PAR-1 inhibition results in reduced inflammation. However, this effect occurs without increasing protective pathways. This is an important finding as it leads to the idea that a combined approach of stimulating protective pathways while inhibiting pro-inflammatory ones may have a synergistic effect. To advance this idea, we are now examining the effect of combined PAR-1 inhibition and S1P-r1 agonist. Simultaneously we are continuing our experiments to determine the optimal timing of PAR-1 inhibition to ameliorate renal IR injury.

**Leader and Team**

*Leader: Dr Jonathan Erlich*, Senior Lecturer and Nephrologist

*Team: Dr Sean Kennedy*, Senior Lecturer, School of Women’s & Children’s Health, co-investigator and co-supervisor; *Mr Anthony Chuang*, medical student
Neuroscience Research Group

The aim of our clinical research group is to investigate the mechanisms, prevention and treatment strategies for neurological disease including motor neurone disease, multiple sclerosis and stroke. We also have a research focus covering chemotherapy-induced neurotoxicity and inherited neuropathies. We are involved in a number of clinical trials aimed at preventing or slowing the progression of neurodegenerative diseases.

Our research is intrinsically linked to the provision of clinical services — particularly the Multidisciplinary Motor Neurone Disease Clinic, the Hereditary Nerve and Muscle Clinics and Diagnostic Clinical Neurophysiology Clinics — all operating at Prince of Wales Hospital. Neurological consultation and clinical neurophysiological services are also provided at the UNSW Professorial Suite.

Current projects

- Investigator driven clinical trials in Motor Neurone Disease and Multiple Sclerosis funded by the National Health and Medical Research Council (NHMRC) of Australia

- NEU-HORIZONS is an investigator-initiated clinical trial investigating the potential new treatment for nerve dysfunction in patients receiving oxaliplatin chemotherapy, again supported by NHMRC

- Development of clinical biomarkers for diabetes neuropathy, the influence of dialysis in uraemic neuropathy and possible neuroprotective therapies

Progress in 2011

- Recent discoveries from our lab have prompted the initiation of therapeutic treatment trials, supported by NHMRC. The first investigator driven study has focused on a ‘neuroprotective’ medication for use in patients diagnosed with motor neurone disease

- Novel physical therapies are being explored in a clinical trial setting. One of these therapies incorporates a respiratory training device that aims to maintain breathing muscle function in motor neurone disease patients. As part of this process we have initiated and developed a clinical trials consortium, and are currently enrolling patients from across Australia into these trials

- In tandem with the aforementioned clinical trials, the Australian Motor Neurone Disease Registry is filtering large amounts of clinical data from motor neurone disease patients, enrolled in the registry from sites throughout Australia. This transcontinental registry forms part of a growing worldwide trend to obtain epidemiological and natural history information for motor neurone disease, and provides a hub for collaborative approaches. Through this approach we hope to improve the multidisciplinary care of motor neurone disease patients

- Our research hub runs in tandem with the Multidisciplinary Motor Neurone Disease Clinical Service, supported by the Motor Neurone Disease Association of NSW. The Service was recently funded by the Federal Department of Health and Ageing to develop training programs for health care professionals to assist with their involvement and care of motor neurone disease patients

- In separate studies in children who develop an early form of the disease known as spinal muscular atrophy, the team is exploring the pathophysiology of this devastating childhood disease

Highlights

- In August 2011 we were very proud to host the inaugural Sydney-Chiba Neurological Symposium. We were honoured to host Prof Satoshi Kuwabara and his team. This has strengthened our relationship with our sister research node in Chiba, Japan

- The team organised the Australian and New Zealand Association of Neurologists Clinical Neurophysiology Workshop held in Queensland, with Professor Matthew Kiernan, Chair of the Scientific Program

- The team organised and hosted the International Motor Neurone Disease Symposium in Sydney, attended by 1,000 clinical neuroscientists and neurologists

- Launch of three new clinical trials — dexprimipexole for patients with motor neurone disease, fampridine for patients with Multiple Sclerosis and chronic inflammatory demyelinating polyneuropathy, and riluzole for chemotherapy patients to prevent neurotoxicity (NEU-Horizon)

Leader and Team

Leader: Prof Matthew Kiernan

Team: Dr Cindy Lin, Senior Research Officer, Senior Lecturer UNSW; Dr Arun Krishnan, Senior Research Officer, Senior Lecturer Translational Neuroscience; Dr Steve Vucic, Senior Research Officer, A/Prof in Neurology; Dr Robert Bolland, Senior Research Officer; Dr Jennica Winhammer, Research Officer; Dr Michelle Farrar, PhD Student; Mr Ben Cheah, PhD Student; Ms Natalie Kwai, PhD Student; Dr William Huynh, PhD Student; Dr James Burrell, PhD Student; Mr Ben Cheah, PhD Student; Ms Ria Arnold, PhD Student; Ms Susanna Park, PhD Student; Dr James Burrell, PhD Student; Ms Ria Arnold, PhD Student; Ms Natalie Kwai, PhD Student; Dr Eneida Moishi, PhD Student; Dr Michael Lee, Post Doc; Dr Jong Bae, International Visitor; Dr Neil Simons, PhD Student; Ms Hannah Pickering, Research Assistant; Ms Jenna Murray, Research Assistant; Dr Margie Zoing, Research Officer; Ms Dianne Tyson, PA to Prof Kiernan; Ms Eleanor Ramsey, Clinic & Research Coordinator
The Psychosocial Research Group (PRG) comprises of a research team dedicated to the exploration of the interrelationship between psychology and health. PRG’s two major research strengths are in the area of the psychosocial implications of genetics and the psychological impact of cancer (psycho-oncology). The PRG’s research program in the psychosocial implications of genetics comprises several themes, including — the psychosocial impact of genetic counselling and testing for hereditary disease, psychological adjustment and behavioural impact of hereditary disease, and the design and evaluation of interventions in the cancer genetic counselling setting – in particular decision aids as an innovative means of patient education.

In relation to its research program in psycho-oncology, PRG is a leading international research centre in the area of the psychological and behavioural implications of cancer genetics. Other areas of national and international recognition include the psychosocial support and information needs of younger women with a diagnosis of breast cancer, fertility and menopause related implications of cancer therapy as well as cultural aspects of cancer.

Current projects
• An online hereditary prostate cancer decision aid (HPC-DA) for men with a family history of prostate cancer
• Randomised controlled trial (RCT) comparing the efficacy of educational materials regarding treatment-focused genetic testing (TFGT) to that of standard pre-test genetic counselling in preparing women newly diagnosed with breast cancer for decision-making about TFGT

Progress in 2011
• Completed baseline data collection for a randomised controlled trial (RCT) evaluating an online hereditary prostate cancer decision aid for men with a family history of prostate cancer who are considering their prostate cancer screening options
• An ongoing multicentre study comparing the efficacy of educational materials regarding treatment-focused genetic testing (TFGT) to that of standard pre-test genetic counselling in preparing women newly diagnosed with breast cancer for decision-making about TFGT

Highlight

*Making hard choices easier: a prospective, multicentre study to assess the efficacy of a fertility-related decision aid in young women with early-breast cancer.*


**PURPOSE:** To prospectively evaluate the efficacy of a fertility-related decision aid in women aged 18-40 years with newly-diagnosed early-stage breast cancer.

**PATIENTS AND METHODS:** From 19 Australian oncology clinics, 120 patients with early-stage breast cancer aged 18-40 years who desired future fertility were recruited. Participants were allocated using a block design to receive either a fertility-related decision aid or usual care. Patient reported measures were administered shortly after diagnosis and at 1 month and 12 months follow-up to evaluate the impact of the decision aid on fertility-related decisional conflict, decision regret, and patient satisfaction.

**RESULTS:** The decision aid was associated with significantly reduced decisional conflict over 12 months about fertility-related treatment decisions compared with usual care (p=0.004), adjusted for education, desire for more children, and uncertainty at baseline. Women who received the decision aid had significantly lower decisional regret about fertility-related treatment decisions at 12 months, compared to women who received usual care (p=0.034), adjusted for education. Women who received the decision aid were more satisfied with the information received on the impact of breast cancer treatment on fertility (p<0.001 and the different fertility options (p=0.005), and considered it more helpful (p=0.002), compared to those who received usual care.

**CONCLUSION:** This decision aid was effective in reducing decisional conflict about fertility-related treatment decisions and should be offered routinely to young breast cancer patients interested in future fertility shortly after diagnosis.

**Leader and Team**

**Leader:** A/Prof Bettina Meiser

**Team:** Mr Justin Chau, ILP Student; Ms Jenny Clough, Administrative Officer; Ms Denise Edwards, Administrative Officer; Ms Margaret Gleeson, Research Officer; Ms Sophie Lawrence, Administrative Officer; Ms Belinda Rahman, Research Officer; Ms Kishani Townsend, PhD Student; Dr Kaaren Watts, Research Officer; Ms Mimi Xu, ILP Student; Dr Elvira Zilliacus, Research Officer; Ms Lilian Zou, ILP Student
Pulmonary Inflammation Group

The major theme of research in this group is the study of inflammatory mediators in the pathogenesis of asthma and other lung diseases, including mechanisms of development of disease, clinically useful markers of inflammation, and novel approaches to intervention.

Projects include: mechanisms underlying inflammation and airway wall remodelling in animal models of chronic asthma and acute exacerbations of asthma; the influence of early-life infections and environmental injury in an animal model of the pathogenesis of childhood asthma; and studies of potential therapeutic interventions in asthma.

Translational research is a particular focus of the group, notably with respect to breath analysis of oxidative stress and other markers of disease activity, especially in asthma, but also sarcoidosis, chronic obstructive pulmonary disease (COPD) and lung cancer.

Current projects
- Asthma
- Lung Cancer
- COPD
- Sarcoidosis

Progress in 2011
Innovative research has emerged from our studies on non-invasive methods of studying airway diseases:
- Asthma: We have shown that exhaled nitric oxide is a method by which we can monitor lung diseases such as asthma. In addition, multicentre collaborative projects funded by NHMRC are being conducted with University of Melbourne applying these techniques
- COPD and lung cancer: We are studying methods of detecting and monitoring lung diseases such as COPD and lung cancer by using breath analysis
- Sarcoidosis: Novel studies in sarcoidosis have demonstrated markers of disease activity in the exhaled breath of the patients, as well as novel observations upon the peripheral lymphocyte profile and activation

In addition, the lung burden of mineral fibres secondary to asbestos exposure is being studied with current NHMRC funding.

Leader

Leader: Professor Paul Thomas
The Surgical and Orthopaedic Research Laboratory’s (SORL) overall goals are:

- to identify areas of clinical need from surgical, biomaterial and biomechanical perspectives and apply the scientific method to improve patient outcome
- to explore and understand the pathways and mechanisms involved in healing of connective tissues as well as strategies to augment the healing response.

The multidisciplinary approach of SORL furthers the understanding of the interactions of biomaterials and therapies related to connective tissues in normal, injured and diseased models using molecular biology, histology, chemical analyses, radiography, image analysis, computer modeling and biomechanical evaluations.

Our collaborations with surgeons across many sub-specialties combined with industrial and academic colleagues around the world provide for an exciting environment for cross fertilisation and progress for Australian research that has global reach.

Current Projects

- Bone ingrowth, ongrowth and implant fixation in total joint replacements
- Synthetic and tissue engineering scaffolds for tendon and ligament applications
- Biomechanical, kinematic and molecular biology of spinal fusions
- In vivo and in vitro evaluations of flexor tendon repairs
- Allograft sterilization, biomechanical and in vivo performance
- Osteoinductivity and osteoconductive bone graft materials
- Carbon fibre total hip replacements
- Patient specific arthroplasty surgery techniques
- Molecular biology of cancer treatments
- Platelet rich plasma concentrate and connective tissue healing
- Hard bearings in total joint replacements
- Shape memory alloys in orthopaedics and vascular surgery
- Design and evaluation of new implantable devices for use in sports medicine, trauma and spinal applications
- Molecular biology of fistulas in vascular surgery
- Segmental defect healing in long bones
- Spinal cord injury and bone loss
- Collaborative study with CSIRO

Progress 2011

- Best Scientific Paper - NSW Hand Surgery Association - Biomechanical assessment of a novel tendon junction
- SORL videos with Flying Fox Films
- Continued successful filings for implants to the Food & Drug Administration (FDA)
- Expansion of mechanical and kinematic biomechanical testing
- Expansion of histology and tissue culture laboratories
- Australian Orthopaedic Association – Australian Undergraduate Week at SORL and UNSW

Leader and Team

Leader: Professor W.R. (Bill) Walsh, PhD, Director

Team: Mr. John Rawlinson, Laboratory Manager and Section Head of Pre-Clinical Models; A/Prof Yan Yu, Section Head, Molecular Biology and Conjoint Senior Hospital Scientist; Dr Rema Oliver, Research Fellow, Section Head, Histology, OH&S Supervisor; Dr Matthew Pelletier, Research Fellow, Lecturer, Co-Secti-

on Head, Biomechanics and Engineering; Dr Nicky Bertollo, Research Fellow, Lecturer, Co-Section Head, Biomechanics and Engineering; Dr Alain Rives, Research Associate, Section Head, Chemical Analysis and IT; Dr Adrian Low, Research Associate; Dr Chris Christou BScVet, Staff Veterinarian; Mr Vedran Lovric, MS, Research Associate; Mr Gregory Mitchell, Animal and Research Technician; Ms Samar Saliba, Research Technician; Mr Nick Russell, MS, Research Technician; Mrs Manuela Winkler, Business Manager and Administrative Supervisor
Soft tissue sarcomas (or tumours) and bony tumours can occur almost anywhere in the body. These tumours are usually high grade aggressive cancers that result in poor survival rates. The Surgical Oncology Research Group (SORG) focuses on translational studies using small molecule inhibitors directed against new therapeutic targets to improve treatment of human sarcomas. The Sydney Sarcoma Unit has also been examining novel ways of reducing treatment side effects from surgery and radiotherapy, which are the mainstay treatments for soft tissue sarcoma. We are also analysing the management pathway of patients with retroperitoneal sarcoma (or a tumor of the far back abdomen).

Current projects

- Effect and mechanism of concurrent inhibition of EGFR and STAT3 in treatment of soft tissue sarcoma
- Effect of pan-Her inhibitor in human sarcoma
- Significance of inhibition of MEK/ERK signalling in soft tissue sarcoma
- Outcome of patients with retroperitoneal sarcoma: influence of pre-treatment biopsy

Progress 2011

- Significance of IGF-1R and its signaling pathways in human sarcoma (2011 American Association for Cancer Research presentation)
- Prognostic/therapeutic significance of EGFR in human soft tissue sarcoma (2011 Annual Cancer Symposium of the Society of Surgical Oncology presentation)
- STAT3/EGFR targeted therapy in soft tissue sarcoma (Australian Sarcoma Group 2011 Best Poster Award)
- IGF1R targeted therapy enhances chemotherapy in sarcoma
- MEK/ERK signalling and lung metastasis of osteosarcoma
- New gene groups in osteosarcomagenesis
- Adjuvant radiotherapy in the treatment of extremity soft tissue sarcoma

Highlights

**Combination targeted cancer therapy**

Much of the SORG’s efforts this year have been devoted to combination sarcoma targeted therapy. This study was initiated with the support of the Ross Trust Foundation. The study found that blocking EGFR signalling alone can’t inhibit JAK-STAT by-pass signalling for sarcoma cell survival. The solution is to concurrently inhibit both EGFR and STAT3 leading to cancer cell death in vitro.

The presentation of this study was awarded the Choong-Dickinson Best Poster Prize at the Australian Sarcoma Group meeting in Melbourne in October 2011. This finding justifies further studies in an animal model as well as investigating the mechanism behind this finding.

Leader and Team

**Leaders:** Prof Philip Crowe; A/Prof Jia-Lin Yang, Dr Shing Wong, Senior Lecturer

**Team:** Prof David Goldstein, Oncology Consultant; Dr Peter Luk, Research Associate; Ms Xiaochun Wang, MSc Student; Ms Kathleen Batty, ILP Student; Ms Chun-Jek Tan, ILP Student
Turnour tissue banks are vital for cancer research. The Lowy Cancer Research Centre has purpose-built, state of the art Biobank facilities for the reception and processing of human biospecimens. The Biobank contains biospecimens, including blood and tissue samples, taken with consent from both healthy individuals and patients diagnosed with cancer. Clinical information from the donors is also collected and linked to the specimens via a secure, web accessible database. The aim of the Biobank is to provide translational cancer researchers with high quality biospecimens and related clinical data, in order to facilitate discoveries that will lead to improvements in cancer diagnosis and treatment.

Progress in 2011
• caTissue v1.2 upgrade implemented
• Establishment of molecular processing laboratory
• Long term cryo storage area opened up for clients outside of POWCS and Lowy Cancer Research Centre

Highlights
The Biobank took delivery of a second 95,000 vial capacity Vapour Phase tank early in 2011. This tank is now available to internal and external researchers for long term storage of biospecimens.

Using caTissue, the biospecimen inventory and tracking module of the cancer Biomedical Informatics Grid (caBIG) developed by the US National Cancer Institute (NCI), the Biobank is currently supporting 23 active collection protocols.

We have over 23,000 specimens stored. This includes:
• 10,476 tissue samples
• 3,233 cell samples
• 2,746 fluid samples
• 8,614 molecular samples (6,952 DNA & 1,662 RNA)

Leader and Team
Leader: Dr Anusha Hettiaratchi

Team: Ms Diane Schipp, Research Data Manager; Miss Genevieve Bennett, Research Nurse; Mrs Sarita Tiwari, Research Assistant; Mrs Allison Arndt, Research Assistant
Adult Cancer Program - Biostatistics Group

The Biostatistics Group supports high quality research across the cancer research spectrum by providing expert statistical advice on experimental design, analytic plans and data management. Members of the Adult Cancer Program and Translational Cancer Research Network are provided support through the Biostatistics Services and Consulting program.

The Group also offers statistics lectures open to all staff and students of the school. The application of statistical methodology often raises interesting statistical questions and, as such, the group also has an active interest in statistical methodology as it relates to the analysis of cancer data.

Current projects

The Biostatistics Group is actively involved with providing data management and statistical support to several projects within the Adult Cancer Program. These include the following:

- Elements of Cancer Care cohort study
- Cancer in Department of Veterans’ (DVA) Clients in NSW

Leader and Team

**Leader:** Dr Jake Olivier

**Team:** Mr Ben Daniels, Biostatistician; Mr Michael Falster, Biostatistician; Dr Preeyaporn Srasuebkul, Research Fellow

Translational Cancer Research Network

The Translational Cancer Research Network (TCRN) was established in September 2011 funded by a Cancer Institute NSW grant. The TCRN will create an innovative and supportive environment for the translation of research findings into improvements in patient care and outcomes. Our vision is to create a culture that empowers our members to formulate and implement research-led improvements in patient care. The overall goal of the TCRN is to develop a sustainable translational research engine and to apply it to identified areas of need, in a logical and focussed manner.

Current projects

- Administer and support Cancer Challenge of the Year
- Administer PhD Scholarship Top-ups

Progress in 2011

- Established the Terms of Reference for the TCRN
- Launched the PhD Scholarship Top-up funding program for 2012

Outlook for 2012

- Launch the 2012 Cancer Challenge of the Year funding program
- Grow our membership base to 120 members
- Launch a biostatistical service for our members

Leader and Team

**Leader:** Ms Lena Caruso, Centre Research Manager

**Team:** Mr Jitendra Jonnagaddala, Information Manager; Ms Anna Palagy, Project Officer
The Clinical Teaching Unit (CTU) oversees the clinical teaching and assessment of undergraduate students attached to the Prince of Wales Clinical School. It is primarily an administrative unit to coordinate the placement of all students, organise clinical teaching activities, organise clinical examinations, ensure compliance with University and NSW Health policies and support teaching staff, including conjoint teachers, and students. Overall there are more than 200 students who complete part of their clinical training in the clinical units of the Prince of Wales Hospital each year.

Phase 1

By Dr Barbara-Ann Adelstein, Phase 1 Coordinator

One hundred and forty five medical students in Phase 1 (years 1 and 2) of the Medical Program attended clinical tutorials at Prince of Wales Hospital during 2011. These tutorials give students the opportunity to practice their clinical examination skills on patients in a clinical setting. The tutorials were taught by clinical facilitators drawn from Hospital consultants, registrars and resident as well as local general practitioners. In addition, two Phase 1 clinical examinations were successfully conducted during the year: one in May for the 2010 Phase 1 cohort, and the second in November for the 2011 cohort.

In recognition of their teaching commitment in the Phase 1 program, the Prince of Wales Clinical School presented 2011 Teaching Awards to Dr Phil Kemp, Dr Emily Chong, Dr Naomi Jacobs and Dr Regina Skvirsky, all of whom are general practitioners who have taught clinical skills to Phase 1 students consistently for the last 8 years.

Phase 2

By Dr Melvin Chin, Phase 2 Coordinator

Phase 2 builds on Phase 1 and has a practice based learning context. Phase 2 comprises of the Independent Learning Project (ILP) and clinical courses namely Health Maintenance (HM), Ageing and Endings (AE3), Society and Heath (SH) and

School Programs
Undergraduates
Beginnings, Growth and Development (BGD). This phase provides an opportunity for students to individually participate in supervised research projects in the form of the ILP or the Honours Program. There were 38 ILP Students and 8 Honours students enrolled throughout the Prince of Wales Clinical School and affiliated research institutes in 2011.

The clinical courses integrate Campus based learning such as lectures and practical classes with clinical placements in hospital wards and departments and community centres. The clinical placements are designed for students to develop clinical skills, particularly diagnostic skills. The clinical and campus learning are complimentarily set out in themes so that students can relate what they see in a clinical setting with biomedical learning which forms the foundation of clinical medicine. We are thus very fortunate to be closely located with the main Campus, the Royal Hospital for Women and the Sydney Children’s Hospital. Students are examined on submitted case presentations through the clinical placements and an end-of-course Clinical Skills exam.

We received 46 students for the clinical courses (HM and AE3) at the Prince of Wales Clinical School in 2011. We wish to thank the numerous clinicians from various hospital departments who have selflessly contributed to the valuable clinical teaching to realise the practice based part of the integrated curriculum. In particular, we wish to thank the facilitators of the HM and AE3 terms, most of whom have done so over a number of years. The Aged Care component was facilitated by Associate Professor Jacqueline Close. The Oncology term was facilitated by Dr Elizabeth Hovey, who handed that responsibility over to me at the start of 2011. The HM terms were facilitated by Professor Phil Jones, Dr Silas Taylor, Professor Phil Crowe and Dr Shing Wong.

2012 will see a slightly redesigned Phase 2 course. The HM term will be expanded and split into two 6 week terms named Adult 1 and Adult 2. Adult 1 will be comprised of topics corresponding to a “visceral” theme (such as cardiorespiratory and gastrointestinal systems) while Adult 2 will have an “appendicular” theme (such as neuroscience, rheumatology and orthopaedics). The AE3 term will be split into Oncology and Aged Care which will follow Adult 1 and Adult 2 terms respectively. The redesign will result in Summer Term being the last for Phase 2.

Phase 3

By Dr Shing Wong, Phase 3 Coordinator

At Prince of Wales Clinical School (POWCS), students are offered Medicine, Surgery, Emergency and Selective Phase 3 courses. In all courses, students are allocated to clinical units where they are expected to participate in unit activities. There are regular tutorials throughout the different courses. In Year 6, weekly medical and surgical viva tutorials are provided to students. This year, POWCS have offered regular psychiatry tutorials as well as a Preparation for Examinations Day which included obstetrics and gynaecology, and paediatrics refresher sessions. Students have enjoyed their placements at POWCS and have performed well at the examinations.

Leader and Team

Leader: Professor Philip Jones, Director, Clinical Teaching Unit
Team: Dr Barbara-Ann Adelstein, Phase 1 Coordinator; Dr Melvin Chin, Phase 2 Coordinator; Dr Shing Wong, Phase 3 Coordinator; Ms Jenny Ryall, Senior Administration Officer; Ms Justine Perry, Administration Officer
POWCS has a long tradition of integrating research, teaching, and clinical care. A primary focus of our research is translational medicine – bench-to-bedside. We have world class research facilities in the Prince of Wales Hospital which include the disciplines of neurology, nephrology, surgery and oncology. We also have close affiliations with many centres of renown such as Neuroscience Research Australia, the Lowy Cancer Research Centre and the Garvan Institute. We offer higher degrees in clinical medicine as well as laboratory and public health research.

POWCS provides excellent infrastructure and support to postgraduate students to allow them to pursue high quality, innovative research. We have experienced and dedicated academic staff to supervise, mentor and educate our students. With access and exposure to a diverse range of academic disciplines, our graduates receive all-round training in scientific research. We ensure that students realise their full potential and experience the thrill of scientific discovery. Our postdoctoral scholarships, biostatistics training scholarships and travel scholarships demonstrate our commitment to postgraduate students.

There were 74 postgraduate students enrolled in our School, 59 PhD Students, 14 Masters by Research students and 1 MD students. We had 12 successful completions: 8 PhD, 3 Masters and 1 MD. Fourteen students earned federally funded competitive scholarships in 2011, 13 local and 1 international student.

Two students, Christina Esposito and Hazem Abuhusain, received the 1 year Prince of Wales Clinical School Postgraduate Research Student Scholarship worth $20,000. Melinda Tursky won the 2-3 year Prince of Wales Clinical School Research Student Scholarship worth $22,500 each year, for up to 2 years for Masters and 3 years for a PhD. Congratulations!

Ms Jia (Jenny) Liu, in the final year of her PhD at the School, won the strongly contested Faculty of Medicine 3 Minute Thesis Competition. Jenny then went on to win first place in the UNSW Interfaculty Final, and she gave a stellar performance at the Australia and New Zealand Competition in Perth. The School is very proud of this achievement and Jenny’s research on the relationship between folate and aberrant DNA methylation in colorectal cancer. Jenny submitted her thesis in December and she has returned to study at UNSW to complete her medical degree.

If you are a prospective student, please read the research section of this annual report to identify potential supervisors and research groups, and to get ideas for your research project. Then visit our postgraduate student ‘How to Apply’ section of the School website for instructions on the admission application process for POWCS before you undertake the general admissions application via https://my.unsw.edu.au.

Team

Team: A/Prof Claire Vajdic, Postgraduate Coordinator; Dr Jonathan Erlich, Postgraduate Coordinator; Ms Caitlyn Granse, Administrative Assistant
Conjoints

Prince of Wales Clinical School has over 200 conjoints – both medical and research professionals with various specialties, many based on Prince of Wales Hospital campus in Randwick – they actively support the teaching, research, student supervision and other critical functions of the School and the Faculty of Medicine at UNSW. The School acknowledges the enormous contribution our conjoints make to the community and learning experience of our school. We thank them all very much for their efforts.

Three of our Conjoints who were selected in recognition of their contributions are introduced below:

Professor Lynne Bilston
Conjoint Professor, UNSW; Senior Principal Research Fellow, Neuroscience Research Australia; BE, MSE, PhD

Major projects: Injuries to vehicle occupants – crash factors, biomechanics; biomechanics of spinal cord injury and brain injury; imaging studies and biomechanical factors in obstructive sleep apnoea; neural tissue biomechanics.

Biography: Lynne began her career as a mechanical engineer, after deciding a medical degree and clinical life was not for her. However, her love of all things physiological drove her to adopt engineering techniques in studying the mechanisms of spinal cord injury in her early research career. She has extended this to include research covering many aspects of how the soft tissues of the body, particularly neural tissues, respond to mechanical loading – both physiological and injurious. She came to UNSW and Neuroscience Research Australia in 2002, after 7 years as a teaching academic in Engineering at the University of Sydney. She is now an NHMRC Senior Research Fellow, and leads research programs in injury biomechanics and biomechanical methods in imaging.

Career highlight: Doing the underpinning research for introducing mandatory child restraint legislation to protect children in car crashes, and seeing this work translate through to national legislation and reduced child injury rates.

Maintaining work/life balance: Fortunately for me, my work helps answer the endless stream of questions from my kids — although explaining the concept of magnetic spin to my 11 year old would-be-physicist son was a challenge.

Factors which drove choice of career: My research is a combination of my interests in medicine and engineering mechanics. The body is the most fascinating mechanical machine on the planet!

Dr Michelle Peate
Conjoint Lecturer, UNSW; Research Program Manager, Psycho-Oncology Co-operative Research Group (PoCoG); BSc(Bioinformatics), GradDipSci(Biology), MScMed(Reproductive Health and Human Genetics), PhD(Medicine)

Achievements: My biggest achievement to date has to be my PhD which required no corrections – with one examiner commenting: ‘This examiner has seldom read a document so well qualified for immediate transference of the award’. My thesis was also awarded the prestigious APS Award for Excellent Higher Degree Thesis in Health Psychology (2010). It made all that blood and sweat worthwhile.

Major projects: My primary research focuses are the psychosocial and reproductive issues of young women with cancer, and more generally in cancer patients as a whole. I also have a burgeoning interest in the psychosocial issues of adolescents and young adults with cancer.

Proudest moment (so far): The moment that the Decision Aid (an information tool designed to assist with decision-making) I developed as part of my PhD is publically available will be one of my proudest. In many ways this was a four year labour of love, and I consider it my ‘baby’. It will soon be accessible to young women with breast cancer.

Associate Professor Yan Yu
Conjoint Associate Professor, UNSW; Principal Hospital Scientist, POWH; Section Head, Orthopaedic Pathology & Molecular Biology, Surgical & Orthopaedic Research Laboratories (SORL), Prince of Wales Clinical School; MBBS, PhD

Most satisfying aspects of working for UNSW: Being able to supervise surgical fellows and research students to complete their postgraduate degrees, then seeing them graduate at the end of a long journey! As a primary supervisor I have supervised 4 PhD, 2 Masters, and 2 ILP Students. I have also co-supervised and mentored over 30 postgraduate students and 14 ILP or Honours students.

In return, I have learnt a lot from my students: weird and wonderful medical knowledge, computers, popular culture, sports, travel, fashion, food, as well as new ideas in research. They are my additional source of motivation to design more projects and to keep publishing my research.

I am proud to be a member of SORL led by Prof Bill Walsh. We have three strong wings: animal surgery, mechanical testing, and histo/molecular biology which allows for students to learn multiple skills in-house.
Awards and Grants

Adult Cancer Program - Bioactive Lipid Signalling

Awards
- Don AS; NHMRC Project Grant; Altered myelin sphingolipid homeostasis in Alzheimer’s Disease; 2012-2014; $608,375
- Don AS; Cure Cancer Australia/Cancer Council NSW Innovator Grant; Developing sphingosine kinase 2 inhibitors to block glioblastoma cell proliferation; 2012; 98,648

Grants
- Biostatistical Genomics Group
- Adult Cancer Program - Cancer Drug Development Group

Grants
- The Cancer Council NSW; Research Program Grant; 2011-2015; $2,250,000
- Faculty of Medicine, University of New South Wales, Faculty Research Grant 2011; 12 months; $20,000

Adult Cancer Program – Coagulation in Cancer Group

Awards
- Hua M; Australian Society for Thrombosis and Haemostasis Travel Award; CDI-1 is a novel marker for platelet apoptosis; 2011; $1,000
- VMY Chen; Kanematsu Memorial Award, Contribution of platelet apoptosis to thrombus formation in vivo; 2011; $20,000
- VMY Chen; Early Career Researcher Award, UNSW; 2011; $20,000
- VMY Chen; Silver Star UNSW award; Mechanism of thromboembolism in cancer; 2012; $20,000
- VMY Chen; IL Thompson Award, RACP; Platelet apoptosis and thrombus formation in vivo; 2012; $3,000

Grants
- VMY Chen (PI), E Hardeman, W Jessup, L Kritharides, S Thomas; Major Research Equipment and Infrastructure Initiative; Laser ablation, high speed, multichannel fluorescence intravital microscope; 2011; $300,000
- VMY Chen; Cancer Australia and Cure Cancer Project Grant; Thromboembolism in Cancer; 2012; $90,000
- VMY Chen; Haemophilia Foundation Australia Project Grant; Von Willebrand Factor lateralisation defects: a previously unidentified cause of bleeding; 2012; $20,000
- VMY Chen; Ramaciotti Establishment Grant; Mechanism of thromboembolism in cancer; 2012; $75,000
- NHMRC CJ Martin Overseas Biomedical Training Fellowship; 2008-2012; $407,391

Adult Cancer Program – Cure for Life Neuro-oncology Group

Awards
- McDonald KL; Cancer Institute NSW Career Development Award; 2010-2013

Grants
- McDonald (PI); Combining microRNA with cilengitide: A novel therapeutic approach to impede brain tumour cell migration; Cancer Institute NSW Career Development Fellowship; 2010-2013
- McDonald (PI); The role of IQGAP1 in actively migrating glioma cells and its regulation by miR-124; Cancer Council NSW Project Grant; 2009-2011
- McDonald (Co-PI); Clinical Outcomes and Genetic Epidemiology of High Grade Glioma; AGOG; Cancer Council NSW Strategic Partnership Grant; 2008-2012

Adult Cancer Program – Medical Epigenetics Group

Grants
- H Megan, M Kerrie, H Nicholas; Cancer Council NSW Project grant; 2012-2014; $311,000

Adult Cancer Program – Ovarian Cancer Group

Grants
- GO Research Fund, RHW Foundation; $65,000

Adult Cancer Program – Sarcoma Research Group

Awards

Grants
- Pfizer Investigator Initiative Research Grant for 2011-2012, $108,626
- Ross Trust Research Fund for 2011, $60,000
- Strategic Learning & Teaching Development Funding for 2011, $15,000
### Adult Cancer Program – Wnt Signalling & Metastasis Group

**Grants:**

- Cure Cancer Australia Grant #1008633; Targeting the Wnt signalling pathway – a new metastatic and epigenetic therapy for ovarian cancer; 2011; $90,000
- NHMRC Project Grant #630458; Wnt-5a signaling – a novel therapy for triple negative and Tamoxifen resistant breast cancer patients; 2010-2012; $318,750
- NHMRC CJ Martin Fellowship #466005; 2007-2011; $314,589

### Clinical Pharmacology & Toxicology Group

**Grants:**

- Buckley NA, Senanayake N, Isbister G, Dawson A, Karaliulde L, de Silva J; NHMRC Project Grant 1030069; Neurotoxicity after acute anticholinesterase pesticide poisoning and envenomation; 2012-2015; $970,970
- UNSW Major Research Equipment & Infrastructure Scheme – NHMRC, 2012

### Diving and Hyperbaric Medicine Group

**Grants:**

- UHMS Research Foundation; Sudden sensorineural hearing loss; $7,400
- Australian DHM Foundation; Sudden sensorineural hearing loss; $15,000

### Headache Research Group

**Awards:**

- Cheah B, Fulbright scholarship, Department of Biostatistics at Johns Hopkins Bloomberg School of Public Health; 2011

**Grants:**

- Ross Trust Research Fund, Strategic Learning & Teaching Development Funding; 2011-2013; $60,000

### Neuroscience Research Group

**Awards:**

- Ria Arnold was awarded the Novartis Award for the Best Free Communication at the Australian and New Zealand Association of Neurologists Clinical Neurophysiology Workshop
- Prof Matthew Kiernan was awarded the Paul Brock Fellowship for Cross Disciplinary Research in Neurological Conditions, from the NSW Office of Science and Medical Research
- Dr Susanna Park was awarded the RG Menzies Fellowship for ranking top applicant across Australia for the NHMRC CJ Martin Fellowship
- Dr William Huynh was selected for the Young Investigator Award at the Annual Scientific Meeting of the Australian and New Zealand Association of Neurologists for his work investigating brain plasticity in stroke patients
- Dr Michael Lee and Dr Cindy Lin were awarded the Brain Foundation Research Grant
- Natalie Kwa was awarded the Australian Postgraduate Travel Grant
- Ria Arnold was awarded the TOW Prize - Best Open Junior Oral Presentation
- Dr Michael Lee was awarded the Spinal Cord Injury Research Fellowship from the NSW Office of Science and Medical Research

**Grants:**

- National Health & Medical Research Council (NH&MRC) project grant 630440; 2011-2013; $444,411
- NH&MRC project grant 630425; 2011-2013; $244,250
- NH & MRC project grant 568743; 2010-2012; $571,175
- NH & MRC project grant 510233; 2009-2011; $297,250
- Motor Neurone Disease Research Institute Australia Grant; 2012; $81,000
- Brain Foundation Research Grant; 2011; $44,000
- Office for Science and Medical Research Grant; 2011; $300,000

### Psychosocial Research Group

**Awards:**

- Prof Carolyn Geczy S; 100 proteins: novel oxidant, scavengers in allergic inflammation; NHMRC Project 1027189; $488,675.00

### Pulmonary Inflammation Group

**Grants:**

- A/Prof S. Dharmage et al; What are the lifetime clinical predictors and risk factors for multiple phenotypes of adult Asthma, COPD and Sleep Disordered Breathing? Following up the TAHS cohort from 1st to 6th decade; NHMRC Project 1021275; $1,865,879.00

### Surgical Oncology Research Group

**Awards:**


**Grants:**

- Pfizer Investigator Initiative Research Grant; 2011-2012; $108,626
- Ross Trust Research Fund; 2011; $60,000
- Strategic Learning & Teaching Development Funding; 2011; $15,000
**Adult Cancer Program – Bioactive Lipid Signalling**

**Publications**


**Presentations**


**Adult Cancer Program Bioinformatics and Protein Mass Spectrometry Group**

**Publications**

Adult Cancer Program – Aetiology and Prevention Group

Publications


Presentations

- Vajdic CM, Olivier J, Park Y, Purdue MP. Number of siblings and site-specific cancer risk in two large prospective studies. *Australasian Epidemiology Association*, September 2011, Perth

Adult Cancer Program – Drug Development Group

Publications


Presentations

- Decollogne S, Ramsay EE, Joshi S, Hogg PJ and Dildia PJ. Tumour cell expression of y-glutamyl transpeptidase positively correlates with the anti-tumour efficacy of the metabolism inhibitor, GSAO. *Lorne Cancer Conference*, February 10-12th 2011, Lorne

Adult Cancer Program – Cure for Life Neuro-oncology

Publications


Adult Cancer Program – Medical Epigenetics Group

Publications

Adult Cancer Program: Ovarian Cancer Group

Publications


Adult Cancer Program – Sarcoma Research Group

Publications

- Pereira LA, Wong MS, Mossman AK, Sourris K, Janes ME, Knezevic K, Hirst CE, Lim SM, Pimanda JE, Stanley EG and Elefanty A. Pdgfra and Flk1 are direct target genes of Mxi1 in differentiating embryonic stem cells. *Stem Cell Research* 2012 (in press)

Clinical Pharmacological & Toxicology Group

Publications


Diving and Hyperbaric Medicine

Publications

• Bennett M. Hyperbaric oxygen therapy improved both pain scores and range of motion in patients with early idiopathic femoral head necrosis (Ficat stage II). *Diving and Hyperbaric Medicine* (2011) 41(2):105

**Headache Research Group**

**Publications**


**Neuroscience Research Group**

**Publications**


**Psychosocial Research Group**

**Publications**


**Pulmonary Inflammation Group**

**Publications**

- Ye X, Aziza S, Gomes S, Lancashire W, Thomas PS A case of vocal cord dysfunction with takotsubo cardiomyopathy: is there a link? *Chest Disease Reports* Accepted 22/7/11.

**Surgical Oncology Research Group**

**Publications**


**Conference abstracts**
