



Westmead Millennium Institute  
for Medical Research

ANNUAL REPORT 2009/10

LIFE CHANGING DISCOVERIES



# OUR DISCOVERIES TRANSLATING TO LIFE CHANGING OUTCOMES.

## COVER STORY

A skinny ten-year-old when diagnosed with type 1 diabetes, Stuart was put on insulin three times a day. A call came on Christmas Eve, a suitable set of islet cells had been isolated and his transplant would go ahead. The former bowling champ and father of three is no longer insulin dependent.



Image

Pancreas Islet cells

The Westmead Millennium Institute is one of the largest medical research institutes in Australia conducting research into a wide range of important human disorders affecting both adults and children.

Our research spans infectious and immune diseases; cancer and leukaemia; liver and metabolic diseases; eye and brain related disorders and heart and respiratory disorders.

Closely affiliated with both Westmead Hospital and the University of Sydney, our research

extends from the laboratory to the patient, using the basic tools of molecular and cell biology, genetic epidemiology, imaging technology and clinical research.

This 'Bench to Bedside' approach enables greater translation of research from biomedical discovery to the development of new prevention strategies, diagnostics and more effective treatments.

#### OVERVIEW

- 02 Chairman's Report
- 03 Director's Report
- 04 Research Highlights
- 06 Infection and Immunity
- 12 Cancer
- 16 Liver and Metabolic
- 18 Neuroscience and Vision
- 22 Cardio-respiratory
- 26 Advisory Board
- 27 Organisation Structure
- 28 Westmead Medical Research Foundation
- 29 Funding and Funding Organisations

#### RESEARCH REPORT

- 32 Infection and Immunity
- 42 Cancer
- 47 Liver and Metabolic
- 50 Neuroscience and Vision
- 53 Cardio-respiratory
- 55 Publications
- 68 Staff
- 72 Westmead Millennium Institute at a glance

# ADVISORY BOARD CHAIRMAN'S REPORT

Breakthroughs in medical research are the core of all new therapies, prevention strategies and clinical treatments. Benchmark research at Westmead Millennium Institute has always been focussed on research which will ultimately provide patients with a variety of conditions and disorders with a positive health outcome. This approach has helped build WMI's reputation as a medical research Institute of excellence and innovation.

To be successful modern medical research is dependant on collaboration, the sharing of knowledge and the passing on of information from one team of researchers to another. This year it has become more apparent that WMI's success is embedded in its ability to work collaboratively. Throughout the Institute a number of research disciplines have joined forces, linking conditions and disorders and working together to find a solution. This has produced some outstanding results.

The Institute received international acclaim for its work on genetics and the treatment of chronic hepatitis C, a transmittable virus which has a worldwide prevalence of nearly 300 million. Researchers from the immunology and allergy group joined WMI hepatitis C experts to lead an international team which discovered that there is a link between the interferon gene IL28B and the treatment of hep C.

Similarly, heart researchers, have worked with vision researchers on 'The Australian Heart and Eye Study' looking at whether the minute blood vessels at the back of our eyes can

warn doctors if patients could be at risk of cardiac problems in their future. Likewise virus and cancer researchers combine their efforts to unravel the mechanisms of cytomegalovirus and its deadly consequences for leukaemia patients.

As Chairman of the WMI Advisory Board I am delighted to commend the commitment of the scientists and staff of WMI. I know it is their work that continues to inspire my fellow board members.

This year the WMI Advisory Board worked closely with the WMI Executive, Sydney West Area Health Service and The University of Sydney on a number of issues affecting the growth of the Institute including the pursuit of additional funding for the new WMI building. Planning is well under way for an independent WMI with the Advisory Board assisting in the development of a Constitution and an independent structure for the new organisation. These plans were well on track and scheduled to be finalised by mid-2010. I would like to thank all the Advisory Board members for their positive contributions.

Finally I would like to congratulate Professor Tony Cunningham and his staff for their outstanding work throughout the year and wish them continued success. From this world-class team come life changing discoveries.

Mr Paul Bell

# DIRECTOR'S REPORT

The research productivity of the Institute continues to rise and this year the Institute was firmly ranked by the peak industry body Australian Association of Medical Research Institutes, as among Australia's top ten medical research institutes in terms of published output.

This year particular success was achieved by our kidney, liver and infectious diseases researchers. Each group secured several National Health and Medical Research grants, coupled with two enabling grants and an Australia Research Council grant. During the year, the Institute's research outcomes were published in more than four hundred papers. Several of our researchers were recipients of the year's 'Premier's Awards for Outstanding Cancer Research' including Dr Rosemary Balleine the Translational Oncology group leader who was awarded a Clinical Research Fellowship aimed at strengthening and supporting clinical research in hospitals. At the same time Dr Liang Qiao from the Storr Liver Unit received a Development and Support Fellowship of Future Research Leaders and his colleague Dr Sarah Walker was awarded a Research Scholar which supports outstanding students. In one of our collaborative projects Associate Professor Graham Mann accepted the award for Excellence in Translational Cancer Research on behalf of Sydney Melanoma Unit and the Westmead Millennium Institute for groundbreaking and internationally recognised research into melanoma and translating their findings into clinical practice.

These outcomes have helped us to continue to attract and retain of the best researchers and scientists, who wish to be a part of a top-class research environment. It has also led to an increase in the number of PhD students. Consequently we continue to grow as an Institute physically, academically and scientifically.

Unfortunately we remained scattered around several locations on the Westmead campus with scientists and researchers working in cramped and over-crowded conditions.

However plans and most of the funding for our new building are underway with strong support and leadership from the NSW Government and also the University of Sydney. The Minister for Science and Medical Research, the Hon. Jodi McKay continued to support our work and the NSW Premier, the Hon Nathan Rees pledged \$30 million toward our building. The building site was designated as a site of State significance. A Project Director has already been appointed and planning is well under way. The building will also house the Westmead Research Hub high technology centres in genomics, proteomics, cell imaging and flow cytometry. This will ultimately bring benefit to the whole of Western Sydney, one of the fastest growing regions in Australia.

A major development for WMI has been the implementation of the NSW Government Wiltshire report recommending WMI move to independent governance. Our Board will include nominees of our major partners, Sydney West Area Health Service/Westmead Hospital and the University of Sydney (see Chairman's report).

All this has been achieved through the work of a dedicated team of scientists and supporters. I would like to thank both Paul Bell and our Advisory Board members, and Pat Wilde, President of the Westmead Medical Research Foundation, for their continuous support throughout the year. Without their efforts and dedication much of our achievements would not have been possible. Likewise I would like to extend my thanks to the members of both Boards, all of whom contribute to our work in a voluntary capacity.

Finally to my colleagues at WMI, congratulations on a very successful year. It is your efforts that bring the accolades to the Institute. I look forward to working with you all in the coming year as we focus on research outcomes that will bring better health care to all.

Professor Tony Cunningham

### INFECTION AND IMMUNITY

An international team of scientists led by molecular geneticist Dr David Booth and hepatitis C expert, Professor Jacob George identified a variant in the interferon gene IL28B, linking it with the treatment of chronic hepatitis C virus. The team examined the genomes of more than 800 individuals (including 300 Australians) receiving treatment for chronic HCV. Results of the study published in the Nature Genetics article "IL28B is associated with response to chronic hepatitis C interferon-and ribavirin therapy" reported that IL28B encodes an interferon-lambda that is involved with suppression of viruses including HCV.

The Centre for Virus Research has previously discovered HIV enters the female genital tract using host cells known as dendritic cells and has in the past 12 months been continuing to unravel how the virus alters the function of these critical cells which can start an immune response to the virus. Although there has been little success in developing traditional injection vaccines against the virus, researchers are looking at a mucosal vaccine under the principle that when used in the female genital tract it

would provide greater protection rather than just systemic immunity alone. In December 2009, Professor Tony Cunningham presented a paper at an international conference for the Gates Foundation on this work, and how it could make dramatic inroads into treating the disease in places like Africa, Asia, New Guinea and India.

### CANCER

Several of our cancer researchers were among those to receive accolades at the 'Premier's Awards for Outstanding Cancer Research'. Dr Rosemary Balleine, Translational Oncology group leader, was awarded a Clinical Research Fellowship aimed at strengthening and supporting clinical research in hospitals for her project 'Molecular grade as prognostic indicator in invasive breast cancer'.

Associate Professor Graham Mann accepted the award for 'Excellence in Translational Cancer Research: on behalf of Sydney Melanoma Unit' and the Westmead Institute for Cancer research for their groundbreaking and internationally recognised research into melanoma and translating their findings into clinical practice. A/Prof Mann's melanoma research team are primary collaborators with the Sydney Melanoma Unit.

The Breast Cancer Tissue Bank was awarded a prestigious Cancer Institute of NSW Infrastructure Grant to assist with the collection, entry and auditing of clinical, pathology and specimen data, as well as data management solutions. The Breast Cancer Tissue Bank was established three years ago to collect and distribute specimens and information to breast cancer research projects.

#### LIVER AND METABOLIC

Also recipients of 'a Premier's Awards for Outstanding Cancer Research' were Dr Liang Qiao, of the Storr Liver Unit who received a Development and Support Fellowship of Future Research Leaders for her research work using notch signalling to identify and characterise liver cancer stem cells and Dr Sarah Walker who received an Research Scholar supporting outstanding students enrolled in a higher degree. Dr Walker is investigating the role of adiponectin in hepatocellular carcinoma (liver cancer)

#### NEUROSCIENCE AND VISION

iSPOT-D the first study to look at brain and gene measures as well as clinical information to identify these objective 'markers' for predicting treatment response is now close to 50

per cent complete and on track for completion in 2011. There are no objective tests or 'markers' that help doctors to reliably recommend the right treatment for the right person at the right time.

As part of the Blue Mountains Eye study – one of the largest eye disease studies in the world – a 15-year follow up of participants has just been completed, and from this researchers at the Vision Centre have been able to positively link eye disease not just with hearing loss, but also microvascular disease in the kidneys.

#### CARDIO-RESPIRATORY

This year Associate Professor John Wheatley was also awarded an NHMRC Practitioner Fellowship to support the centre's research, the first one to be awarded to a researcher at the Westmead Millennium Institute.

The Centre for Heart Research in collaboration with the Centre for Vision researchers commenced a world-first study investigating whether tiny blood vessels in the eyes can be used as predictors of cardiac problems.

The work of the Infection and Immunity division covers a diverse range of pathogens and infectious diseases, autoimmunity and other immune disorders as well as oral infection and progressive renal diseases and transplantation.

### THE CENTRE FOR TRANSPLANT AND RENAL RESEARCH

For a diabetic, being able to control your disease without daily injections sounds like a fairytale. But research by the Centre for Transplant and Renal Research is proving that it is indeed a future possibility. The centre's research into transplanting pancreatic islet cells into insulin dependent Type 1 diabetes sufferers is progressing with 12 patients so far undergoing the procedure.

Transplanting donor pancreatic islet cells allows patients to produce their own insulin. The transplanted islet cells are isolated in the laboratory and then run into the patient's portal vein so they will lodge in the liver. This procedure is done around three times to optimise the outcome. So far, the majority of patients who have undergone the procedure no longer have hypoglycemic episodes, improving their quality of life. The patients in the study have suffered from Type 1 diabetes for more than 25 years and many could not detect when their sugars were low, however, with the transplant they have been able to enjoy a quality of life most people take for granted such as not having to stick to a regimented eating routine. The islet cells are harvested from organ donors and the centre can realistically only complete three or four transplants per year presently, but they are working on ways to improve the efficiency of the isolation process so that more patients can be transplanted and more patients are free of insulin injections.

In a related study, the centre is also conducting collaborative research with the Storr Liver Unit to study what effect transplantation of insulin producing cells has on the liver of islet transplant recipients. When the insulin producing cells or islets are infused into the portal vein they lodge in the liver. This means that the adjacent liver cells are exposed to relatively high concentrations of insulin which may have detrimental effects. By conducting biopsies on the livers of patients who have undergone the procedure the transplant centre and the Storr Liver Unit is ascertaining the long term affect this may have on the organ. In 2009, as part of the research program to improve transplant outcomes, Dr Toshi Akima from the

centre had a paper published in the American Journal of Transplantation about his work in trying to identify new therapeutic options to prevent the early islet destruction that occurs in the initial transplant period. His study used two new anti-coagulant agents to get better protection of transplanted islet cells. He found that the combination of these two agents had better results at preventing the clotting reaction that occurs when those cells were exposed to blood.

To overcome the lack of donors for possible islet transplantation, the unit is also working with international research centres on developing a genetically modified pig from which islets can be harvested.

In association with their collaborators in Melbourne and South Australia, researchers are hoping to genetically modify pigs so the islet cells are accepted by the patient's own immune system into thinking they are human. So far the research has been ongoing for more than 20 years and presently has reached the stage where researchers are testing various genetic modifications. They have already identified that two of the changes they have successfully made in the genetically modified pig have made a big difference in the immediate islet destruction. The next strategy is to produce islets in the pig that can secrete their own immunosuppressant molecule to eliminate the need for patients to be on a lifetime regime of anti-rejection drugs.

Concurrently researchers are also taking part in a large National Institutes of Health-funded study looking at genomics, and specifically the genetic control that leads to chronic graft loss in kidney transplants.

Using protocol renal transplant biopsies researchers are investigating tens of thousands of genes at one time, and in collaboration with researchers at the Mount Sinai Medical Centre in New York and others in the US are collecting large numbers of patients to understand the causes to chronic graft loss in the hope of designing treatment to prevent it. It is the largest collection of such patients in the world and all the collected data is hoped to be finalized next year.

#### HIGHLIGHTS

- Groundbreaking work to improve treatment for herpes simplex 1 and 2 continues with researchers identifying three components for a novel vaccine.
- Scientists have identified a number of molecular targets within fungus-specific secretion pathways that may constitute new drug targets.
- Dental researchers have shown that individuals with certain blood groups may be more prone to infection from damaging oral bacterium.

### CENTRE FOR INFECTIOUS DISEASES AND MICROBIOLOGY

Discovering which patients admitted to intensive care units are at highest risk of the serious fungal infection, invasive candidiasis, could save hospitals hundreds of thousands of dollars per year in resources and time. Invasive candidiasis is caused by a yeast (fungus) called *Candida*, which infects the bloodstream and then other parts of the body such as the kidney, eyes or heart.

Researchers have seven hospitals involved in a study, and around 5000 patients enrolled, to develop a model to predict the level of risk patients have for developing invasive candidiasis.

Researchers are hoping to use the predictive model to improve outcomes for patients by assisting health professionals select the best treatment strategy if infection is found while at the same time saving resources used for constant checking of patients for the fungus or treating those not actually infected.

The risk predictive model will be developed from clinical information and colonization data collected 72 hours after admission to ICU and twice weekly thereafter. In a sub-study being conducted by PhD student, Anna Lau, standard culture

Researchers have shown that the hydrolytic enzyme phospholipase B1 is one of the specialised proteins that help maintain the structure of the cell wall in the fungus *Cryptococcus neoformans*. They are using this information to synthesize better antifungal drugs.



DR XIAO MING ZUO

Image  
*Cryptococcus neoformans* cells

and a new molecular rapid method (multiplex tandem PCR) for detection of *Candida* will identify how heavily and how soon patients coming into an ICU become colonised with *Candida* and whether MT-PCR is more cost-effective than culture.

Initial accrual of patients will be complete in December 2010, when the data will be analysed and the model developed. A subsequent validation study will be conducted to see if the new model holds true. If it does, the team will be able to then initiate clinical trials of different treatment strategies – preemptive (patient does not have symptoms of candidiasis but there is evidence of occult infection), empiric (patient has symptoms of infection but no evidence of candidiasis) and prophylaxis (patient is at high risk, but has no evidence of occult or symptomatic infection).

New classes of antifungal drugs are urgently needed to combat serious fungal infections which are increasing in prevalence due to the increase in immunocompromised individuals. Research in Dr Julie Djordjevic's fungal pathogenesis laboratory has three objectives: identification of novel molecular targets for antifungal drug development, delineating at the molecular level, the mode of action of miltefosine a compound which is structurally related to the membrane phospholipid, phosphatidyl choline, and using this information to synthesize and patent new, better antifungal drugs.

Miltefosine is used to treat patients with a serious parasite infection (leishmaniasis) in developing countries, and WMI found that it has antifungal activity when tested in the laboratory.

Dr Katrina Joliffe from the Sydney University chemistry faculty, working with the infectious diseases researcher, has synthesized a number of compounds structurally related to Miltefosine. By testing their antifungal activity we are now beginning to understand which regions in miltefosine are important for antifungal potency. Some of these structural variants of miltefosine have similar or stronger antifungal

potency than the parent compound. Preliminary toxicity testing of the most promising analogues against mammalian cells is underway.

In collaboration with US and UK colleagues, researchers have identified a number of molecular targets within fungus-specific secretion pathways that may constitute new drug targets. In addition, Dr Djordjevic's group has shown that miltefosine is rapidly taken up by fungal cells. It interacts with the mitochondria, (the energy powerhouse of all living cells) and induces a type of programmed cell death called apoptosis.

Meningitis caused by infection by another fungus, *Cryptococcus neoformans*, is common in patients with AIDS especially in developing countries, and infection due to a second species, *Cryptococcus gattii*, though less common, is endemic in Australia and certain other countries. Professor Sorrell, A/Professor Sharon Chen and A/Professor Wieland Meyer this year initiated a collaborative study with colleagues in Vancouver to compare brain infection due to *C. gattii* in both countries. In Australia the red gum species of eucalypt appear to harbour the fungus, which causes disease following inhalation. The researchers are hoping to clarify whether neurological infection due to this species has different

Image  
Nucleus of HIV cell



DR. MIN KIM

clinical features than already known species to help design better treatment strategies for those who may get infected. Although only about 60 patients a year in Australia develop serious disease due to *C. gattii*, by correlating its clinical features and response to therapy with fungal genetic markers, researchers in both countries are hoping to discover key fungal determinants, as well as if there is a mechanism that prevents people becoming ill if they are exposed to the fungus. The relatively low number of infections in humans, suggests that their predisposition to meningitis or resistance to contracting the disease is inherited.

In related research Associate Professor Wieland Meyer is using new molecular methods to distinguish between species and molecular types in the *Cryptococcus* complex to determine whether there are more species than are currently designated and if so, how these species evolved and the clinical significance of each.

### CENTRE FOR VIRUS RESEARCH

Discovering the ways in which vaccines stimulate immune response will lead to more advanced ways to prevent some of the world's most common viral infections.

The Centre for Virus Research has been undertaking studies into this for nearly 20 years and has been opening the doors to understanding viral infection and vaccine response that will help some of the world's most underprivileged populations.

HIV is still one of the globe's most significant causes of death and disease. Our scientists are conducting world-leading research into a mucosal vaccine that could make dramatic inroads into treating the virus.

The centre is continuing on its groundbreaking research into finding a way to improve the current vaccine for Herpes Simplex virus, of which there are two types. HSV-1 is the major cause of oral herpes and HSV-2 causes genital herpes.

Although a herpes vaccine already exists, researchers at the centre are working on formulating an even better one that can stimulate a much stronger immune response. They are working on three components of the vaccine, two of which have proved successful. The third and final component is still under investigation, and when it too has been investigated and trialled successfully, the study team can move onto working out the best way to combine the three components to create a much more powerful vaccine.

Work is also progressing into another Herpes virus – herpes zoster, which causes Shingles, an infection predominantly found in older people. One of the effects of shingles is persistent neuralgic pain on the nerve ends affected by the virus, which can last for up to five months in some patients.

An early stage vaccine, a modification of the chicken pox vaccine, is already being tested and proving to be successful in a percentage of cases, but researchers led by Dr Allison Abendroth are working on trying to discover a way to improve this vaccine by looking at immune response to the infection. To do this they are taking a novel approach by looking at the nerve cells that are affected by the virus on patients who have died with Shingles. From this, researchers have been able to define the types of immune cells that infiltrate the ganglia – or nerve ends - adjacent to the spinal cord and relate those immune

cells to virus infection. They have also been able to isolate time points to see the sequence of this infiltration. They suspect that the immunity of people who don't get associated neuralgic pain is different to those that do, and from that hope to discover a way to stimulate the right type of immunity through a vaccine to eliminate neuralgic episodes.

HIV is still one of the most significant causes of death and disease in the developing world and the Centre for Virus Research has been leading the world in studies of the virus, most specifically in trying to develop a cream that can be used to stop or inhibit the transfer of the disease through women.

The Centre has previously discovered HIV enters the female genital tract using host cells known as dendritic cells and has in the past 12 months been continuing to unravel how the virus alters the function of these critical cells which can start an immune response to the virus. Although there has been little success in developing traditional injection vaccines against the virus, researchers are looking at a mucosal vaccine under the principal that when used in the female genital tract it would provide greater protection rather than just systemic immunity alone.

In December 2009, Professor Tony Cunningham presented a paper at an international conference for the Gates Foundation on this work, and how it could make dramatic inroads into treating the disease in places like Africa, Asia, New Guinea and India.

In other studies into HIV, the centre is working on understanding how vaccines infiltrate cells using the Vaccinia Virus, a strand of the Small Pox vaccine. What they are trying to determine is how the Vaccinia virus is able to use the proteins of other viruses to induce an immune response when used in hybrid vaccines. This is more common in adult and adolescent vaccinations and the researchers are trying firstly to discover

how the body controls infections like HIV and Herpes virus and once having determined that to improve the current vaccines on the market. In the past vaccines have used only viral proteins in a hybrid mix, but scientists now have adjuvants - an agent that may stimulate the immune system and increase the response to a vaccine. The theory is that by using adjuvants to direct immune response they will be able to learn more about immunology and refine existing vaccines.

#### INSTITUTE FOR IMMUNOLOGY AND ALLERGY RESEARCH

A simple injection of modified T cells – the cells that help fight disease, but that can also cause autoimmune diseases – could help Multiple Sclerosis sufferers manage their disease, if not present a cure in the not too distant future. Following on from the research the institute has done in previous years, in isolating the genes that cause MS, the team at the Institute for Immunology and Allergy Research are now working at discovering what it calls the 'Holy Grail' of autoimmune disorders - trying to grow specialised T cells in a laboratory setting that may be used to help treat a wide range of autoimmune disorders, including MS.

Until 2007 only one gene had been linked to MS – now there are about 20, and the research centre was instrumental in helping to undertake the genome-wide studies of the disease that made these discoveries. Previously, using different techniques, they had discovered that the IL7 receptor was associated with MS, which was later confirmed in the genomic studies. They have since been trying to establish why this gene is associated with MS. In January 2010 the team will have a paper published in the Journal of Immunology about the likely basis for the IL7R association with disease. They identified that the most likely role was in its generation of protective T cells.

With the number of known genes associated with MS increasing, the immunology research team is now working to

find the links between them and test whether the information can be used to generate T cells that might be useful in therapy. Using information it is also gathering from researching the MS treatment drug interferon beta, the team is hoping to culture cells in a laboratory setting in the hope of generating protective T cells that can work to wipe out the rogue cells causing the disease. The aim of the research is to find a way to use these special T cells therapeutically.

If the team can devise a way to create these T cells artificially using novel molecules and strategies, it could lead to not just a treatment for MS, but to many other autoimmune disorders like arthritis, motor neuron disease and Parkinson's Disease.

#### INSTITUTE OF DENTAL RESEARCH

New research from the Dental Research Centre has found that individuals with certain blood groups may be more prone to infection from a bacterium known to cause soft tissue and bone damage in the mouth.

The pathogenic bacterium *Porphyromonas gingivalis*, which is one of the major causes of destructive disease of the soft tissues and bone that support the teeth, has also been linked to the development of fatty changes in blood vessels and to autoimmunity where the immune system attacks the tissues.

The centre has been trying to understand how the organism causes disease, who may be susceptible to its infection and how to eliminate it. So far researchers have found that one of the major disease causing properties of *P. gingivalis* are surface located gingipains - powerful enzymes that also contain adhesion domains which help the bacteria latch on

to molecules and surfaces. But what the bacteria also needs to flourish is the capacity to obtain the haemoglobin pigment, haem, from blood.

Working with the Schools of Molecular Biosciences and Chemistry at the University of Sydney, the group has unravelled the crystal structures of the adhesin domains of the gingipains which they found were surprisingly similar to adhesion molecules that determine tissue integrity in humans. Their analysis also discovered the precise structure of a blood group binding region which could explain why people with blood group A are infected by all strains of *P. gingivalis* while those with blood Group O are only infected by a limited number of strains.

Ultimately the discovery explains why even by sharing things like toothbrushes or drink bottles, not everyone in one family will be infected by this microbe. Using the information they learned about the haem binding properties of the microbe, researchers have also been able to design effective anti-microbial drugs by creating a library of synthesised modified haem molecules linked to antibiotic. These are selectively taken up by *P. gingivalis* as a 'Trojan horse', that is the organism is tricked into taking up a toxic antibiotic by the gift of a blood component. This concentrates the anti-microbial leading to highly efficient control of *P. gingivalis*.

DIVISION

## CANCER

OVERVIEW

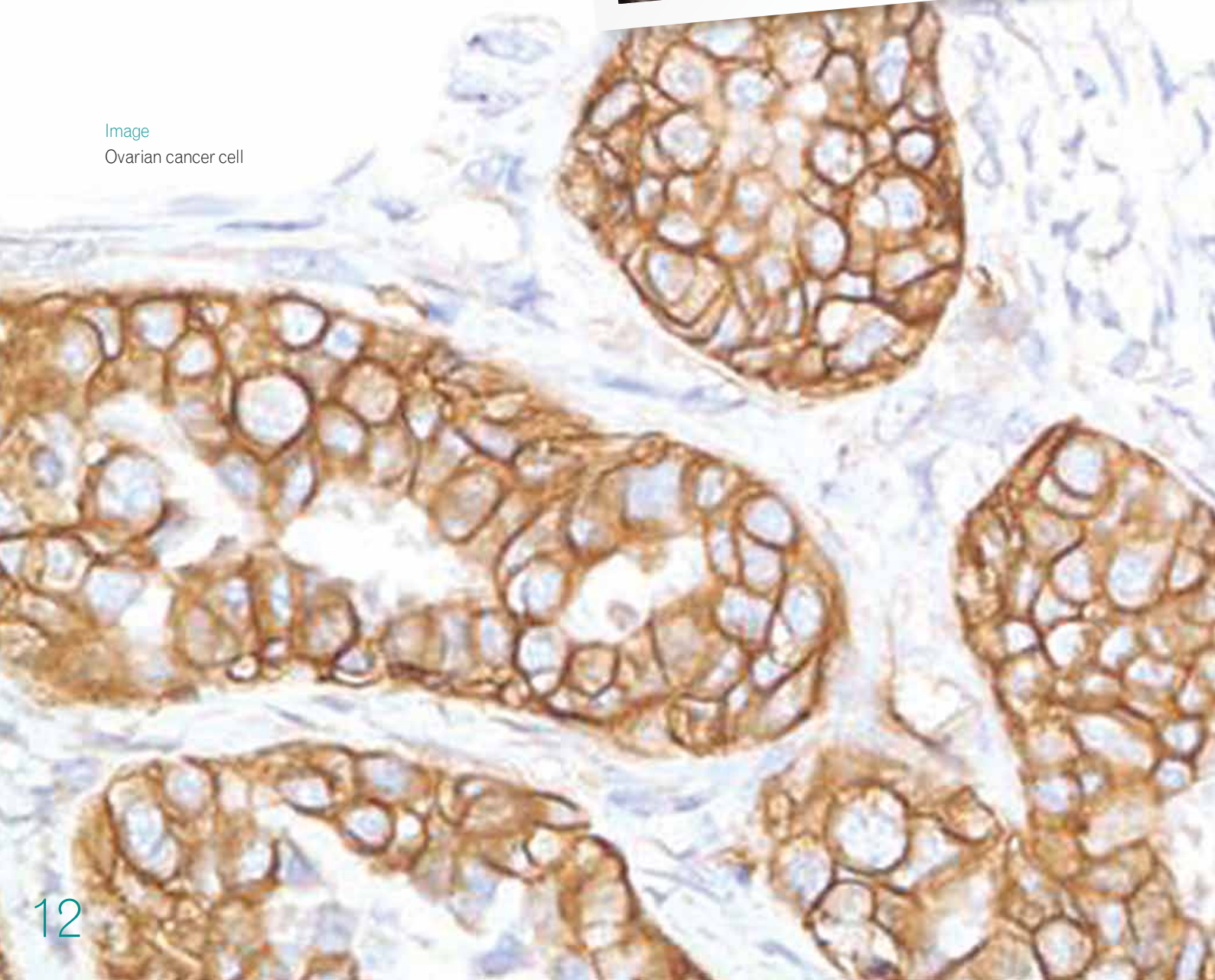
The Cancer division's groundbreaking research is aimed at improving prevention and treatment strategies and establishing cures for cancers common to many Australians.

A bubbly fifty-seven year-old Rhonda was diagnosed with early stage ovarian cancer last year. Her family history of cancer prompted her to enrol in the Deep C study. Previously our researchers have identified different genetic make-ups and now are investigating how various genotypes process drug therapies differently.



Image

Ovarian cancer cell



#### HIGHLIGHTS

- Researchers have now identified various molecules that can be targeted in treatment by looking at genomes associated with tumours.
- A more accurate methodology for functional screening of the mutant melanoma p16NK4a gene has been designed.
- Researchers have identified a molecule – the SDF-1 molecule, critical in the treatment of ALL patients.

## WESTMEAD INSTITUTE FOR CANCER RESEARCH

Researchers at the Westmead Institute for Cancer Research are now testing a new drug that could stop the growth of melanoma and save thousands of lives.

Scientists and researchers in the centre's melanoma program have made a number of significant breakthroughs in the past 12 months in the development of targeted therapy in the treatment of melanoma. In collaboration with the Melanoma Institute of Australia, the team is at the forefront of clinical trials of new drugs that can stop a critical pathway in the growth of melanoma tumours. Scientists identified the MAP kinase pathway which appears to be critical in the growth of metastatic melanoma. They have discovered that if this pathway is blocked with selected inhibitors it can shut down the tumour which then subsequently dies with very few side effects.

The research is now in the first phase of clinical trials for a new drug that can inhibit this MAP kinase pathway and the team will be presenting their findings at the international American Society of Clinical Oncology conference in June. They are also

now doing phase two and three clinical trials of a different inhibitor - PLX 4032 - which acts in a very select way to stop a different critical pathway essential for the growth of melanoma tumours.

The Melanoma Program has also identified a new melanoma gene - WMCR 0 - which was identified as part of one of the largest studies in melanoma in the world involving looking into the risk factors in developing the cancer. Blood samples taken from people who did not have melanoma were used in two major gene studies that identified several genes that make a large contribution to the risk of melanoma. Researchers have found that these genes seem to be involved in skin pigmentation. The study used the blood samples to then compare 300,000 genetic markers of people with melanoma and those without tumours. The study is an international collaboration involving the Australian Melanoma Family Studies and the GenoMEL consortium which has researchers in 15 countries.

Together the melanoma targeted therapy and the identification of the new melanoma genes have been important components in success of the WICR team lead by Professor Rick Kefford and have been awarded a \$12.6 million NHMRC grant which will start in 2011 – the largest NHMRC grant awarded to the University of Sydney. The studies were also reported in the Journal of Nature Genetics in 2008 and 2009 highlighting the contributions WICR researchers are making to melanoma research around the world. The team was also recognized for its work with the 2009 Premier's Excellence Award in Translation Research.

In further research into melanoma, the Cell Cycle Research Group led by Dr Helen Rizos has made critical advances after investigating claims that a specific molecule acted as a suppressor in melanoma.

A paper published in 2008 pinpointed a molecule – IGFBP7 – which allegedly initiated a cascade of responses to stop damaged melanocytes from developing into melanoma. The Cell Cycle Research Group, as part of its work, double checked the findings in this paper to ensure it was also on the right track with its own research. But what this team found was that the IGFBP7 molecule was not in fact the key in the process of stopping the growth of cancer cells. The impact of its own research has implications for other studies around the world by ensuring that work investigating the key molecules and pathways that limit melanoma proliferation continues. These vital molecules may prove to be important therapeutic targets in the treatment of melanoma.

The group was also instrumental in formulating a standardised test for genetic screening of mutant p16INK4a genes and is hopeful that it will be instituted internationally to ensure patients who undergo screening are given consistent and accurate information. Generally mutant or faulty genes can occur in families and genetic testing for certain diseases is becoming more frequent. The Cell Cycle Research Group has designed a standardized methodology for the functional screening of p16INK4a which is not only more accurate, but simpler than those previously used. It also means that data retrieved from screening using this method is more reliable and thus easier for genetic counsellors to understand and disseminate to clients.

Work has also continued on breast cancer and the role ovarian hormones play in the development of the cancer. After discovering in 2008 that progesterone increases the rate of growth of the cell type in the breast that gives rise to breast cancer, research is now focusing on finding out why.

Although it has been known for some time that ovarian hormones are responsible for driving breast cancer, the way in which they work has not been well understood and the research team, headed by Professor Christine Clarke, is now working to understand how hormones can control the activities of the normal breast cell. A worldwide study group called the Women's Health Initiative identified women who had taken Hormone Replacement Therapy that contained synthetic progesterone had an increased risk of breast cancer, compared to those who were using HRT containing only estrogens. That discovery identified progesterone as a major participant in the increased breast cancer risk that occurred when women were taking hormones and pointed to a natural link between the natural hormone and breast cancer associated with the normal hormonal cycle. It also led to the hypothesis that women who don't have children or start their menstrual cycle early and finish it late in life have an increased risk of breast cancer. The breast cancer research group is working under the premise that the ovarian hormones are not causing breast cancer but somehow facilitating the growth or survival of cells that have received a carcinogenic hit. What they are now trying to determine using a model that closely resembles a normal breast, is the initial factor that triggers a cell onto road to becoming cancerous. The research is taking a different route than previous studies by using healthy breast tissue and exposing it to the normal hormonal cycle to try and identify points of vulnerability and determine how ovarian hormones are stimulating the growth of cancerous cells.

The Leukaemia Cell Therapy Group has made significant progress in improving the current treatment for children and adults with Acute Aplastic Leukaemia (ALL). This is the most common childhood cancer and although 80 per cent of children who contract the disease can be cured with chemotherapy about 20 per cent of those relapse and the survival rate for those patients is poor. Scientists have been working at identifying what it is that actually stops the current treatment working for all ALL patients and have identified a molecule – the SDF-1 molecule – which seems to promote the survival and growth of ALL cells by activating an enzyme called mTOR. Animal models show there is a drug – EVEROLOMUS - which can inhibit mTOR enzymes and slows the growth of ALL cells, increasing the chances of patient survival. Clinical trials in adult patients who have relapsed with ALL are underway and the translational benefit is that researchers and their clinical colleagues hope the addition of EVEROLOMUS to current treatment regimes will improve outcomes for ALL patients. The trials will also help them to understand why some patients develop a resistance to chemotherapy treatment.

The Gynaecological Oncology Research Group has been investigating why some women who have ovarian cancer respond well to chemotherapy while others don't by looking at the genetic and molecular features of ovarian cancer tumours. The five-year survival rate for patients with ovarian cancer is only about 40 per cent and researchers have now identified various molecules that can be targeted in treatment by looking at the genomes associated with the tumours to see if there are any missing or amplified parts – in other words, to see if patients have gained or lost part of the genome responsible for the tumour. So far they have discovered there is a critical

gene involved in the growth of the tumours and that when it is amplified – or has multiplied – those patients did not respond well to chemotherapy. The team is continuing to investigate the mechanism and translate that knowledge into better treatment outcomes for patients. By identifying which patients have this particular gene, doctors will be able to predict who will respond best to certain treatments. The team has also had a paper on its work published in the prestigious New England Journal of Medicine as part of their participation in an international collaboration to identify the driver mutation of a particular rare type of ovarian tumour.

The Familial Cancer Research Group has this year been continuing its work on identifying women at risk of developing cancer due to genetic predisposition. After identifying patients with a predisposition to familial cancer, the team has enrolled patients in a genetic epidemiology study and as part of this work have identified that males who have a genetic predisposition to breast cancer are also at an increased risk of developing prostate cancer. The study is being conducted in collaboration with IMPACT and is looking at whether screening for prostate cancer would be beneficial for men who have been identified with this particular genetic predisposition. The preliminary results of the study will be published this year in British Journal of Urology.

This division explores causes of liver injury, such as viruses and toxins and metabolic factors. The long term goal of the division is to improve outcomes for patients with chronic liver diseases by reducing liver injury and fibrosis and to prevent liver cancer.

### STORR LIVER UNIT

It is a well known fact that hepatitis C can predispose patients to Type 2 diabetes but until this year, the reason why, was a mystery. The Storr Liver Unit, in conjunction with its collaborators, have recently published a paper in the prestigious US journal Gastroenterology that unravelled the mystery and will hopefully lead to preventative treatment for hep C patients.

Hepatitis C is a blood-borne virus and in Australia is caused mainly by injecting drug use, but also by unsterile tattooing or body piercing. There is no vaccine for hepatitis C, unlike hepatitis A and B. Around 212,000 Australians suffer from chronic hepatitis C and there are about 10,000 new infections each year.

The Storr Liver Unit and the Garvan Institute studied 29 people with hepatitis C, and found that these patients have a high level of insulin resistance, a precursor to diabetes. However, what was unusual was that almost all the insulin resistance occurs in muscle, with little or none in the liver - a very surprising finding given that hepatitis C is a liver disease. In the study, researchers gave patients intravenous glucose, a specific

stimulus to insulin secretion, and showed insulin secretion was not impaired in hepatitis C patients. The results show people with hepatitis C who develop diabetes probably have susceptible insulin-producing cells, and would more than likely develop Type 2 diabetes anyway, albeit much later. Although more work needs to be done into why hepatitis C causes insulin resistance in muscle, the study gives researchers a better insight into the behaviour of the disease and is helpful for people with hepatitis C who may have relatives with Type 2 diabetes and therefore are at risk themselves.

The Storr Liver Unit has also had a major paper published in Nature Genetics that identified IL28B polymorphisms as predicting treatment responses in hepatitis C.

This has been a major milestone in hepatitis C research and a diagnostic test to predict treatment response based on this gene is being developed.

Continuing its cutting edge research into non-alcoholic fatty liver (NAFLD) disease and liver cancer, the unit is working to develop a way to earlier predict the occurrence of the disease. NAFLD is a growing problem with Australia's, and the world's, increasing obesity epidemic, and can range from a mild 'fatty

Researchers are developing uniform liver cancer treatment guidelines and are looking at the outcome of patients with liver cancer. The B-Positive project, aims to treat chronic hepatitis B infection with the goal of reducing the risk of developing liver cancer. Screening is now underway of more than 1000 patients.



RESEARCHERS KENNY IP  
AND GEORGE WILSON

#### HIGHLIGHTS

- In milestone research, hepatitis C scientists identified IL28B polymorphisms as predictor of treatment responses in the disorder.
- Liver fibrosis studies found that adiponectin inhibited wound healing, but the application of anti-TIMP-1 antibodies hastened recovery.
- Researchers are now in the process of recruiting patients for a serum bank aimed at developing early biomarkers of liver cancer.

liver' to inflammation of the liver which can destroy liver cells and cause scar tissue that can lead to cirrhosis and even liver cancer. Researchers had already found by studying a group of adolescents that overweight girls had a more than double chance of developing NAFLD and that 40 per cent of obese boys had the condition.

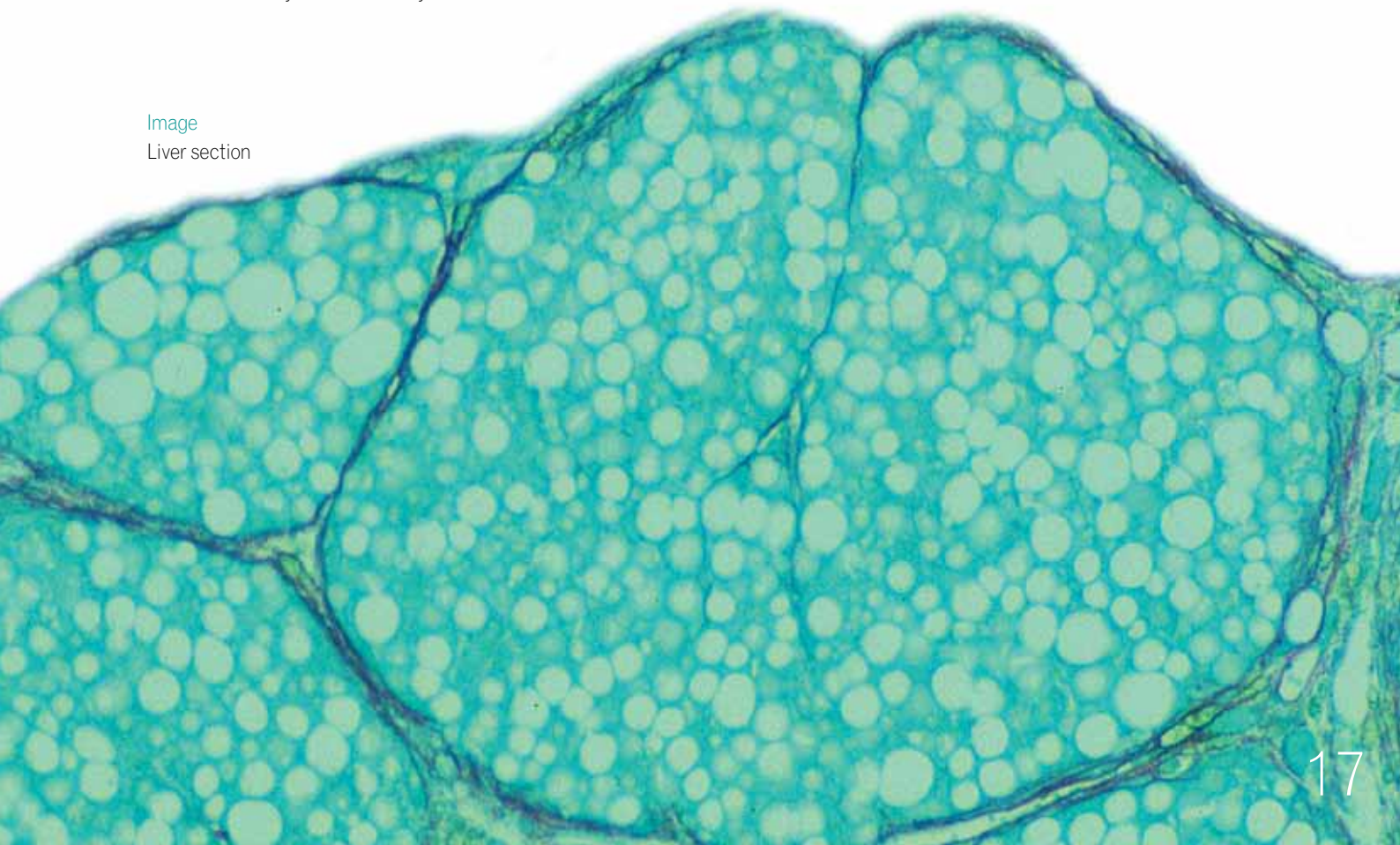
In the next phase of this study, the unit's researchers have now determined the normal range of certain liver enzymes that can make it easier to predict who may have the condition. The challenge scientists now face, and on which researchers at the unit are working, is to translate these findings into clinical practice at the primary care level, in the hope they can help doctors to reduce the long-term liver complications, cardiovascular and diabetic risks associated with NAFLD.

Researchers are now in the process of recruiting patients for a serum bank to ultimately develop early biomarkers of liver cancer in a study it started last year in association with the

NSW Cancer Council. The surveillance program (that now has 650 patients with advanced liver disease) will be able to determine the costs and benefits of liver cancer screening in the era of potent anti-viral therapies.

Scientists are also in the process of developing uniform liver cancer treatment guidelines and are looking at the outcome of patients with liver cancer. The B-Positive project, another study being completed in association with the NSW Cancer Council, has also moved forward in the past 12 months. The project hopes to treat chronic hepatitis B infection in the hope of reducing the risk of developing liver cancer. Screening is underway now of more than 1000 patients using ultrasound and blood tests, and the unit is at the same time working on developing a desktop management tool to allow GPs to optimise their management of patients with hepatitis B including treatment and cancer surveillance.

Image  
Liver section



The Neuroscience and Vision division focuses on the causes of emotional disorders, mental illness and visual disorders, using a combination of imaging technology, molecular biology and epidemiology.

### THE BRAIN DYNAMICS CENTRE

Depression accounts for 27.8 per cent of all mental health disability adjusted life years (DALYs) and in Australia there is a staggering loss of \$4.3 billion in lost productivity each year due to depression. So the research being conducted by the Brain Dynamics Centre on antidepressant medication has far reaching implications not just for the health of those suffering from depression but for all sectors of the community.

The iSPOT-D study, which was started last year, is a world first and is being done simultaneously in Australia, the USA, Europe, and South Africa.

Important landmark studies so far have shown that antidepressant medications are effective, but they are currently selected on a trial-by-trial approach. There are no objective tests or 'markers' that help doctors to reliably recommend the right treatment for the right person at the right time.

This means only about 50 per cent of patients show improved symptoms after taking antidepressant medications and only about one in three will achieve remission (virtual absence of symptoms) within the first eight weeks of treatment.

Image

Brain neurons

#### HIGHLIGHTS

- Brain dynamics researchers have completed their first ADHD study and which identifies ADHD with 96% accuracy.
- Researchers have been able to positively link eye disease not just with hearing loss, but also microvascular disease in the kidneys.
- 'Negativity bias', a genetically associated disposition and earlier exposure to stress was confirmed as a risk factors for depression.

Not only is it important for sufferers of depression to get the right medication for their mental health it is extremely important to find markers for optimal treatment, because those who do not improve are at greater risk of chronic problems and serious medical conditions including cardiovascular disease, obesity and diabetes.

iSPOT-D is the first study to look at brain and gene measures as well as clinical information to identify these objective 'markers' for predicting treatment response. The study is now close to 50 per cent complete and is on track for completion in 2011.

Treatment solutions or strategies for depression could give my daughter a brighter future says mum, Desley. With the condition prevalent on both sides of the family she was happy to take part in the groundbreaking study of the family members of people with depression.

At the Brain Dynamics Centre, already more than 50 people experiencing depression have been assessed before and after treatment for measures of cognition - thinking and emotion functions; brain function - EEG and MRI scans; and genes - for those genes that may affect how different individuals are more sensitive to one medication versus another.

The centre is also undertaking a collaborative study with the Westmead Children's Hospital to study very early onset schizophrenia in children and adolescents from as young as eight years. This is a unique collaboration and a world first to



study these children at their first experience of psychosis. Early onset schizophrenia has a prevalence of one child in 10,000 before the age of 12. It usually indicates a more severe course of illness and identifying biological 'markers' that define early onset of schizophrenia is important for ultimately developing preventative programs, and treatments that limit the chronicity of the illness. Thirty young people with very early onset schizophrenia have been assessed, using cognitive and brain measures.

Preliminary findings show alterations in thinking and emotional functions of cognition that define the onset of schizophrenia. These include difficulties in memory and recognizing emotions on other people's faces.

Importantly, these difficulties may not always improve with medication. So this research is helping develop assessments to monitor when children may continue to have thinking/emotional problems even when their symptoms have improved which is important to understanding ongoing difficulties in school, or moving into work and when there is a need for additional therapies.

The centre has also just completed the first ADHD study and has identified a profile that identifies ADHD with 96 per cent accuracy (known as 'predictive power').

This profile can be assessed with a straightforward computerized test that can be easily done in the doctors' waiting room. The results have also formed the evidence base for a web-based version of the same test.

The study is now being followed up in three ways. Firstly to test a replication of the findings in an independent sample of ADHD

children/adolescents, then to identify whether this profile also helps identify which children/adolescents with ADHD will respond well to stimulant medications.

A new controlled trial study is also underway to identify which profile helps identify children/adolescents with ADHD who will respond to alternative non-stimulant medications.

Finally the centre's research into fear and anxiety has found a number of interesting things. Following the study, the research has found that people with a 'Negativity Bias' compared to a 'Positivity Bias' are more at risk of depression, anxiety and related stress conditions.

Negativity Bias is a genetically associated disposition to expect negative outcomes, and a related vulnerability to stress so that even normal daily events seem stressful.

It was found two other risk factors interact with a Negativity Bias to further increase the risk for depression-anxiety - genetic variants that affect emotional brain chemistry and brain maturation and environmental exposure to stresses early in life, when the emotional brain is maturing

People with a Negativity Bias and these risk factors show a hyper-reactivity in the way their brain respond to fear. This hyper-reactivity is like being on 'alert' all the time, and in a state of biological stress. The results of the study were published in three papers including one in *Molecular Psychiatry* and two in the *Neuroimage* journal.

One of the ways the Brain Dynamics Centre is able to tie this information together across studies is by using new brain modelling methods, supported by the Centre's physics researchers. This work has contributed to a prestigious Federation Fellowship.

## CENTRE FOR VISION RESEARCH

Educating older people and their doctors about the impact of vision and hearing loss is one of the aims of a study being conducted by the Centre for Vision Research.

Research has previously shown older adults with visual impairment are also more likely to have a hearing loss, and that combined sensory loss cumulatively affects health related quality of life. These findings provided the impetus to develop a partnership project with Vision Australia (VA) and funded by the NHMRC to identify how many of VA's clients with low vision also experience hearing loss and to assess whether carrying out hearing tests during low vision appointments can help facilitate better integration of rehabilitation services to improve the quality of life of these people.

In a related study, researchers at the centre found that people with this dual sensory loss were more likely to have negative impacts on their health in terms of loss of independence and an increased risk of depression.

As part of the Blue Mountains Eye study – one of the largest eye disease studies in the world – a 15-year follow up of participants has just been completed, and from this researchers have been able to positively link eye disease not just with hearing loss, but also microvascular disease in the kidneys. The link has never been described before, but the study found that there was almost a doubling of the likelihood of hearing loss in people with chronic kidney disease.

One of the other findings of this lengthy study related to dietary relationship to hearing loss. A paper has just been accepted for publication in the American Journal of Clinical Nutrition which outlines the group's findings that omega three fatty acids found in fish were protective in terms of the development of hearing

loss. In a separate paper to be published in Age and Ageing, researchers outlined the link between hearing loss and overall health, and more specifically the relationship between hearing loss and depression. The findings emphasized the importance of detecting, recognizing and treating hearing loss before it can impact on a patient's mental health. It will hopefully lead to educating general practitioners on the importance of identifying individuals with hearing loss who may be at risk of depression.

In another of its long term studies – the Sydney Childhood Eye Study – researchers are now conducting five-year follow up on the children who were tested in Years 1 and 7 investigating the link between eye health and future vascular diseases.

The purpose of the study was to look at the frequency of different eye conditions in children of those two age groups, and its baseline data found there was a correlation between high blood pressure and narrowing of the retinal eye calibre and obesity and the narrowing of retinal vein calibre vessels. The follow up study is aiming to investigate whether as the children have aged whether these early signs of vascular changes relate to a marker for an increase risk of vascular problems such as hypertension.

DIVISION

## CARDIO- RESPIRATORY

OVERVIEW

Combining laboratory research and clinical studies the Cardio-respiratory Division is investigating common cardio and respiratory disorders like abnormal heart rhythms and sleep apnoea.

### CENTRE FOR HEART RESEARCH

They say the eyes are the window to the soul, but eyes may also be able to help doctors predict if patients are at risk of coronary episodes.

The Centre for Heart Research, in a collaborative study with the Centre for Vision Research has started a study looking at whether the tiny blood vessels at the back of our eyes can warn

doctors if patients could be at risk of cardiac problems in their future.

Already 600 patients have been enrolled into the study which will use a specially developed technology that can photograph the network of tiny blood vessels at the back of an eye to see if there are any changes that could indicate whether larger, coronary arteries may be at risk.

Image

Healthy retina



#### HIGHLIGHTS

- In world leading research a study testing the effect of a nasal dilator strip started measuring the quality of sleep of patients with nasal complaints.
- World's first Australian Heart and Eye Study commenced looking at blood vessels at the back of our eyes as predictors of cardiac disorders.
- The largest single centre trial addressing a cure for atrial fibrillation commenced looking at minimally invasive procedures.

Not only have the two centres developed a special camera which can photograph these very small branches of blood vessels they have also developed the equipment to take pictures in time with a patient's heartbeat.

Bleeding in the eye from these blood vessels is one of the more common signs of hypertension, but what the study is trying to ascertain is whether there is also any change to the size of the blood vessels. Studies have been done on the larger arteries and vessels related to cardiac episodes but this is the largest study to compare the small blood vessels in the eye with the larger vessels within the heart. The centres hope to recruit about 2000 patients to the study and publish their initial results in around six months.

The Heart Research Centre has also recently completed enrolment for one of the largest single centre trials addressing

The optimal surgical technique for minimally invasive procedures designed to cure atrial fibrillation. The clinical trials are to look at ways to improve treatment for atrial fibrillation, the most common abnormal heart rhythm which affects 20 per cent of people at some stage in their lives. Atrial fibrillation may cause disabling symptoms and is a common cause of strokes. Already the centre has performed a number of trials to develop and improve curative techniques for treatment of this condition and the initial results of this trial will be available in late next year.

Another major study has also just been started looking at new technology for a catheter to look at the inside of the heart in a similar way to that of a gastroscopy. Until now, there was no way in which to see clear pictures of the inside of the heart, but the heart research centre has been investigating a new type of catheter which allows doctors to see the internal parts of the heart including the wall and surrounding muscle. Previous trials on animals have been completed and the heart research centre is one of the first sites in the world to use the new catheter that would be used on patients with complex heart rhythm problems.

Tammy agreed to take part in the Australian Heart and Eye Study following her admission to hospital with abnormal heart rhythms. Researchers believe the blood vessels in the retina may reflect the changes in blood vessel in the heart.



The Centre for Heart Research also continued to expand its work investigating the molecular basis of cardiac conduction. Using high-end molecular techniques, involving viral based gene delivery and regulatory RNA transfer to somatic cells, the group genetically manipulated cells and tissues in animal models.

This allowed the researchers to characterise the effects of these manipulations on heart rhythms. The work is deliberately translational in nature with researchers hoping to uncover new molecular targets for the treatment of cardiac arrhythmias.

#### LUDWIG ENGEL CENTRE FOR RESPIRATORY RESEARCH

For people who have trouble sleeping because of a blocked nose, the Ludwig Engel Centre for Respiratory Research could be on the way to helping them with just a simple strip.

The centre has been leading the world in research on sleep-related respiratory diseases and last year began a study targeting 50 patients to test the effect of a nasal dilator strip on the quality of sleep for patients complaining of nasal symptoms or difficulty in sleeping because of a blocked nose.

The dilator strip would help in opening blocked nasal passages and airways and is one of the biggest studies of its kind with researchers aiming to finish collecting data by September.

One of the centre's major projects in the past 12 months has been looking for a connection between snoring, sleep apnoea and carotid artery atherosclerosis.

In 2008, researchers started to investigate whether snoring could be isolated as an independent risk factor for carotid artery atherosclerosis and endothelial dysfunction.

This year researchers took their work further, using a model of an artery wall to which they applied snoring like vibrations for six hours before looking at the biochemical results under a microscope.

The results show that although structurally there seemed to be no damage to the cells, functionally, the endothelial cells – or those lining the artery wall that act as a barrier between the blood and body – no longer reacted as they should.

The vibrations, which are similar to those that occur in chronic snorers, had interrupted the way in which the endothelial cells react, leading to endothelial cell dysfunction.

Endothelial dysfunction is one of the well recognized precursors to carotid atherosclerosis which is the first step along the pathway to stroke. The research demonstrated that snoring-like vibrations can produce this dysfunction, and was very supportive of the clinical study the centre conducted in 2008.

The data continue to point to heavy snoring as a common cause of stroke. For doctors, the presence of heavy snoring could indicate a patient is at increased risk of stroke.

Researchers are now looking at finding a way to block the defective signal in the cell to prevent endothelial damage.

In a different but related study, the centre has been taking a slightly different approach to understanding sleep apnoea and the role that upper airway surface forces play. Already the centre has completed a couple of pilot studies on the effect of surfactant on the upper airways. In patients with sleep apnoea upper airway walls collapse onto each other and remain stuck together, reducing the size of the airway.

This study is looking at lowering the surface tension of liquid in the upper airways, by applying a surfactant onto the airway walls, decreasing the possibility of them sticking to each other by decreasing the adhesive pressure.

Two approaches are being taken - one looking at the effect of the surfactant on patients while they are awake, and the other an overnight study.

In the first instance an MRI is taken of the airways while the patient is awake after a surfactant has been applied to determine if it acts to increase the size of the patient's airway. On overnight studies, researchers have been measuring whether a surfactant can work at decreasing surface tension, making the airway bigger, and reducing the frequency of apnoeas.

This year Associate Professor John Wheatley was also awarded an NHMRC Practitioner Fellowship to support the centre's research, the first one to be awarded to a researcher at the Westmead Millennium Institute.

## ADVISORY BOARD

**Mr Paul R Bell**  
Chairman

**Professor Tony Cunningham**  
Director, Westmead Millennium Institute

**Professor Steven Boyages**  
Chief Executive, Sydney West Area Health Service

**Emeritus Professor Peter Castaldi AO**

**Mr Philip Chronican**  
Group Executive, Westpac Institutional Bank

**Associate Professor Michael Fearnside AM**

**Dr Michael Spence**  
Vice-Chancellor, University of Sydney

**Mr James Wakim**  
Managing Director, Arab Bank Australia

**Mr Patrick Wilde**  
President, The Westmead Medical Research Foundation

OVERVIEW

## ORGANISATION STRUCTURE

Image

Chicken pox virus

### Chairman

Mr Paul R Bell

### Director

Professor Tony Cunningham

### DIVISIONS

#### INFECTION AND IMMUNITY

##### Centre for Infectious Diseases and Microbiology

Director, Prof Tania Sorrell

##### Centre for Transplant and Renal Research

Director Transplantation, A/Prof Phillip O'Connell

Director Renal Medicine, Prof David Harris

##### Centre for Virus Research

Director, Prof Tony Cunningham

##### Institute of Dental Research

Director, Prof Neil Hunter

##### Institute for Immunology and Allergy Research

Director, Prof Graeme Stewart

#### CANCER

##### Westmead Institute for Cancer Research

Director, Prof Rick Kefford

#### LIVER AND METABOLIC

##### Storr Liver Unit

Director, Prof Jacob George

#### NEUROSCIENCE AND VISION

##### Brain Dynamics Centre

Director, Prof Lea Williams

##### Centre for Vision Research

Director, Prof Paul Mitchell

#### CARDIO-RESPIRATORY

##### Centre for Heart Research

Director, Dr Pramesh Kovoor

##### Ludwig Engel Centre for Respiratory Research

Director, A/Prof John Wheatley

### Chief Operating Officer

Mr Mark Dado

### Operations and I.T

Manager, Dr David Facey

### Facilities and Grant Administration

Manager, Mr Mark Smith

### Finance

Manager, Mr Mark Wissam

### Human Resources

Manager, Mr Lloyd Smith

### Communications

Manager, Ms Victoria Hollick

### Administration

Executive Officer, Mrs Margot McEwan

### Science Council

Chair, Dr Anna de Fazio

## THE WESTMEAD MEDICAL RESEARCH FOUNDATION

Westmead Medical Research Foundation (WMRF) is the major fundraising organisation for Westmead Millennium Institute (WMI) and Westmead Hospital.

Through the support of the community, WMRF helps transform lives by supporting outstanding medical research and clinical care. In addition, it is WMRF's mission to advocate excellence, promote collaboration and foster talent.

WMRF reports to a financial year and, in 2008-09, the Foundation raised more than \$4.1 million and dispersed close to \$2 million in research grants, equipment funding and other donations.

WMRF was previously known as The Millennium Foundation. However, an extensive brand review revealed that the name lacked widespread recognition and failed to communicate the Foundation's mission.

Significant research, consultation, testing and planning was committed to finding a new name that succinctly defined the Foundation's purpose, and harnessed the strong brand equity of Westmead.

The new name, Westmead Medical Research Foundation, leverages the powerful reputation of a campus renowned for research and medical excellence. The words 'medical' and 'research' in the name illustrate the core purpose of funding Westmead's important research and clinical care services.

During WMRF's flagship gala event, A Night with the Stars, the NSW Government pledged \$30 million to WMI towards its new WMI building on the Westmead campus, in addition to \$380,000 raised on the night with the help of Yum! Restaurants International.

The Foundation awarded a total of \$230,000 to 50 promising WMI research students at the Grants and WMI Science Awards Night, while the annual Clubs Race Day at Rosehill Racecourse raised a further \$50,000.

Under the leadership of Executive Director Eric d'Indy, WMRF diversified its fundraising portfolios in 2009, to focus more heavily on philanthropic giving, corporate partnerships and clubs. This strategy helped contribute to a total of \$1.1 million raised from corporate, high net worth individuals and community partnerships during the 2008-09 financial year, to support the important medical research and clinical care undertaken at Westmead.

The Foundation also launched a new, online-driven campaign, called The Move Movement, to attract new generations of supporters and donors. The Move Movement directly targets members of Generations X and Y, who are characterised in marketing terms by their responsiveness to experiences rather than causes.

Complementing WMRF's more traditional fundraising activities, The Move Movement engages young people and corporate teams by advocating healthy lifestyle, sport and adventure travel as means by which they can have fun, prevent disease, and at the same time contribute to the important work at Westmead.

## FUNDING AND FUNDING ORGANISATIONS

### Funding 2009 (figures in millions)

NHMRC Grants	\$ 10.6
Other Grants	10.6
Infrastructure Grant	3.0
Other Income	2.5
<b>Total</b>	<b>\$ 26.7</b>

\*Excludes donations through the Westmead Medical Research Foundation

During 2009 the Institute received research funding through the following organisations and we thank them for their support.

Allergan Australia Pty Ltd	Multiple Sclerosis Research Australia
American Health Assistance Foundation	National Breast Cancer Foundation
Anthony Rothe Memorial Trust	National Health and Medical Research Council
Australia and New Zealand Intensive Care Foundation	National Heart Foundation of Australia
Australian Centre for HIV and Hepatitis Virology Research	National Institutes of Health (USA)
Australian Cystic Fibrosis Research Trust	Novartis Pharmaceuticals Australia Pty Ltd
Australian Dental Research Foundation	NSW Office of Science and Medical Research
Australian Health Ministers' Advisory Council	Pfizer Australia Pty Ltd
Australian Research Council	Robert W Storr Bequest
Australian Rotary Health Research Fund	Roche Products Pty Ltd
Australian Society for Psychiatric Research	Sanofi-aventis Australia Pty Ltd
Biogen Idec Australia	Schering-Plough Pty Ltd
Bristol-Myers Squibb Australia Pty Ltd	The Australian Lung Foundation
Cancer Institute NSW	The Cancer Council of New South Wales
Cure Cancer Foundation	The Cardiac Society of Australia and New Zealand
Diabetes Australia	The Westmead Medical Research Foundation
Eli Lilly Australia Pty Ltd	University of Sydney
Janssen-Cilag Pty Ltd	University of Sydney Cancer Research Fund
Juvenile Diabetes Research Foundation	
Juvenile Diabetes Research Foundation International	
Kidney Health Australia	
Leukaemia Foundation	



A woman with dark hair, wearing a white lab coat and a colorful patterned scarf, is looking through a white and black microscope. The background is a blurred laboratory setting with shelves containing various items. A semi-transparent white box in the top right corner contains the text 'RESEARCH REPORT'.

## RESEARCH REPORT

### CONTENTS

- 32 Infection and Immunity
- 42 Cancer
- 47 Liver and Metabolic
- 50 Neuroscience and Vision
- 53 Cardio-respiratory
- 55 Publications
- 68 Staff

Researchers in the Centre for Transplant and Renal Research are isolating islet cells for transplantation into type 1 diabetes patients.

## INFECTION AND IMMUNITY

### CENTRE FOR INFECTIOUS DISEASES AND MICROBIOLOGY

#### Fungal pathogenesis

The fungal pathogenesis group headed by Dr Julie Djordjevic, has shown that hydrolytic enzyme phospholipase B1 (PLB1) is one of the specialised (GPI-anchored) proteins that help maintain integrity of the cell wall in the fungus *Cryptococcus neoformans*. *Cryptococcus neoformans* causes potentially fatal meningitis especially in patients with HIV infection, an estimated 4-10 million of whom are affected. Furthermore PLB1 protein released to the exterior of the cell from both the membrane and cell wall facilitates penetration of *Cryptococcus* into lung and brain. We have recently found that a key enzyme involved in PLB1 secretion, phospholipase C, also regulates production of another virulence determinant, laccase, which is itself responsible for production of the cell wall-protective molecule, melanin, and that PLC1 is essential for growth of *Cryptococcus* at physiological temperatures. We are now studying signalling pathways involved in regulating the production and release of PLB1 from the cell surface and investigating PLC as a potential antifungal drug target. This fundamental knowledge will lead to new understanding of cryptococcal biology and help us to identify new target molecules for development of drugs to treat fungal infections.

#### Antifungal drug development

The group has an NHMRC project grant to make and test new chemical compounds that act on fungal enzymes which are important in virulence (and hence initiation of disease). In collaboration with Dr Kate Jolliffe, a synthetic chemist at the University of Sydney, novel compounds in 3 chemical classes have been made and tested against a range of fungi that cause disease in humans. Particular interesting are compounds in two of these classes. These have been patented and are undergoing further evaluation as potential antifungal drugs. A lead compound from the third class is marketed as miltefosine, which was developed as an anti-cancer drug and is now used for treatment of a parasite infection (leishmaniasis). We have synthesised and obtained related compounds and are investigating their antifungal potential and mode of action. This work will be extended in 2010.

#### Bacterial pathogenesis, antibiotic resistance and novel diagnostics

The group has characterised the genetic basis of local transmissible resistance to carbapenem, extended-spectrum beta-lactam, and the common aminoglycoside antibiotics, including novel gene variants, and defined the basis for most major antibiotic resistance genes relevant in ICU in Australia.

These have begun to be incorporated into novel high speed multiplexed assays in collaboration with industry partners. Assays have also been developed for rapid detection of pathogens in blood culture, and common viruses including influenza (including "swine flu" and "bird flu") have been tested and are available for high-throughput assays. Our work has been presented in major international conferences (eg ICAAC) and journals (eg *Lancet Infectious Diseases*, *Nature Reviews Microbiology*). New areas include bacteriophage therapeutics (in collaboration with industry) and novel immunofluorescence methods (funded by ARC, in collaboration with Macquarie University).

#### Nuclear magnetic resonance spectroscopy

Investigation of NMR spectroscopy as a rapid diagnostic tool in microbiology has continued. We have now shown that this platform has great potential for reducing the time needed to test drugs for their antifungal effect and hence allow earlier institution of therapy and better patient outcomes. Additional studies in animal (rat) models of meningitis have shown that analysis of cerebrospinal fluid by NMR spectroscopy can distinguish streptococcal from cryptococcal meningitis and from normal CSF. This suggests that with further development, it should be possible to achieve an etiologic diagnosis (determine the organism causing the infection) within a few minutes of placing CSF samples in the magnet.

#### Improved outcomes in immunosuppressed haematology patients - CCRE

This is a large NHMRC Centre of Clinical Research Excellence Program now in its final year and involves three themes - prevention, diagnostics and treatment, and ethics. Highlights to date include a study of the occurrence, transmission and prevention of community respiratory virus infections in patients with cancer of the blood. New viruses with the potential to

cause pneumonia have been identified. Our work with highly multiplexed rapid diagnostics has been particularly fruitful, with platforms for rapid identification of bacteria and fungi and for testing for bacterial and viral pathogens in respiratory samples now ready for adoption in the clinical laboratory. Several key ethics studies are nearing completion including assessing the response of patients to living with cancer, the ethics of creating “saviour siblings” as bone marrow transplant donors and the psychological effect of physical isolation during times of very low function of the immune system (in order to prevent serious infections). Other key programs are proceeding in vaccine research, the epidemiology of invasive fungal infections and the role of rapid molecular methods to inform infection control practice.

## CENTRE FOR TRANSPLANT AND RENAL RESEARCH

### Pancreatic islet cell transplantation

Following the units pioneering clinical trial of pancreatic islet transplantation they have been chosen to lead an Australia wide consortium with the aim of developing pancreatic islet cell transplantation as a mainstream therapy for patients with difficult to control diabetes. The current trial involves patients with severe metabolic complications from their diabetes. Patients have shown marked improvement in metabolic outcomes after successful pancreatic islet transplantation with the ultimate outcome being that patients no longer require insulin injections for substantial periods of time. This trial is also identifying progressive loss of islet graft function and complications from the anti-rejection drugs as the major impediments to its more widespread application. The study, which has been funded by the Federal Government and the JDRF aims to identify factors that cause graft damage and to develop a safer immunosuppressive regimen. Currently 10 patients have received islet transplants in this new trial. Early data suggests that successful transplantation abolishes severe hypoglycaemia leading to a marked improvement in quality of life. The study is still ongoing and involves a large Australian collaborative effort to advance this exciting technology.

### Pancreatic islet xenotransplantation research

Currently pancreatic islet cell transplantation is the only known cure for Type 1 diabetes. If this therapy is to be more effective

sources of insulin producing cells other than organ donors needs to be found. In collaboration with researchers in Melbourne and Adelaide we are investigating the use of pig pancreatic islet cells for future transplantation in human patients. The group's current research is focused on identifying molecular targets that can be used in the development of genetically modified pigs for transplantation. Currently we are focusing on genes that are involved in down regulating clotting and inflammation. Our data suggests that producing pigs whose islet cells express several human proteins that regulate these aspects of the immune system may be sufficient to allow this tissue to be used safely in patients. This information has been used to develop a new line of pigs that have been genetically modified so that they may be better suited to clinical transplantation. Australia is the world leader in pig transgenesis and this ambitious collaborative project between four research institutes is making substantial progress in the development of pig islet cell xenotransplantation. Recently it received a major funding boost by being awarded a special NHMRC/JDRF special program grant in Type 1 diabetes.

### Transplantation immunity and tolerance

The aim of this group is to better understand the mechanisms of rejection of pancreatic islet xenografts and to develop novel strategies for suppressing this immune response. The group has made several findings in understanding the role macrophages play in the rejection of pig islet grafts. In particular they have shown that macrophages have a surprisingly specific and sophisticated recognition response for identifying pig tissue. At present, work in this area is focusing on understanding the molecular mechanisms responsible for this recognition. Currently the group is focusing of receptor-ligand incompatibilities between pigs and humans to determine if signals that regulate macrophage function are switched off.

The group is also investigating novel strategies to induce tolerance to transplanted islet tissue and to further reduce the requirement for long-term immunosuppression. In particular they are focusing on the role of a regulatory T cell called CD4CD25+ T cells. They have found that these cells are capable of inducing tolerance to islet allografts and have begun investigating their role in maintaining tolerance to pig islet cells.

### Chronic allograft nephropathy research

The aim of this group is to increase knowledge about the mechanisms for the long-term loss of renal transplant. Current treatment strategies are very good at preventing acute cellular rejection but over time renal transplants are still lost to a complex process known as Chronic Allograft Nephropathy. The group has been at the forefront of this research internationally and by studying protocol biopsies has identified several novel factors responsible for this chronic graft loss. The focus of the group is to understand the molecular mechanisms responsible for this loss using a genome wide analysis of biopsy specimens using genomics or gene chips. This had allowed us to identify early mechanisms of graft fibrosis and glomerulosclerosis. Which in turn has allowed us to better understand the early pathology that ultimately leads to chronic allograft nephropathy. Ultimately it will assist us to develop a diagnostic test that predicts those patients that will develop this condition and to design new treatments. Our group is part of a large collaborative study between 4 US centres and our centre at Westmead which is funded by the National Institutes of Health in the US. Its aim is to identify the molecular basis of Chronic Allograft Nephropathy from a large patient cohort of over 300 transplant recipients.

### Renal failure research

This research is focused on novel therapies for reducing kidney inflammation in chronic kidney disease. New approaches to treatment that are currently being tested in animal models of human kidney disease include the administration of protective cells (regulatory macrophages, dendritic cells and T lymphocytes) which reduce inflammation and structural and functional injury. In addition, vaccination using genes of molecules that drive the inflammatory response is also being tested. The gene targets include chemokines (such as CCL2 & fractalkine), chemokine receptors and costimulatory molecules (including CD40). A separate series of protocols is examining the role of key molecules, macrophages and proteinases in causing transition of renal epithelial cells into mesenchymal cells which can cause kidney fibrosis. We have exciting results in a number of models of chronic kidney disease. These novel strategies are bringing new understanding about the progressive nature of kidney disease. It is likely that such strategies will in the future be applied to the treatment of human kidney disease.

### Polycystic Kidney Disease

Polycystic kidney disease (PKD) is the most common fatal inherited renal disease in the world. Both adults and children are affected. In adults, currently there are no effective treatments to prevent kidney failure due to PKD. The PKD group at Westmead have identified that kidney cell proliferation and cell cycle activation are a key mechanism of cyst growth in humans and experimental PKD. The focus of the group is the development of novel drug inhibitors (cyclin-dependent kinases, mammalian target of rapamycin protein kinase, vitamin D receptor signalling) to suppress cyst growth in preclinical small animal models of PKD. Magnetic resonance imaging as a non-invasive marker of disease progression is also under investigation. The group is also involved in multi-centre clinical trials of humans with PKD using vasopressin receptor antagonists, and is collaborating with the Mayo Clinic to determine the role of modifier genes in predicting disease progression in human autosomal dominant PKD. The work is supported by the NHMRC as well as collaborators at Radiology Department of Westmead Hospital, Macquarie University (Sydney), the Mayo Clinic (USA) and the Institute of Molecular and Cell Biology (Singapore).

### Cellular regeneration in glomerulonephritis

Diseases of the renal glomerulus are the most common cause of kidney failure throughout the world. A key feature of progressive renal injury in glomerular disease is the proliferation, dedifferentiation and eventual loss of podocytes and tubular epithelial cells in response to disease inducers. The group has identified that the mammalian target of rapamycin (mTOR) pathway and cyclin dependent kinases have a key role in intrinsic renal cell turnover, and that modulation of mTOR suppresses disease progression in models of focal segmental glomerulosclerosis and crescentic glomerulonephritis. Ongoing work aims at developing further precision in understanding the role of mTOR in mediating glomerular injury and proteinuria in human and experimental glomerulonephritis, as well as its future application in cellular regeneration. This work is supported by Kidney Health Australia, Cyclacel (United Kingdom), Wyeth-Ayerst and external collaborators at Monash University (Melbourne).

## CENTRE FOR VIRUS RESEARCH

### HIV molecular pathogenesis

The HIV molecular pathogenesis group's primary focus is to understand the very early interactions of the HIV virus with host cells of the body, predominantly human dendritic cells (DCs). These are the first cells to come into contact with HIV within the genital tract.

Our group has utilised microarrays to assess the global effects of HIV on the DC transcriptome. In doing so we have gained an understanding of the many ways that HIV shapes the intracellular environment and manipulates these cells to facilitate its own transport and subsequent transfer to CD4-T lymphocytes, its primary target cell. We have shown that HIV triggers two distinct phases of gene expression in DCs, one early in infection (6hrs) corresponding to viral entry and second burst later in infection (48hrs) corresponding to viral replication. Based on this data we are currently following three main avenues of research.

In 2009 we published in Blood journal (PMID: 19436054) that HIV is able to down regulate lysosomal enzyme activity in DCs after infection. We are currently investigating the functional consequences of this i.e. enhanced viral survival within the DC and reduced HIV antigen presentation to T-cells.

Our microarray studies have also indicated that HIV is able to induce the expression of discrete subset of interferon stimulated genes (ISG) in absence of any interferons. We are currently investigating the mechanism by which HIV i) inhibits the production of interferon by DC and ii) how the virus induces ISG expression. We are specifically focussing on the role the interferon regulatory factor family in the process .

The global gene changes that HIV induces in dendritic cells continue to be investigated using DNA microarray technology, and investigations are now being broadened to include the effects that HIV has on the proteins regulating the expression of interferons, subverting the effect of these antiviral substances and inducing a subset of interferon stimulated genes, probably to boost its own replication.

In addition to microarray studies we are conducting proteomic studies on DCs. We are particularly interested in the oligomeric structures of the DC surface receptors (C-type lectin receptors)

that bind HIV. We have published two papers in the Journal of Biological Chemistry (PMID: 15385553 and 19224860) looking at DC-SIGN and the mannose receptor respectively. We are currently conducting similar studies on Langerin.

We are also investigating ways to prevent initial infection of the female genital tract via DCs in skin/genital mucosa. The methods employed include using soluble receptors as decoys binding to the virus as well as direct antagonism of the HIV binding receptors by blocking. Preliminary studies indicate that these can be effective

### Cytomegalovirus

Cytomegalovirus (CMV) is a medically important virus which infects a vast majority of the world's population. Although infection is usually mild in healthy individuals, it is a frequent cause of serious, life-threatening disease in neonates and immunosuppressed individuals such as solid organ and bone marrow transplant recipients, and in people with HIV AIDS. After initial (primary) infection, the virus is not completely cleared by the host's immune system, but rather has the remarkable ability to remain inside the body for the life of an individual in a dormant (or latent) form. Periodically, the virus may reawaken from this latent state by a process called reactivation, resulting in the production of new infectious virus. It is this reactivation from the latent state in immunosuppressed individuals which is thought to be the major cause of serious, often fatal disease in these people. Despite the critical importance of latency to resulting disease, this phase of infection remains very poorly understood.

The CMV Research Group is working to discover the fundamental basis by which CMV is able to remain hidden in the human host in a latent form. The group has applied a variety of molecular and cell biology and proteomics approaches to identify both viral genes and human genes that play important roles during CMV latent infection of human cells. These studies include identification of a viral gene active latent infection which renders latently infected cells "invisible" to the immune system. Identifying the critical virus and host cell components of latency and reactivation will provide a rational basis for the design of drugs and therapies to limit the consequences of CMV disease in immunosuppressed individuals. There is currently no vaccine against CMV, so the Group is also seeking to develop a

CMV vaccine with enhanced capacity to stimulate protective immunity to infection.

### Retroviral Genetics

The Retroviral Genetics Laboratory focuses on several different aspects of HIV pathogenesis aimed at unveiling genomic and proteomic interactions of HIV with its host.

We are working on the innate and adaptive immune factors, which are found in untreated HIV+ patients with non-progressive disease, especially the ones who have naturally controlled HIV disease for >20 years with strength of their immune system. One such combination of factors has been characterized and recently patented, which will be the subject of in vitro human clinical trial. Our main goal is to understand what guides the path to non-progressive HIV disease in a subset of HIV+ individuals and whether these natural factors, which provide them protection against HIV, can find some use as therapeutic agents/vaccines. We are adopting a variety of immunological, virological, proteomic and genomic techniques to identify and characterize novel immune factors, which underlie non-progressive HIV disease.

Recently we have extended our studies to cell transcriptome level, where we are investigating the whole human genome (>47,000 genes) in different cell types, such as CD4+/CD8+ T cells, Monocytes and NK Cells derived from viremic and aviremic HIV+ therapy naïve and therapy experienced individuals in order to understand how HIV guides different stages of HIV disease by differentially and systematically subverting the cellular gene machinery within the same host. Our objective is to define genomic and proteomic imprints of HIV in HIV-infected progressing and non-progressing individuals. Also, since the majority of HIV+ individuals receive highly active antiretroviral therapy (HAART), our lab is most interested in unveiling the pharmaco-genomic imprints of drug toxicity in HIV+ individuals and genetic mechanisms 1. Which can partially restore the host immune system during treatment and 2. Which can the success and failure of HAART treatment. All the aforementioned genomic and proteomic studies using microarray will be complimented by analysing microRNA in each of the cell types discussed above, which associate with HIV virus infection in humans. This detailed mapping of cellular

transcriptomes of HIV-infected cells will guide the development of new generation of biomarkers/prognostic and diagnostic tools, along with providing a detailed snapshot of virus-host interaction at the genomic and proteomic levels.

The group is also highly focused on current trends in viral epidemiology (such as emerging viruses and HIV-HCV co-infections) and developing novel diagnostic and prognostic molecular technologies for HIV, influenza, Hepatitis C virus (HCV), Human Papilloma virus (HPV), SARS virus and most recently Influenza Swine Flu (H1N1) virus, etc. The Retroviral Genetics lab also runs services for drug resistance and epidemiologic testing of HIV in Australia.

### HIV Biology

The HIV Biology team aims to improve our understanding of how HIV can spread rapidly between cell types, which are known to be important for HIV transmission. HIV transmission begins as a chain of events that enables a critical infection threshold to be reached. By researching this spread, a greater understanding can be attained with respect to mechanisms of HIV migration and amplification. In doing so strategies designed specifically at breaking any part of the chain of transmission can be used in future scenarios for HIV prevention and/or therapy.

Current studies of the group include the genetic manipulation of HIV vectors to spy on HIV in live cells using fluorescent microscopy and the generation of HIV vectors for visualization at the electron microscopy level. It is through the generation of such tracking devices, that the group has observed cellular "needle like" projections are used by the virus to initiate the process of jumping from cell to cell. The work would not be possible, if it were not for two criteria: Firstly the genetic engineering of viruses that permits visualisation over time in living cells and secondly the use of cutting edge microscopy to capture these events. For the latter, the HIV biology group has been instrumental in acquiring this technology in collaboration with chief investigators from the Westmead Research Hub.

Recently the group has aligned with several collaborators from the University of Sydney (School of Chemistry) and CMRI, to develop new therapeutics that act at blocking viral entry and spread throughout the body. For the latter the HIV Biology group has been successfully awarded a translational grant through

the Australian Centre for HIV and Hepatitis Virology Research scheme, to study the role of a common cellular protein, Dynamin II, in HIV entry and spread. This collaboration with Professor Phil Robinson at CMRI, will potentially short-list existing drugs targeted towards this cellular protein for use in future HIV therapeutics and prevention strategies.

### **Molecular viral transport and assembly**

Herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) are important human pathogens, causing encephalitis, blindness and severe neonatal infection. They also enhance the acquisition of HIV three-fold. The transport of HSV-1 and HSV-2 to and from the periphery within the axons of nerve cells is a key component of their life cycle.

The group aims to define a molecular interaction network or infectome at the protein level during the course of infection of a host cell by HSV-1. This will unlock the mechanism(s) involved in the entry, axonal transport, assembly and exit of HSV-1 from nerve cells. In addition, this will assist in a general understanding of host cell function. Recent work has identified crucial molecular interactions, involving viral and host cell proteins, required for viral assembly and transport. Such information on viral replication will allow development of inhibitors of key steps within this process. These may then be used as antivirals for control of recurrent herpes simplex. A similar approach is also being undertaken with HIV.

### **Varicella zoster virus**

Despite its significant impact on the community, little is known about the molecular basis of Varicella zoster virus (VZV) infection, due in part, to VZV only infecting humans. To more closely examine the interaction of VZV with host cells, the group has established several models of infection using human cell-types which are targets for infection and are relevant to those that suffer from either Varicella or herpes zoster/PHN because each of these cell types are likely to play different, but essential roles in the disease process. These include human fibroblasts (skin cells), neurons (nerve cells) and specialized immune cells (T cells and dendritic cells).

The group has shown that human nerve cells infected with VZV do not undergo programmed cell death (apoptosis). This is an important finding because it suggests the nerve cell damage

observed when VZV reawakens from its "silent" state in nerve cells to cause shingles is not due to programmed cell death. Another implication from this observation is that VZV encodes a function to interfere with the death response in human nerve cells, thus providing a possible mechanism by which the virus can establish and maintain its life-long dormant infection. We went on to identify the first VZV encoded anti-apoptotic gene ORF63. To further our understanding of VZV with human nerve cells the group has developed and recently published a novel model of VZV infection of intact human explant ganglia. The group has shown for the first time that VZV can infect intact human ganglionic cells and this is a novel way of studying the interaction of this virus with human nerve cells.

These features of intact ganglionic infection can now be studied in further detail to better define the molecular mechanisms that underlie VZV infection of ganglionic cells. For example, this model provides a means to rapidly test viral gene mutant viruses and new candidate vaccine strains containing targeted gene disruptions to define viral genes that may play critical roles in VZV neurotropism and to examine in detail the outcome of infection of both neurons and non-neuronal cells with respect to apoptosis and cell function.

Significantly, we have now obtained rare naturally infected ganglia samples at autopsy from patients who suffered from herpes zoster close to the time of death, but who had died from unrelated causes. We are now uniquely placed to extend our earlier work by examining the interaction of VZV with ganglionic cells in both experimentally and naturally infected settings. These studies will be important for the development of better therapies to lessen the impact of VZV disease on the community.

Given the importance of the skin as a site of VZV infection and the role skin DC play in the induction of anti-viral immunity, there is good reason to study infection and modulation of DC in human skin during VZV infection. To date, the group has determined the DC subsets that may participate in VZV pathogenesis by immunostaining sections of chickenpox and shingles skin lesions for immune cell markers. In VZV infected skin, Langerhans cells (LC), were decreased and plasmacytoid DC (PDC), DC that produces high levels of IFN-alpha, were increased in frequency compared to uninfected skin. We

investigated whether these DC subsets support VZV infection in vivo by dual immunofluorescently staining sections of VZV infected skin lesions for LC/PDC markers and VZV proteins. Notably, a proportion of LC and PDC were positive for VZV proteins, suggesting these cells can be infected. Further assessment of skin DC infection, immune function and viability will define the mechanisms underlying cutaneous infection. These studies will enable a critical definition of the mechanistic basis of VZV modulation of host cell functions which is needed for development of a "second generation" vaccine to lessen the impact of VZV disease on the community.

### Herpes Neuropathogenesis

Transmission of Herpes simplex viruses (HSV) occurs from close contact with an individual who is actively shedding virus. Viral shedding generally occurs from lesions but can occur even when lesions are not apparent. Herpes infection can be treated but not cured, as the virus infects nerve cells and lies dormant in these cells during the lifetime of the human host. HSV can awake or reactivate frequently and its reactivation can be triggered by a number of factors including stress or illness. Our laboratory has established several models for culture and HSV-1 infection of primary human fetal and rat nerve cells in vitro. Our studies aim to understand how HSV-1 invades and replicates in nerve cells and the mechanisms used by the virus to travel along nerves for efficient virus spread during primary infection and after reactivation. We have used fluorescent-tagged viruses to visualize how the virus enters, travels along axons (nerves) and exit nerve cells using fluorescence and real time imaging. We have also used electron microscopy in order to elucidate, at an ultra structural level, the mechanisms used by the virus to travel along nerves and for virus assembly and exit from nerve endings. Our findings have led to the establishment of a model in which virus components are transported separately along nerves and the virus is assembled at axonal swellings and nerve endings before the virus exit the nerve cell. Our studies have shown that the virus has evolved to utilize existing neuronal vesicles and secretory pathways for transport of its components and for its exit from nerve cells.

Understanding the mechanisms used by HSV for entry, transport along nerves, and assembly in nerve cells will assist in the development of new strategies for antivirals for control of recurrent herpes disease. In addition, elucidation of the mechanisms of how HSV-1 utilizes the existing transport pathways in nerve cells for virus spread from nerve cell to nerve cell will further assist in the use of HSV as gene therapy vector to deliver drugs to the nervous system.

### INSTITUTE OF DENTAL RESEARCH

#### Analysis of advanced caries as a polymicrobial infection

Degradation of tooth enamel leads to exposure of the underlying vital dentine matrix to infection. Recent studies using molecular techniques have detailed the complexity of the polymicrobial flora associated with dentinal caries where consortia of bacteria preferentially migrate along the tracts normally occupied by cell processes of the odontoblasts that line the pulp chamber of the tooth. Characteristics of the microflora associated with infected necrotic pulps have been actively investigated but the phases of infection by dentine microorganisms remain obscure. In the present study fluorescence in-situ hybridisation on tissue embedded in resin and based on probes for 16S rRNA corresponding to the major groups of bacteria in carious dentine, was used to provide information on the characteristics of pulp infection. Lactobacilli were prominent in pulps determined to be at the early stage of infection. Established infection showed a more complex profile with lactobacilli persisting in all of the lesions but with invasion of the necrotic regions of tissue by Bacteroidetes, Fusobacteria, Lachnospiraceae and Coriobacteriaceae in particular. Advanced infections were characterised by mixed anaerobic species but with strong representation by Coriobacteriaceae and Lachnospiraceae. Lactobacilli were sparsely represented at this stage. Typically groups of organisms were spatially isolated within the infected pulp tissue. Analysis indicated that *Lactobacillus rhamnosus* could invade vital pulp tissue to achieve a very high biomass that was not associated with detectable local inflammatory infiltrate. The findings establish that early invasion of the dental pulp can be associated with a pronounced selection from the complex microbial populations within carious dentine, suggesting specific pathogenicity. Further, that extension of infection occurs according to defined sequence of invading bacterial species.

There is considerable interest in the potential of infected demineralised dentine to undergo repair thereby avoiding destructive surgical removal of infected matrix. The potential to disrupt the polymicrobial flora within carious dentine by sealing over the infected matrix, was investigated. This approach is made possible by the capacity of new glass ionomer cements to bond to tooth structure forming a molecular seal. Relative to determinations on pre-restoration biopsies, populations of lactobacilli and streptococci were markedly reduced at a 12 month treatment end-point. It was noteworthy that Propionibacteria persisted in the decalcified matrix adjacent to the restoration. As this group are known to express proteolytic activities to utilise protein matrix components of dentine as nutrient sources, it is considered that effective antimicrobial therapy to eliminate Propionibacteria will be necessary to preserve the organic matrix to enable appropriate remineralisation as a component of minimal intervention therapy.

#### **Virulence mechanisms of *Porphyromonas gingivalis***

*P. gingivalis* is implicated as a major pathogen in chronic inflammatory disease of the tissues that support the dentition. This Gram negative anaerobic bacterium is unusual in being deficient in the capacity to synthesise the porphyrin macrocycle of haem. To compensate for this, the organism has acquired sophisticated mechanisms for the sequestration of haem from host components, particularly haemoglobin from captured red cells. Cysteine proteinases, the gingipains, containing extensive adhesin domains, are important for these functions. In collaboration with researchers in the School of Molecular and Microbial Biosciences, University of Sydney, the three structural domains K1, K2 and K3, within the adhesin region of the lysine gingipain have been characterised as members of a new class of carbohydrate binding adhesins. High resolution structural analysis of K1, a haemolysin, and K3, a blood group antigen binding domain, has been achieved by X-ray crystallography. In complementary studies, Small Angle X-ray Scatter was used to provide an informative topographic outline of the adhesin complex in solution. More detailed analysis of binding sites and molecular shape changes related to binding will facilitate our objective of achieving selective control of this organism within oral polymicrobial biofilms.

While these functional determinants play major roles in the pathogenicity of the organism in disease sites, eradication of *P. gingivalis* from the oral cavity necessitates removal of organisms from numerous mucosal sites that constitute reservoirs of infection. Studies at IDR have identified a secreted haem receptor (or haemophore) released by *P. gingivalis* in response to limited environmental haem, as expected in most mucosal surfaces colonised by the organism. This haemophore, termed HusA, displays high affinity binding of haem and is essential for growth under haem limitation. It is noteworthy that HusA has no functional homologues in other bacteria, reflecting the highly adapted biology of *P. gingivalis*. The unique structure of HusA provides favourable indication of potential for specific inhibition of this haemophore to augment strategies to eradicate the organism from the oral cavity.

#### **Regulation of epithelial integrity by bacteria**

The integrity of the epithelial attachment to the tooth and that of the lining epithelium of the lesion of chronic periodontitis critically restricts the ingress of microbial products and therefore governs the inflammatory reaction to these products. Excessive response associated with immunopathology is considered to be a key driver of destructive disease. The gingipain proteinases of the pathogen *Porphyromonas gingivalis* concentrate at these surfaces and were demonstrated to disrupt model epithelial monolayers. The mechanism includes direct attack, for instance degradation of the key intercellular bridging molecule e-cadherin, and potentially, indirect mechanisms, including activation of latent transforming growth factor-beta 3 isoform which is strongly expressed by these tissues. This growth factor was shown to potently down-regulate e-cadherin and an array of tight junction proteins, a property linked to suppression of the CD24 receptor. Studies at IDR have shown that CD24 maintains epithelial barrier integrity by up-regulating expression of intercellular junction components and directing these components to the cell periphery to form functional intercellular junctions. It is proposed that lectin-like molecules of commensal organisms including *Streptococcus gordonii*, bind to sialic acid residues on CD24 to regulate intercellular junctions and epithelial permeability.

### Analysis of streptococcal genes associated with tolerance to low pH and DNA repair

Comparative proteome analysis of *Streptococcus mutans*, a key pathogen in dental caries initiation, has highlighted a number of genes associated with this bacterium's tolerance to acidic conditions. These genes and their protein products are currently the subject of ongoing studies. The aim is to determine novel biochemical sites that will allow the growth of *S. mutans* to be selectively inhibited and hence will prevent cariogenic conditions from arising without disrupting the general microbial population of dental plaque that creates a protective environment on the tooth surface.

Proteome studies have also confirmed an enhanced role for competence (DNA uptake) in *S. mutans* biofilms. These studies have identified a number of genes including ones previously designated as coding for "hypothetical" proteins. The way in which *S. mutans* can exchange genetic information is being studied by sequentially eliminating these genes from the bacterial chromosome. This research is enabling a better understanding of how more virulent strains of *S. mutans* can arise as well as how the transmission and proliferation of antibiotic resistance genes can occur in dental plaque. Uptake of DNA is also essential for the survival of *S. mutans* under extreme stress conditions when chromosomal damage can only be repaired with extraneous strands of DNA from the environment. This is known as the SOS response and allows chromosomal replication to proceed under circumstances where this would otherwise be impossible, thus enabling the bacterium to survive and proliferate under adverse conditions that are potentially lethal, such as the acidic conditions that give rise to carious lesions.

### Immune development in the tammar wallaby

In association with collaborators at ANU, UWS, CSIRO and University of New Mexico, aspects of the development of immunity in the tammar wallaby are being investigated. The tammar wallaby is an ideal model for undertaking these studies as the new born marsupial remains immune intolerant for the first 120 days. Prior to birth, salivary bacteria have been shown to be suppressed by the pregnant mother which licks the pouch clean in preparation for the new born. Molecular and histological studies have shown that a unique antimicrobial

peptide, a cathelicidin, is expressed by both the adult and new born wallaby which is capable of suppressing bacteria and hence protecting the young animal from a range of bacterial infections.

Changes in the early populations of the colonizing bacteria of the gastrointestinal tract have also been determined as the pouch young develops. Unique bacterial genera, that have not previously been described and which are not detected in the adult animal, have been identified using the same molecular strategy used in analyzing polymicrobial populations in advanced caries. These microbial studies represent the first comprehensive analysis of bacterial populations associated with any marsupial. By studying the changes in bacterial populations as the young animal develops, a better understanding will be gained into the role played by specific bacterial species during the development of immunity and tolerance in this mammal, as it is known that the immune system of gnotobiotic animals does not develop to maturity.

## INSTITUTE FOR IMMUNOLOGY AND ALLERGY RESEARCH

### Multiple sclerosis

Two large scale genome wide screens (GWS) for inherited susceptibility factors in multiple sclerosis, in which we play a major role, have been completed and discovered new genetic associations. The screen carried out by the Australian New Zealand MS Genetics Consortium (ANZGene) identified CD40 and a novel region in chromosome12, published in Nature Genetics in June 2009 (ANZgene, 2009). We are now engaged in fine mapping the chromosome 12 region, and working out how CD40 affects MS. The second GWS, in collaboration with the International Multiple Sclerosis Consortium and the Wellcome Trust, is the largest ever undertaken, and has identified virtually all the genes which increase risk by more than 20%. This study will be submitted for publication in mid 2010. We aim to determine the basis for these new genetic associations in the next few years, and it is expected this knowledge will contribute to the development of new therapeutic strategies.

In addition to our group's contribution to the genome screens, David Booth has led the associated gene expression studies, the largest such study in MS carried out to date. This work has identified a T cell activation signature characteristic of MS, and

which may prove useful as a biomarker to monitor response to therapy, to predict who might be susceptible to MS and other autoimmune diseases, and define a molecular type of MS.

### The IL-7R gene

IL-7R is the second gene unequivocally confirmed worldwide to be associated with MS susceptibility. We have shown that the MS-susceptibility variant of the gene produces more of a soluble form of this receptor, which can reduce cell-surface receptor signalling (McKay et al, 2008a). The IL-7R gene is produced in many cell types within the immune system, but how does the susceptibility variant cause a predisposition to MS?

Experiments have been aimed at determining the context in which the MS-susceptibility variant behaved most differently from the other IL-7R variants within the immune system. We examined T cells, important mediators of tissue damage or tissue protection in MS, in 9 different states of activation/ differentiation. However, the greatest difference in behaviour of the MS-susceptibility variant of IL-7R was observed in dendritic cells, an important class of cells which process and present antigen to the immune system. In dendritic cells IL-7R responds to TSLP signals to suppress autoimmunity, and we showed that dendritic cells with MS-susceptibility variant of IL-7R may receive less of this signal. The challenge is to use this knowledge to correct autoimmunity in MS. This work is now published in the *Journal of Immunology* (Hoe et al, 2010).

Our patent application for MS therapy is based on removing immune cells from a person with MS, and re-educating them via TSLP signalling through IL-7R to prevent immune reactivity to central nervous system antigens in MS. We have secured funding for 2009 from Merck-Serono to examine new ways to generate tolerising dendritic cells in vitro using cytokines in combination with IL-7R signalling and other agents to suppress autoimmunity.

### Molecular response to therapy

As part of our ARC Linkage project with Biogen-Idec we continued to provide Australia's only IFN bioactivity service, which tests if people with MS using this therapy have a biological response to the drug, which is necessary if they are to respond to therapy. Over 2000 people have now had samples tested under this service.

In addition, we have recently shown that IL-7R is up regulated by IFN in peripheral blood cells in vitro, including both naïve and memory T cells. However, this effect is not seen amongst individuals carrying the haplotype 4 IL-7R variant. We hypothesise that haplotype 4 carriers may be less responsive to the antiviral effects of IFN, and possibly the therapeutic effects of the drug (Hoe et al, *Journal of Interferon and Cytokine Research*, 2010).

### Allergy and Asthma

During 2009 we continued our focus on PHF11, investigating how this gene contributed to the changes in the immune system in allergic individuals. We were the first group to independently confirm a link between the inheritance of specific genetic variants in PHF11 and the risk of developing allergic disease. Several recent studies from other research groups also support a link between heritable genetic variants in PHF11 and allergy.

We are at the beginning of a revolution in the understanding of the genetic basis of complex heritable disorders that can involve many genes interacting in a complex manner with the environment. This is being achieved by the use of genome-wide association studies, allowing scientists to evaluate differences in common genetic variants between thousands of healthy and affected individuals. Several genome-wide association studies have already been published on asthma and allergic eczema and an Australian genome-wide association study is currently being done, for which we have assisted in the collection of several hundred samples as part of a collaboration with the Childhood Asthma Prevention Study (CAPS).

Although such genome-wide association studies have the potential to deliver novel insights into the pathogenesis of allergy with the promise of improved diagnosis and therapy, much work must still be done to fully understand the function of many of the genes identified in these studies. The PHF11 gene is a good example of this, which was identified in a genetic association study prior to any knowledge of its function. Using an array of genetic, molecular and cell biological techniques we published the first functional study of PHF11 in 2008 and in 2009 we completed a new functional study of PHF11, providing additional detail on how PHF11 turns on the expression of genes in T-cells of the immune system.

New work from our laboratory on the function of PHF11 has now revealed an unexpected link to how cells cope with stress. A cell can encounter stress in a number of ways with one common route involving the cellular response to infection by viruses. This is particularly interesting as a recent genome-wide association study of asthma has identified a novel gene, called ORMDL3, that also appears to be important in how cells respond to stress. These findings are now leading us to examine the role of PHF11 in cells that are at the interface of contact with the environment; these include cells that line our airways and digestive system that come into contact with environmental irritants and infectious agents.

Since the response of our immune systems to these agents is determined in part by the inheritance of genetic variants in genes such as PHF11, the continued genetic and functional investigation of genes linked with allergy will play an important role in understanding the risk of developing allergies.

## CANCER

### WESTMEAD INSTITUTE FOR CANCER RESEARCH

#### Breast Cancer

The Breast Cancer Research Group is studying the influence of the ovarian steroid hormones, estrogen and progesterone, in the normal breast and in breast cancer. The causes of breast cancer are largely unknown, yet the crucial role of ovarian hormones in normal breast development and function, and their links to breast cancer are undeniable. Large clinical studies of women exposed to progesterone in hormone replacement therapy have unequivocally demonstrated that exposure to progesterone in these formulations increases a woman's risk of developing breast cancer.

We are investigating the effects of ovarian hormones in normal breast development. Using an innovative three-dimensional model we have developed previously, we are investigating development of the normal breast with treatment regimens mimicking the menstrual cycle. In 2009 we gained valuable knowledge as to how the ovarian hormones individually and in concert regulated normal breast development. Using primary

normal tissues and methods optimized in our lab, we are employing high throughput digital immunofluorescent image analysis to investigate the effects of oral contraceptive and hormone replacement formulations on normal breast biology.

Progesterone exerts its effects through the progesterone receptor, which resides in the cell nucleus and, when bound to progesterone, associates with specific sites on chromosomal DNA to regulate expression of specific target genes. We have previously shown that normal progesterone receptor function is dependent on the formation of aggregates between the receptor and important co-factors in the nucleus. In 2009 we specifically identified one of these key co-regulators, which showed higher expression in cancer cells compared to normal breast cells, suggesting that these co-factors may form abnormal aggregates with the progesterone receptor in cancer. We also utilised a powerful technique that uses high throughput sequencing, across the entire human genome, to predict which genes the progesterone receptor binds to and regulates. We have now identified new target DNAs with which the progesterone receptor interacts, and work is continuing on this analysis to identify further targets, as well as comparing these interactions between normal and breast cancer cells.

Although progesterone is critical in normal breast development, it has since emerged that it is also a major driver of breast cancer risk. Despite this, healthy women are still regularly exposed to synthetic progesterone analogues, such as in the oral contraceptive pill and hormone replacement therapy. Therefore, it is critical that we understand the mechanisms by which progesterone influences breast cancer development so that we can devise strategies to circumvent this increased breast cancer risk.

#### Breast Cancer Tissue Bank

In 2009 the Breast Cancer Tissue (BCTB) has continued its activity, recruiting donors and collecting and processing specimens from breast cancer patients at BCTB collection centres located across both metropolitan and regional areas of NSW. In addition, a new collection centre based in the ACT began operations and collects from donors in Canberra and South East NSW.

The BCTB headquarters are located within WMI, and management of an extensive clinical and specimen data base is maintained and is being continually enhanced within the WMI facility. Clinical follow up data on donors is also facilitated within WMI. During 2009 almost 1,000 new donors were recruited to the Bank bringing the total number of donors at the end of the year to over 2,500.

By having actual patient material and data available which has been collected and stored in accordance with world best practice guidelines, the BCTB can support breast cancer research programs across Australia and thus expedite the research effort with the ultimate aim of the translation of research knowledge into clinical practice.

Applications to the BCTB for material and data are subject to scientific scrutiny ensuring the high quality of projects supported. In 2009 a number of applications were received and a total of 2,200 individual specimens were dispatched to research projects across Australia.

### Melanoma cell cycle research

We now know that cancer is caused by genetic changes, or mutations, in cells. However, the precise sequence of mutations required to transform a dormant melanocyte into a melanoma remains unresolved. In recent years the group's work has contributed to the identification of several critical pathways crucial to this process. In particular, the p16INK4a/p14ARF locus, which encodes the tumour suppressor proteins p16INK4a and p14ARF, is altered in 39% of melanoma-prone families and a single base change that activates the BRAF oncogene is found in 50-70% of melanomas.

Unexpectedly, this activating BRAF mutation is also found in 80% of benign acquired naevi on sun-exposed skin. High numbers of naevi are associated strongly with melanoma risk but the vast majority of benign naevi never form melanomas, remain arrested for decades and many gradually disappear. Thus, although aberrant activation of BRAF plays a role in melanoma, it also triggers a permanent form of growth arrest, known as senescence, in normal melanocytes. This apparent paradox can be reconciled by the observation that BRAF-induced senescence is bypassed by additional genetic alterations. The Melanoma Cell Cycle Research Group is

investigating the mechanisms responsible for BRAF-induced growth arrest, which is clearly critical in protecting against melanoma formation. In addition, our research will resolve the molecular events that occur during melanoma development and progression.

The team recently confirmed that activated BRAF promotes senescence in human melanocytes. More importantly, they showed that the BRAF-induced protective growth arrest did not require the accumulation of the p14ARF or p16INK4a tumour suppressor proteins. In particular, when p14ARF and p16INK4a expression was silenced in human melanocytes, activated BRAF retained its potent growth inhibitory activity. They also confirmed that the p53 tumour suppressor, which is inactivated in most human cancers, is not necessary for BRAF-induced senescence in melanocytes. These data suggest that additional genes regulate BRAF activity and protect melanocytes from abnormal proliferation and transformation. The group is exploring potential candidate genes that regulate BRAF-induced arrest in human melanocytes.

In recent work secreted factors, such as IL-6 and IGFBP7 have been found to play a significant role in senescence. Our group readdressed the role of IGFBP7 in BRAF induced senescence in human melanocytes. We found no correlation between BRAF mutational status and IGFBP7 expression levels in a series of melanoma cell lines and benign naevi. Furthermore, we found that BRAF potently induced senescence in the presence and absence of IGFBP7. Therefore, the molecules required for BRAF-induced senescence in human melanocytes remain to be defined.

The Melanoma Cell Cycle research team have also shown that accumulation of the p16INK4a tumour suppressor promotes rapid cell cycle arrest that leads to a senescence program characterized by the appearance of DNA foci, activation of acidic  $\beta$ -galactosidase activity and p53-independence. The team also developed a rapid and accurate functional screen to determine the functional significance of melanoma-associated p16INK4a mutations. The ability to determine variant functional activity accurately would identify disease-associated mutations and facilitate effective genetic counselling of individuals at high risk of melanoma.

The BRAF, p16INK4a and p14ARF molecules are critical in the genesis of melanoma and this research team continues to investigate their functions. This work is essential to the development of a rational approach to targeted therapy for this destructive disease.

### Familial Cancer Research Group

The Familial Cancer Research Group uses genetic testing to identify individuals at high genetic risk of cancer. In conjunction with this clinical service, many patients are enrolled in collaborative, genetic-epidemiological studies investigating the familial aspects of cancer. As many high-risk individuals have now been identified, the group established a risk-management clinic in 2006 that facilitates co-ordinated, multidisciplinary care of women at high risk of breast and ovarian cancer, as well as providing further opportunities for research. Studies done on the molecular profile of ductal lavage fluid from women at high risk are on-going. By 2010, as part of a new research study, most younger (<50) women with a new diagnosis of breast cancer will be offered rapid turnaround "treatment focussed" genetic testing. This study has now been approved to start at Westmead. The results will guide cancer management decisions and allow for the appropriate use of the newly developed targeted therapies such as the PARP-inhibitors.

The group continues to participate in the international GOG-199 study, aimed at assessing the usefulness of screening versus preventive surgery in women at increased risk of cancer of the ovary and fallopian tubes. The group has maintained its role in the study of tamoxifen in breast cancer prevention for those at higher risk based on family history (IBIS). As a result of such studies, women at increased risk of breast cancer may choose to take Tamoxifen or Raloxifene to reduce the risk of breast cancer. Several new studies have been published as a result of collaborations in the investigation of the psychosocial aspects of genetic counselling for cancer susceptibility, including studies the use of telehealth to provide genetic services to rural areas. The group has successfully applied for new funding to extend work already done in developing an on-line tool to assess risk of bowel cancer based on family history of the disease.

Males from families with a genetic predisposition to breast/ovarian cancer due to germline BRCA1/BRCA2 gene mutations are at increased risk of prostate cancer. The IMPACT study (Identification of Men with a genetic predisposition to ProstAte. Cancer Targeted Screening in BRCA1/2 mutation carriers and controls) is evaluating screening in this population. Preliminary results from this study are about to be published in the British Journal of Urology, indicating that these men tend to develop a quite aggressive form of prostate cancer.

The group's laboratory provides a testing service for individuals in the families described above, primarily for mutations in the BRCA1 and BRCA2 breast cancer susceptibility genes. In addition, there is some testing for susceptibility to melanoma. The laboratory's research program has been successfully directed towards improved screening for BRCA1 and BRCA2 mutations and continues to focus on improvements to testing and the understanding of the gene mutations (and unclassified variants) that are detected by screening.

### Gene expression in cancer

The Gene Expression Laboratory investigates the impact of APC alterations and function in the cell. By employing sophisticated cell biology and microscopic imaging techniques, they mapped fundamental differences in the cellular location and activity of mutated APC proteins. In 2009 they pursued new studies that show a link between APC and DNA replication in the cell nucleus, with implications for understanding why some chemotherapy drugs might have reduced activity in APC-mutated colorectal cancers.

In 2009 other protein regulators of colon cancer were also investigated. In particular, the oncogenic protein beta-catenin was analysed for its movement between the nucleus and cell membrane, and shown to display a rapid turnover at plasma membrane "ruffle" structures involved in cell movement. This work was published and the first to provide a clear analysis of beta-catenin movement in living cells.

This team has also continued their study of the tumour suppressors BRCA1 and BARD1 in breast cancer, and completed new cell imaging studies that characterise the movement of BRCA1/BARD1 to nuclear DNA repair foci and to mitochondria in cancer cells.

### Melanoma Genomics and Genetic Epidemiology

The WICR melanoma genomics and genetic epidemiology group has two major goals. First we want to identify all the genes that most strongly affect melanoma risk, and how that genetic risk interacts with the environment, and we have established a leading role in that field over many years. More recently we have begun systematically searching for the genes and proteins that make some melanomas more dangerous than others. In collaboration with the cell cycle research group we study how these specific genetic changes work to produce melanoma. Our groups are part of a comprehensive research program funded by NHMRC and the Cancer Institute NSW in a multidisciplinary partnership with the clinicians and pathologists of the Sydney Melanoma Unit (now Melanoma Institute Australia), the world's largest melanoma clinical research centre.

Samples and data from thousands of people with a strong family history of melanoma, who have supported our projects over the last twenty years, have been used to identify new melanoma genes. In addition, our Australian Melanoma Family Study (AMFS), one of the world's largest population-based studies of melanoma, has studied people who developed melanoma before age 40 in Melbourne, Sydney and Brisbane, or unaffected controls, plus thousands of their family members. Early-onset melanoma can be indicative of increased susceptibility, but little has been known about what genes contribute to risk in this setting.

We have reported in the prestigious journal *Nature Genetics* two studies that used up to 600,000 DNA markers to compare the genes of people who have had melanoma with those who had not. We identified several genes that make a large contribution to the risk of melanoma in the community; some are involved in skin pigmentation, some in mole development, and others have functions that aren't yet clear. These genome-wide association studies (GWAS) have involved 22 research groups of the international melanoma genetics consortium (GenoMEL) and several million dollars' funding support from the European Union and US agencies such as the National Institutes of Health. They have highlighted the contributions WICR researchers are making to melanoma research around the world.

We have gone on to analyse the effect of the environment and lifestyle in the AMFS and have shown that an alarming number of melanomas under 30 can be attributed to the use of sunbeds or solaria.

As part of our CINSW Program we established Australia's first research clinic for people with a high risk of melanoma in the Sydney Melanoma Diagnostic Centre. It is trialling photographic and other surveillance in a study group of 300 patients whose risk of melanoma is more than ten times the average. We are showing that new melanomas have been detected early but without excessive removal of non-malignant moles. We have continued to report some of the first research anywhere in the world on perception of melanoma risk and the psychological consequences of high melanoma risk in our melanoma families. These studies have major translational significance and have spun off additional grant support from beyondblue, a national mental health initiative.

We are well advanced in wide-ranging studies of all the genetic and protein abnormalities in melanomas themselves. The goals of this research are to understand how apparently similar melanomas can have such different clinical behaviour, whether a greater propensity to relapse after surgery, or differing responsiveness to drug and biological treatment. These studies are showing that specific mutations, proteins and expressed genes have a strong influence on melanoma outcome and point the way to improved diagnostic tests to support melanoma care, as well as to new targets for melanoma treatment.

### Gynaecological cancers

Ovarian cancer is the most lethal gynaecological malignancy. The Gynaecological Cancer Research Group has a program of research which aims to improve our understanding of the progression from healthy cells to ovarian cancer and to improve our understanding of what determines how a patient will respond to chemotherapy.

The Gynaecological Cancer Research Group has continued to work with collaborators on the Australian Ovarian Cancer Study (AOCS), a major national collaborative project involving WICR, the Peter McCallum Cancer Centre (Melbourne), the Queensland Institute for Medical Research (Brisbane) and over

20 cancer treatment centres across the country. During 2009, in collaboration with Prof David Bowtell and investigators at the Peter Mac, regions of the genome were identified that were specifically amplified or lost in ovarian tumours in association with treatment outcome, for instance the genomic region encoding a central cell cycle gene, Cyclin E, was amplified in women that did not respond to conventional chemotherapy. This work was published in the journal *Clinical Cancer Research*, and researchers are continuing to work on the mechanisms underlying this effect so that the results can be translated into improved treatment outcomes.

Another major thrust of the Gynaecological Oncology Research Group is the identification of genes and pathways that are involved in the initial steps leading to ovarian cancer and may modify a woman's risk of developing cancer. In addition to the publication of gene signatures related to ovulation, a major risk factor in ovarian cancer, this work has led to a new pilot grant from the US (Marsha Rivkin Centre for Ovarian Cancer Research) to further examine aberrant gene expression patterns in malignant human ovarian cells and in samples from women at high genetic risk of developing ovarian cancer.

In 2009 the group also participated in an international collaboration led by Dr David Huntsman (British Columbia Cancer Agency, Vancouver) which identified a likely "driver" mutation of the *FOXL2* gene in adult-type granulosa-cell tumors, relatively uncommon neoplasms that account for 3 to 5% of all ovarian cancers. This mutation was one of the first identified using whole-transcriptome paired-end RNA sequencing (also called RNA-seq) and was published in the *New England Journal of Medicine*.

### Leukaemia cell biology

Acute Lymphoblastic Leukaemia (ALL) is the most common childhood cancer and although responsive to chemotherapy, 20% of children and 65% of adults will relapse following treatment. Survival following relapse is poor particularly in adult patients. New treatments for ALL are necessary to improve outcomes for these patients.

ALL cells are highly dependent on the support of other bone marrow cells, generally referred to as stroma, for their growth and survival. These cells also provide protection from the effects

of chemotherapy. The leukaemia cell biology group has been investigating ways in which the bone marrow supports ALL cells with the aim of disrupting this supportive and protective function to enhance currently used therapeutic protocols.

The group has identified a number of stroma-derived factors that modulate ALL cell growth including the cytokines IL-7, VEGF, and PDGF. However the chemokine SDF-1 is the major factor that supports ALL cells. Drugs that can block the effects of SDF-1 mobilize ALL cells into the peripheral blood making them more susceptible to chemotherapy. These drugs inhibit the growth of ALL cells in the laboratory and in a mouse model of human leukaemia. However, normal bone marrow stem cells are similarly mobilized. We have recently determined that ALL cells remain in the circulation longer than normal stem cells providing a window where the administration of chemotherapy would be expected to produce maximal ALL cell kill with minimal effects on normal cells.

SDF-1 activates a number of molecules within ALL cells. Targeting the p38 MAPK signalling pathway specifically mobilizes ALL cells but not normal haematopoietic stem cells. This has the potential to increase the specificity of current used therapies for ALL cells. Inhibition of p38 MAPK also has direct effects on the proliferation and survival of ALL cells and increases their sensitivity to chemotherapeutic agents. This is at least partially mediated by decreasing the production of supportive factors by the stromal cells. The potential utility of p38 MAPK inhibition as a therapeutic strategy is currently under investigation in pre-clinical models.

The PI-3 kinase pathway is also activated by SDF-1 as well as a number of other supportive factors produced by stromal cells. Disruption of this pathway by blocking a central molecule mTOR results the suppression of growth and induction of cell death in ALL cells. The mechanism of cell death is different from that induced by chemotherapy agents, and as a result, blockade of mTOR enhances the efficacy of chemotherapy in pre-clinical studies of mTOR inhibitors in ALL. A clinical trial of drugs that block mTOR in patients with relapsed acute lymphoblastic leukaemia has now been approved.

### Leukaemia cell therapies

The Cell Therapies group focuses on investigating the use of targeted cells for the treatment of infectious and malignant disease in patients with haematological malignancy. In the last 3 years, the group has been enrolling patients into a gene therapy study in which CMV specific T cells are generated using an adenoviral vector containing the entire CMV pp65 gene. T cells are given to patients after allogeneic stem cell transplantation.

More than 30 patients have received T cell infusions from their donors and excellent control of CMV has been observed. The team is now moving to expand the applicability of T cell infusions to other areas and shortly will introduce infusions that have specificity for a number of other opportunistic infections including EBV and VZV viruses that are common in immunosuppressed individuals.

Immunity to the BK virus that causes bladder and kidney problems in both stem cell and renal transplant recipients is being actively investigated and appears also to be amenable to cell therapy. It is anticipated that clinical trials in these areas will also commence shortly.

Recently, permission was obtained from the National Marrow Donor Program of the USA to utilise stem cell products from American Donors for T cell infusions widening the applicability of T cell infusions to patients with overseas unrelated donors and simplifying the production process for T cell generation. These advances will enhance the availability to cell therapies to a wide range of immunosuppressed patients.

### Translational Oncology

The aim of the Translational Oncology is to conduct research that is specifically focussed on important clinical issues in oncology, and a major focus of the group is the pathology of breast cancer.

Mammographic screening for breast cancer is an important part of the strategy to reduce the impact from this disease. It has also created a number of challenges in breast pathology reporting. In particular, there are a range of non-cancerous lesions that may give rise to abnormal mammographic appearances prompting investigation by biopsy. This includes a category known as 'columnar cell lesions' of the breast or

CCLs. While it is clear that CCLs are not themselves malignant, their clinical significance is uncertain and it is important that we learn more about their natural history and any relationship to breast cancer. There have been a number of studies in this area, but progress to date has been hampered by inconsistent nomenclature and classification schemes that make it difficult to directly compare results.

The Translational Oncology group addressed this issue with a study that examined pathologic features of 102 CCLs diagnosed on biopsy following mammographic detection. A systematic analysis approach was applied to determine whether there were natural groupings inherent within the spectrum of screen detected CLLs that might form the basis of a robust classification scheme. A striking finding from this analysis was that there was extreme variability in the pathologic features of CCLs. However, it was possible to delineate a subgroup consisting of about one third of the 102 cases, that had milder pathologic features and a lower proliferation rate. Using a classification algorithm, this CCL type could be identified in a second series of 32 cases and it was concluded that this classification approach could form a basis for future studies on the nature and significance of CCLs. Results of this study have been published in the journal Pathology (1).

## LIVER AND METABOLIC

### STORR LIVER UNIT

#### Hepatitis C

In 2009 we continued our investigation of hepatitis C virus (HCV)-induced insulin resistance. Following our results last year, we recently confirmed increased inhibitory phosphorylation of the PI3 kinase/Akt pathway inhibitor PTEN in HCV infected cells. This suggests a novel mechanism contributing to HCV-induced insulin resistance and a manuscript is currently being drafted. We have known for several years that Hepatitis C, a common cause of liver cirrhosis and cancer, also makes people three to four times more likely to develop Type 2 diabetes. In studying the insulin resistance of 29 people with Hepatitis C, we have now confirmed not only that they have high insulin

resistance, a precursor to diabetes, but also that they have little or no insulin resistance in the liver. This is a very surprising finding given that Hepatitis C is a liver disease. This observation promises to alter the way we consider hepatitis C pathogenesis and its consequences.

To study whether insulin sensitising drugs increase the effect of interferon on HCV we have established cell culture models of replicating virus that incorporate a luciferase reporter. We have shown that drugs that improve cell insulin sensitivity, especially PPAR- agonists, enhance the ability of interferon to suppress virus replication. We are currently determining optimal combination treatment conditions and are planning experiments to investigate the underlying mechanisms.

Cannabinoid receptors play an important role in the promotion of steatosis and fibrosis in chronic liver disease, but there are no data on their role in hepatitis C. We have showed that in HCV infection, CB1 cannabinoid receptors are upregulated, both in patients with chronic hepatitis C and in Huh7 cells infected with HCV (JFH-1). This suggested that the virus may directly up-regulate the endocannabinoid system. Since HCV replication is closely linked to lipid metabolism increased CB1 signalling should increase lipid storage and favour viral replication, which has been confirmed in in vitro studies.

### Fatty Liver Disease

In 100 subjects with NAFLD and 129 matched controls we showed the importance of the novel adipocytokine Adipocyte Fatty acid-binding Protein (AFABP) to the pathogenesis of NASH. Levels of AFABP were independently associated with severity of liver necroinflammation and fibrosis and were predictive of NASH vs simple steatosis. Interestingly, AFABP correlated with insulin resistance and subcutaneous fat. The novel cytokine lipocalin-2 correlated with insulin resistance and its levels were higher in NAFLD compared to control. It was not associated with histological severity of NASH. Finally, we assessed retinol binding protein-4 (RBP-4), but found no association with NAFLD, or indeed with insulin resistance. These data have been published in *Hepatology*. Adiponectin: NASH cirrhosis is characterised by gradual fat loss and a paradoxical increase in serum adiponectin. In 119 patients with NASH we examined whether adiponectin correlated with

hepatic fat loss in advanced NASH. All patients had hepatic fat measured by digital morphometry and adiponectin and leptin measured by ELISA. We showed that in advanced NASH (F3-4) adiponectin levels increased with hepatic fat loss in a highly significant manner. Indeed, in advanced NASH the only associations with reduced hepatic fat were adiponectin, patient age and bilirubin. Adiponectin was the only independent predictor of hepatic fat loss even when controlled for these factors as well as insulin resistance and BMI. These data answer a major clinical conundrum and a manuscript is under preparation.

### Liver Fibrosis

We have extended data from 2008 which examined the role of adiponectin in mediating liver injury by in vitro studies on Hepatic stellate cells (HSCs) and Kupffer cells (KCs). Last year our data suggested an important role for IL10 and TIMP1 in mediating the effects of adiponectin on the liver. In 2009, using scratch wounding migration assays, we found that adiponectin inhibited wound healing and that the application of anti-TIMP-1 antibodies in the presence of adiponectin accelerated wound recovery. In Boyden chamber invasion assays in which the filter was coated with rat tail Collagen 1, adiponectin retarded cell invasion and anti-TIMP-1 antibodies abrogated this effect. Taken together with previous data, we find that adiponectin promotes IL-10 and TIMP-1 secretion which impacts on HSC apoptosis, migration and invasion. We are now examining the potential role of adiponectin's ability to regulate IL-10, TIMP-1 levels and HSC apoptosis in vivo using mouse models.

In 2008, we demonstrated that in KCs, adiponectin induced IL10 mRNA up to 53 fold, but at the same time had an initial pro-inflammatory effect markedly increasing cytokines such as TNF ; continued exposure to adiponectin had the opposite, anti-inflammatory effect. We now find that IL-10 neutralising antibodies abrogate the late phase cytokine down-regulation observed in adiponectin primed KCs. In agreement, the application of recombinant IL-10 negates the cytokine up-regulation observed in non-primed KCs. Mechanistically, we find that the MAP kinase pathways are involved are now testing the relevance of adiponectin and IL-10 treatment on KCs inflammatory response in mouse models. Thus, in sum we find that adiponectin induces IL-10 in KCs and this abrogates LPS-

induced TNF, TGF, PDGF and CTGF expression and in part, mediates its anti-inflammatory and anti-fibrotic effects on the liver. Further in vitro and in vivo studies to examine the molecular basis of these effects are underway.

We have sought to elucidate whether adiponectin mediates nitric oxide (NO) production in nonparenchymal liver cells and whether increased NO modulates the antifibrogenic effects of adiponectin. We find that the gene and protein expression of iNOS in HSCs and KCs is hugely up-regulated by adiponectin treatment (mRNA expression: 1000 fold and 8000 fold, respectively). Protein expression: 7.7 fold and 7.2 fold, respectively). Similarly, eNOS phosphoprotein was increased (1.8 fold,  $p < 0.05$ ). Additional experiments showed that the AMPK inhibitor, Compound C down-regulated adiponectin-induced iNOS gene expression, suggesting that iNOS induction by adiponectin may be AMPK mediated. In further experiments, we show that concentrations of NO metabolites (NO<sub>2</sub>-/NO<sub>3</sub>-) in HSC, KC and SEC cultured medium treated with adiponectin were significantly elevated (36 fold in HSCs, 9 fold in KCs and 1.75 fold in SECs,  $p < 0.01$  and  $0.05$ ). We have confirmed that the above effects of adiponectin are not due to endotoxin contamination. Finally, since HSC contraction plays an important role in mediating intrahepatic sinusoidal size in cirrhosis and contributes to portal hypertension, we determined whether adiponectin modulates endothelin-1 induced HSC contraction. Adiponectin (5 µg/mL) remarkably attenuated ET-1 - elicited HSC contraction, an effect reversed by the NO inhibitor (L-NAME). These exciting results will be further investigated in future

### Genetics of treatment response in hepatitis C

Perhaps the highlight of 2009 has been our seminal paper published in Nature Genetics on the role of host genetics and treatment response in chronic hepatitis C. This paper which followed a genome wide analysis of host factors that influence response to treatment in chronic hepatitis C infection was part of a multinational genetic consortium headed by the Storr Liver Unit and undertaken at the Westmead Millennium Institute. In essence, we showed that polymorphisms in a gene (IL28B) are the most crucial determinant of treatment outcome (success or failure) in chronic hepatitis C. Regarded as one of the most

important advances in hepatitis C in the last decade, this discovery is the subject of a University patent and promises to significantly alter patient management. The paper has received widespread coverage in research journals, lay publications, web sites and in News reports.

### Liver Cancer

A second paper on the use of a novel form of therapy (Yttrium-90 resin microspheres) for the treatment of cancer in the liver was published in the Journal of Clinical Oncology with an editorial comment and has received much attention. A third report (Journal of Hepatology) on the cost effectiveness of cancer screening and treatment of Hepatitis B has had major public health impact and is the basis of a New South Wales Cancer Council and Storr Liver Unit initiative to increase hepatitis B case-finding and treatment in the State. This study has received widespread interest from other States and Territories.

### Disposition of Cancer Drugs

Working with the Department of Medical Oncology and Westmead Hospital we are involved in two projects that seek to develop better dosing regimes for the treatment of serious cancers. The first project involves screening patients receiving a new generation of anti-cancer drugs called 'kinase inhibitors' for a large range of genetic mutations in genes involved in drug metabolism and drug transport using custom gene array technology. These mutations are then statistically compared to adverse treatment outcomes to determine if the poor outcome could have been predicted in advance by a genetic test. Screening for 378 mutations yielded one that was predictive and we are extending this work to determine if this finding can be translated to the clinic for routine patient management. The second project revolves around the observation that the commonly used breast cancer drug Tamoxifen exerts its beneficial effects through a metabolite formed in the liver called Endoxifen. Unfortunately, the formation of Endoxifen is highly variable between patients so not all receive the maximum effect of Tamoxifen. We have set up a mass spectrometry-based assay for Endoxifen for use in a targeted dosing study. Patients will have their Tamoxifen dose varied so that the serum Endoxifen level is within a desired range. Patients will be followed long term to see if this improves breast cancer outcomes.

## NEUROSCIENCE AND VISION

### BRAIN DYNAMICS CENTRE

#### Wellbeing

##### Biological markers of Mental Health in Twins

Reduced wellbeing and resilience is a hallmark risk factor for poor mental health. The goal of the TWIN-RESILIENCE Study is to identify those gene, environment and brain markers that predict resilience over time in a large cohort of 1500 healthy twins. This project is a large national ARC-Linkage project coordinated by the Brain Dynamics Centre (Westmead Millennium Institute, University of Sydney) in collaboration with POWMRI, Flinders University of South Australia, industry partner Brain Resource Ltd, with support from the Australian Twins Registry. This project commenced in 2009 and was very successful in recruiting almost 30% of the target sample by end-2009, with the anticipated completion date of the first wave of testing by end-2010. Participants are assessed on a number of measures of resilience, including genetic, neurocognitive, and EEG/ MRI brain function measures. By comparing MZ to DZ twins, we will also be able to assess the contribution of heritability versus environmental factors in resilience. This information is important given evidence that genetic-environmental interactions are key to our risk and resilience for major mental health conditions such as depression, anxiety disorders, ADHD or schizophrenia.

#### Depression

##### International Study to Predict Optimized Treatment – in Depression

Currently, only 40% of patients respond well to antidepressants and there is no objective test to help clinicians determine which are best to prescribe for an individual with MDD. iSPOT-D is the largest biomarker study ever undertaken in major depressive disorder (MDD) and the first trial to study objective tests of brain and genetics. The iSPOT-D aim is to find a guidance tool which would be most useful to apply in routine practice. This is a global study, with the Brain Dynamics Centre as a leading site. The BDC site of iSPOT-D study saw significant progress in 2009. The year saw our first completed subjects (1 year in duration),

40 MDD patients were enrolled as well as 39 healthy control participants. This impacted globally, making BDC the 3rd highest recruiter world-wide with the 2nd highest retention rate of 86%.

BDC's iSPOT-D study also received significant attention in the community in 2009 with media coverage and feature articles in leading newspapers in Sydney, Canberra, Newcastle and Parramatta, articles in online newspapers (such as ABC News, Nine News, The Age, Virtual Medicine Website, and The West Australian), as well as radio segments on 2GB and NOVA 96.9. 2009 also saw the collaboration of 32 General Practitioners who are referring to our Centre for this study.

##### Study of the family members of people with Depression

Supported by an ARC Discovery grant, this study addresses the current absence of an objective test or set of biological markers that can detect early signs of depression. We are assessing candidate gene-brain-behaviour risk markers in the unaffected first degree relatives of people with depression. Family members are a valuable comparison group because they share biological predispositions with people who have depression, but do not have depressive symptoms. Recruitment of participants is continuing over the course of the year to reach a total of 200. A summary paper on emotion identification as a risk marker has been submitted for publication.

#### Post-Traumatic Stress Disorder

##### Anxiety

This study looks at biological markers of PTSD and prediction of treatment response. Recruitment is ongoing and participants with PTSD will undergo 10 weeks of cognitive behavior therapy (CBT). We aim to identify brain markers associated with response to CBT, as well as genetic variance. The results of this study will be used to identify the specific effects of CBT on psychological, physiological and overall functioning of people with PTSD.

#### NHMRC Centre for Clinical Research Excellence (CCRE):

##### Anxiety and Neuroscience

The aim of this study is to identify biological markers of anxiety disorders and response to treatment in these disorders.

The focus is on cognitive behavioral therapy (CBT), a common first-line treatment for anxiety disorders. We are looking at both cognitive and physiological measures that were specifically designed for the anxiety disorders to allow for a more precise evaluation of the effectiveness of CBT. This study looks at social anxiety disorder, panic disorder, generalized anxiety disorder, post-traumatic stress disorder (PTSD) and depression. The goal of this study is to use the obtained results to improve existing treatments.

## Schizophrenia

### Missing links: cause and treatment of mental illness

This fellowship is supporting research into schizophrenia. Schizophrenia is characterized by high-level breakdowns in connectivity, affecting functioning across domains of emotion, thinking, feeling and self-regulation. The data collected so far under this fellowship has allowed examination across a range of clinical, cognitive and brain function measures.

Publications of this data in 2009, and those forthcoming in 2010, have focused on presenting an integrative view of these measures and highlighting the relationships between them. A measure of particular focus has been "gamma synchrony", which can be recorded with electroencephalographic methods and has been proposed to be involved in binding information together in the brain. The team at the Brain Dynamics Centre has been one of the few groups to look at gamma synchrony in the context of emotional functioning, in addition to thinking tasks.

### Childhood onset psychosis: risk factors and biological markers

In patients with early or childhood-onset schizophrenia, psychotic symptoms develop and present before the age of 18. This is a particularly severe form of schizophrenia, with the potential to severely affect social functioning and quality of life throughout adulthood.

In collaboration with the Children's Hospital at Westmead, The Brain Dynamics Centre is assessing the clinical, cognitive and brain function markers for childhood- and early-onset psychosis. If objective markers can be identified, they may one day be able to provide support for diagnostic and treatment decisions. In

2009, pilot data from this study was presented at conferences, and as of early 2010, 75% of the target sample has been recruited and tested. Data analyses are continuing.

## Disorders of adolescent mental health

### ADHD Controlled Trial Investigation of a Non-stimulant

Attention deficit hyperactivity disorder (ADHD) is the most commonly diagnosed psychiatric disorder in children and young people, and is generally characterized by inattentiveness, impulsivity, and/or hyperactivity. ADHD has traditionally been diagnosed via subjective reports by parents/guardians and observations by a paediatrician, which obviously has its limitations. The Brain Dynamics Centre (BDC), in collaboration with Brain Resource Company and The University of Sydney, has recently validated the use of a computer-based objective assessment tool (IntegNeuro™) for accurately distinguishing children and adolescents with ADHD from those without ADHD. This breakthrough discovery will assist researchers, clinicians, and families with the diagnosis, treatment, and further research of this common and often limiting psychiatric disorder.

Other research currently being conducted at the BDC includes the ACTION study, which is investigating the efficacy of a non-stimulant drug (atomoxetine, ATMX) for thinking and emotional function in ADHD, utilizing the aforementioned IntegNeuro™ assessment tool. The ACTION is due to finish in 2010. Upcoming ADHD studies include iSPOT-A, which will identify any markers capable of predicting those patients who will benefit most from stimulant medication. This study is expected to commence in the second half of 2010.

## CENTRE FOR VISION RESEARCH

### The Blue Mountains Eye Study

This benchmark population-based study in ophthalmology has almost completed 15-year follow-up of the original cohort from 1992. Collecting information on eye health, hearing and other sensory impairments, as well as general health and nutrition, once data entry is completed, this study will examine long-term risk factors for sensory loss as well as systemic diseases.

From blood samples collected at earlier stages of the study, this population sample has recently been genotyped, and we will examine genetic associations with eye disease and systemic traits in 2010. These tasks will involve large scale collaboration with national and international researchers. We have established such collaborations with some researchers but will continue to extend these further. One collaborative project combining the BMES, Beaver Dam Eye Study and the UK Twin Study has led to a well-documented link between the gene EPHA2 and one particular type (cortical) of cataract.

Data collected from previous stages of the study are still being analysed, and findings include a strong association from long-term use of steroids (for example for treating asthma), and an increased risk of developing cataract. Dietary data collected during the BMES baseline have now been used to investigate long-term associations of daily dietary food or nutrients (common environmental exposures) with risk of eye disease and systemic conditions.

#### The Blue Mountains Hearing Study

A number of publications in the area of age-related hearing loss have resulted, including findings published in the Archives of Internal Medicine showing that one in three older adults have hearing loss. Previously unavailable Australia data on the association between several risk factors (i.e. type 2 diabetes, stroke, smoking and alcohol consumption) and hearing loss were assessed, as were the adverse effects of hearing loss on the mental health of older Australians. In collaboration with the Bettering the Evaluation and Care of Health (BEACH) study, novel findings were published in the Medical Journal of Australia, showing relatively low levels of identification and management of hearing loss by GPs in Australia. These data highlight the need for improved education of GPs to better detect and manage older hearing impaired patients.

#### Retinal vessel signs in acute stroke patients

This study investigated the role of small vessel disease in acute stroke, and it is increasingly recognised that acute stroke such as lacunar infarction, deep intracerebral haemorrhage and other subtypes involve not only large vessel but also small vessel disease.

Assuming that retinal vascular changes mirror similar changes in the brain, this study showed that abnormalities in the retinal vessels are strongly linked to some types of stroke (lacunar infarction and deep intracerebral haemorrhage). This study suggests that different types of stroke have different causes, ultimately, highlighting the need for different approaches to treat different stroke types.

#### Cataract surgery and risk of age-related macular degeneration

This study is continuing the long-term follow-up of around 2000 participants, to determine the risk of cataract surgery and development of age-related macular degeneration.

#### Australian Heart Eye Study

Patient recruitment for this study commenced in 2009, from patients attending for coronary angiography. This study aims to examine associations between the microvasculature (as visible from photography of the retina) and coronary heart disease, and hence to determine what the risk signs are. Around 400 patients have been recruited, and have undergone retinal photography and completed the detailed questionnaire.

#### The Sydney Childhood Eye Study

Five year follow-up to the original Sydney Myopia Study which examined children in two age groups, 6- and 12-year-old students, is now well underway, with most primary schools re-visited and high schools booked in for 2010.

Once complete this study will have longitudinal data from children relatively free of pathology, enabling examination into the genesis of eye and systemic diseases.

Associations between retinal vascular calibre and blood pressure, obesity and birth weight that we previously observed in the younger children (6-year-olds), have been confirmed in the older children (12-year-olds). These data suggest that cardiovascular risk factors track from childhood through to adulthood, highlighting the need for better recognition and management of elevated blood pressure and obesity at younger ages, as a potential strategy for limiting the overall disease burden of cardiovascular disease in adulthood.

## CARDIO-RESPIRATORY

### CENTRE FOR HEART RESEARCH

#### Australian Heart Eye Study

The Australian Heart Eye Study is a collaborative research project with Centre for Vision Research. The purpose of the study is to assess whether changes detected in the blood vessels in the back of the eyes (retina) could provide useful information for the diagnosis and management of heart disease. Retinal photography provides the only opportunity to non-invasively examine blood vessels.

The study is enrolling a large number of patients (3,000) presenting to Westmead Hospital for coronary angiography. The patients are undergoing extensive non-invasive risk stratification including retinal photography. We hypothesise that retinal vessel changes will be associated with both ischaemic heart disease secondary to epicardial coronary artery disease and subtypes of ischaemic heart disease associated with microvascular disease.

#### Molecular basis of cardiac rhythm

In 2009, the Centre for Heart Research continued to expand its basic research endeavours. The focus of this group is to understand the molecular basis of cardiac conduction. The group employs high-end molecular techniques involving viral vector-based gene and regulatory RNA transfer to somatic cells to genetically manipulate cells and tissues. These methods permit the characterization of the effects of these alterations on cardiac physiology. Furthermore, mechanistic insights into arrhythmias can be gleaned. The group uses cell culture and animal models. The proposed work is deliberately translational in nature with the hope of uncovering novel molecular targets for the treatment of cardiac arrhythmias.

#### Trial of Ablation Therapy for Atrial Fibrillation

Recently, minimally invasive radio frequency ablation procedures have been shown to treat atrial fibrillation effectively. However, this technique is still evolving and it is not clear how to maximise its efficacy while minimising complications. To clarify this, a clinical trial was initiated at Westmead to compare a novel ablation technique developed here for atrial fibrillation against a more commonly performed

technique. The trial now in progress is also looking at the long term effects of these techniques on heart function. We believe this trial may provide useful insights into how to optimise the treatment of atrial fibrillation and how to minimise patient complications.

#### Development of treatments for ventricular tachycardia

This project aims to understand how post-myocardial infarction substrate precipitates ventricular tachycardia and to develop novel strategies of mapping and ablation of ventricular tachycardia using non-invasive, non-contact electrophysiological mapping.

Non-invasive assessment of myocardial function is clinically performed using electrogram voltage mapping. The group assessed the in vivo effects of myocardial activation on electrogram dynamics in normal sheep hearts and found that the activation sequence of the heart has a significant impact on electrogram voltage and rate of local conduction. This adds to the understanding and interpretation of unipolar electrograms. Future application of regularisation of voltage based on the cardiac activation sequence may be applied to improve the accuracy of assessing myocardial function.

Clinical evidence suggests that ventricular tachycardia often precipitates at the border zone of scarred and non-scarred myocardium. In an ovine model of myocardial infarction the group compared the performance of identifying ventricular scarring using a multimodality of conventional electroanatomical mapping technologies. The group also developed and validated a novel method of non-contact mapping of scar which was validated from functional and structural assessment of the myocardium. The novel method of scarring offered greater accuracy and resolution in identifying ventricular scar tissue over conventional modalities of mapping.

Traditional single chamber noncontact mapping has limited ability to identify and map ventricular tachycardia originating from the septum. In an ovine model of chronic anterior myocardial infarction, the group mapped ventricular tachycardia using simultaneous dual chamber non-contact mapping. The group demonstrated that the septum played a significant role in initiating ventricular tachycardia in this animal model, and were able to identify potential target sites of radio frequency

ablation. Research is currently being undertaken to identify the association of septal scarring and the mechanism responsible for initiation of ventricular tachycardia.

## LUDWIG ENGEL CENTRE FOR RESPIRATORY RESEARCH

### Sleep disordered breathing

Researchers are working to understand the processes associated with the occurrence of obstructed breathing during sleep in order to improve the treatments available for this important disorder.

Snoring has long been thought of as mainly a social nuisance, but there is growing evidence world wide of the possible health implications of habitual snoring. We have published a large study showing an increased prevalence of carotid artery atherosclerosis in heavy snorers. Studies undertaken this year have demonstrated that snoring like vibrations may be a factor responsible for triggering endothelial dysfunction. We are continuing this line of research to further explore the mechanisms by which snoring vibration energy may trigger the endothelial dysfunction and inflammation that may lead to carotid artery atherosclerosis, which is the leading cause of stroke.

Studies undertaken in 2009 include investigation of nasal dilator splints as a treatment to reduce disturbed sleep and sleep disordered breathing, measurements of the surface tension of the upper airway lining liquid in healthy subjects and OSAS patients, the impact of breathing route on the development of sleep disordered breathing, and the development of a computer model aimed at defining the relationships between peri-pharyngeal tissue pressure and upper airway patency. Ongoing studies have continued to explore the role of peri-pharyngeal tissue pressure in the pathogenesis of upper airway collapse, which is the major underlying cause of OSAS. We have also developed and published a new model of the upper airway functioning as a muscular hydrostat.

The group also participated in a study in Samoa demonstrating that CPAP treatment can effectively reduce blood pressure in patients with untreated severe sleep apnoea and hypertension.

### Cystic fibrosis

The researchers have been working on the nasal potential difference (NPD) technique which can diagnose Cystic fibrosis (CF), and LECRR is part of the European CF Diagnostic Network which is examining different groups of patients and comparing the nasal potential difference recordings with the severity of their disease. LECRR staff have recently compared different testing solutions in the NPD test which will allow the NPD to be used more effectively in multi-centre trials.

This NPD test also provides better understanding of the mechanisms involved in salt movement across the human airway and is helping to find new therapies which may bypass the defect in CF by stimulating different chloride channels to move salt in the right direction.

The group has just published a study of fungi in CF, showing the importance of correct analysis for new species of fungi, such as *Scedosporium*.

### Asthma and chronic obstructive pulmonary disease

Asthma now affects the lives of over 2 million Australian children and adults. Despite decades of research into the causes and treatment of asthma the prevalence of asthma in the population continues to rise. A major research interest of the centre is the influence of mouth versus nose breathing on the occurrence of asthmatic symptoms.

Chronic Obstructive Pulmonary Disease is the fourth leading cause of death and third leading cause of disease burden and it has been estimated that 2.1 million Australians have some form of COPD. Research in the Respiratory Ambulatory Care Service focuses on improving the quality of life of patients with COPD and their carers by the prevention of crisis situations in the community, reducing the frequency of avoidable admissions to hospital and improved integration of services.

Research completed over the past 12 months include the outcomes of a community outreach program for patients with COPD and a review of whether patients recently admitted to hospital with an acute exacerbation of their COPD will benefit most from pulmonary rehabilitation. Our study demonstrated that admission to hospital does not necessarily predict a favourable response to pulmonary rehabilitation.

**BRAIN DYNAMICS CENTRE**

Craig A, Tran Y, Hermens G, Williams LM, Kemp AH, Morris C & Gordon E. () Psychological and neural correlates of emotional intelligence in a large sample of adult males and females. *Personality and Individual Differences*, 46 (2) 111-115.

Falconer E, Felmingham K, Allen A, Clark CR, McFarlane A, Williams LM & Bryant RA (). Developing an integrated brain, behaviour & biological response profile in posttraumatic stress disorder (PTSD). *Journal of Integrative Neuroscience*, 7 (3): 439-456

Felmingham KL, Williams LM, Kemp AH, Rennie CJ, Gordon E, Bryant RA. Anterior cingulate activity to salient stimuli is modulated by autonomic arousal in posttraumatic stress disorder. *Psychiatry research*, 173(1):59-62.

Felmingham KL, Kemp AH, Williams LM, Falconer E, Olivieri G, Peduto A, Bryant RA. (). Dissociative responses to conscious and nonconscious fear impact underlying brain function in Posttraumatic Stress Disorder. *Psychological Medicine*, 38 (12) :1771-80

Gatt JM, Nemeroff CB, Dobson-Stone C, Paul RH, Bryant RA, Schofield P R, Gordon E, Kemp A H, Williams L M. (). Interactions between BDNF Val66Met polymorphism and early life stress predict brain and arousal pathways to syndromal depression and anxiety. *Molecular psychiatry* 14 (7):681-95.

Gow R, Matsudaira T, Taylor E, Rubia K, Crawford M, Ghebremeskel K, Ibrahimovic A, Vallée-Tourangeau F, Williams LM, Sumich A () Total red blood cell concentrations of Omega-3 fatty acids are associated with emotion-elicited neural activity in adolescent boys with attention-deficit hyperactivity disorder. *Prostaglandins, Leukotrienes and Essential Fatty Acids*, 80(2), 151-156

Hatch A, Madden S, Clarke S, Touyz S, Gordon E, Williams LM. EEG in adolescent Anorexia Nervosa: Impact of refeeding and weight gain. *Int. J Eating Disorders*.

Joffe RT, Gatt JM, Kemp AH, Grieve S, Dobson-Stone C, Kuan SA, Schofield PR, Gordon E & Williams LM (). Brain derived neurotrophic factor Val66Met polymorphism, the five factor model of personality and hippocampal volume: Implications for depressive illness. *Human Brain Mapping* 30(4):1246-1256

Kemp A H, Hatch A, Williams L M. (). Computerized neuropsychological assessments: pros and cons. *CNS Spectrums* 9, 14(3):118-120.

Kemp AH, Gordon E, Rush A & Williams LM (). Improving the prediction of treatment response in depression: integration of clinical, cognitive, psychophysiological, neuroimaging, and genetic measures. *CNS Spectrums* 13 (12) :1066-1086

Kemp AH, Hopkinson Patrick J, Hermens Daniel F, Rowe Donald L, Sumich Alexander L, Clark C Richard, Drinkenburg Wilhelmus, Abdi Nadia, Penrose Rebecca, McFarlane Alexander, Boyce Philip, Gordon E, Williams LM. Frontotemporal alterations within the first 200 ms during an attentional task distinguish major depression, non-clinical participants with depressed mood and healthy controls: a potential biomarker? *Human brain mapping*, 30(2):602-14.

Koslowska K, Williams LM () Self-protective organization in children with conversion and somatoform disorders. *Journal of Psychosomatic Research* 67 (3) 223-233

Mathersul Danielle, Palmer Donna M, Gur Ruben C, Gur Raquel E, Cooper Nick, Gordon E, Williams LM. Explicit identification and implicit recognition of facial emotions: II. Core domains and relationships with general cognition. *Journal of clinical and experimental neuropsychology*, 31(3):278-91.

Rubinov M, Knock SA, Stam CJ, Micheloyannis S, Harris AWF, Williams LM & Breakspear M. Small-world properties of nonlinear brain activity in schizophrenia. *Human brain mapping*, 30(2):403-16.

Schofield PR, Williams LM, Paul RH, Gatt JM, Brown KJ, Luty A, Cooper N, Grieve S, Dobson-Stone C, Kuan S & Gordon E (). Disturbances in selective information processing associated with the BDNF Val66Met polymorphism: Evidence from cognition, the P300, fronto-hippocampal systems. *Biological Psychology* 80(2):176-188

Whitford Thomas J, Farrow Tom F D, Williams LM, Gomes Lavier, Brennan John, Harris Anthony W F. (). Delusions and dorso-medial frontal cortex volume in first-episode schizophrenia: a voxel-based morphometry study. *Psychiatry research*, 172(3):175-9.

Williams LM, Gatt Justine M, Kuan Stacey A, Dobson-Stone Carol, Palmer Donna M, Paul Robert H, Song Le, Costa Paul T, Schofield Peter R, Gordon E. A polymorphism of the MAOA gene is associated with emotional brain markers and personality traits on an antisocial index. *Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology*, 34(7):1797-809.

Williams LM, Gatt Justine M, Schofield Peter R, Olivieri Gloria, Peduto Anthony, Gordon E 'Negativity bias' in risk for depression and anxiety: brain-body fear circuitry correlates, 5-HTT-LPR and early life stress. *NeuroImage*, 47(3):804-14.

Williams LM, Mathersul Danielle, Palmer Donna M, Gur Ruben C, Gur Raquel E, Gordon E. Explicit identification and implicit recognition of facial emotions: I. Age effects in males and females across 10 decades. *Journal of clinical and experimental neuropsychology*, 31(3):257-77.

Williams LM, Whitford Thomas J, Gordon E, Gomes Lavier, Brown Kerri J, Harris Anthony W F. Neural synchrony in patients with a first episode of schizophrenia: tracking relations with grey matter and symptom profile. *Journal of psychiatry & neuroscience: JPN*, 34(1):21-9.

Williams LM, Whitford Thomas J, Nagy Marie, Flynn Gary, Harris Anthony W F, Silverstein Steven M, Gordon Evian. Emotion-elicited gamma synchrony in patients with first-episode schizophrenia: a neural correlate of social cognition outcomes. *Journal of psychiatry & neuroscience: JPN*, 34(4):303-13.

Williams LM, Gatt JM, Kuan SA, Dobson-Stone C, Palmer DM, Paul RH, Song L, Costa PT, Schofield PR, Gordon E (). A polymorphism of the MAOA gene is associated with emotional brain markers and personality traits on an antisocial index. *Neuropsychopharmacology* 34(7) 1797-1809

**CENTRE FOR HEART RESEARCH**

Kumar S, Sivagangabalan G, Choi MC, Eipper V, Thiagalingam A, Kovoor P. Long-Term Outcomes of Inducible Very Fast Ventricular Tachycardia (Cycle Length 200-250 ms) in Patients With Ischemic Cardiomyopathy. *J Cardiovasc Electrophysiol*. Oct 8.

Sivagangabalan G, Pouliopoulos J, Huang K, Barry MA, Lu J, Thomas SP, Ross DL, Thiagalingam A, Kovoor P. Simultaneous biventricular noncontact mapping and ablation of septal ventricular tachycardia in a chronic ovine infarct model. *Circ Arrhythm Electrophysiol* Aug;2(4):441-9.

Kumar S, Hsieh C, Sivagangabalan G, Chan H, Ryding AD, Narayan A, Ong AT, Sadick N, Kovoor P. Prognostic impact of Q waves on presentation and ST resolution in patients with ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. *Am J Cardiol*. Sep 15;104(6):780-5.

Zaman S, Ramesh N, Kovoor P. Arrhythmogenic right ventricular cardiomyopathy presenting with intra-operative aborted sudden cardiac death and Takotsubo-like left ventricular functional abnormalities. *Hellenic J Cardiol*. Jul-Aug;50(4):330-4.

Zaman S, Sivagangabalan G, Narayan A, Thiagalingam A, Ross DL, Kovoor P. Outcomes of early risk stratification and targeted implantable cardioverter-defibrillator implantation after ST-elevation myocardial infarction treated with primary percutaneous coronary intervention. *Circulation*. Jul 21;120(3):194-200.

Pouliopoulos J, Thiagalingam A, Eipper VE, Campbell C, Ross DL, Kovoor P. Transmural mapping of myocardial refractoriness and endocardial dispersion of repolarization in an ovine model of chronic myocardial infarction. *Pacing Clin Electrophysiol*. Jul;32(7):851-61.

Sivagangabalan G, Ong AT, Narayan A, Sadick N, Hansen PS, Nelson GC, Flynn M, Ross DL, Boyages SC, Kovoov P. Effect of prehospital triage on revascularization times, left ventricular function, and survival in patients with ST-elevation myocardial infarction. *Am J Cardiol.* Apr 1;103(7):907-12.

Barile L, Cerisoli F, Frati G, Gaetani R, Chimenti I, Forte E, Cassinelli L, Spinardi L, Altomare C, Kizana E, Giacomello A, Messina E, Ottolenghi S, Magli MC. Bone marrow-derived cells can acquire cardiac stem cells properties in damaged heart. *J Cell Mol Med.* Nov 13.

Rosselló RA, Wang Z, Kizana E, Krebsbach PH, Kohn DH. Connexin 43 as a signaling platform for increasing the volume and spatial distribution of regenerated tissue. *Proc Natl Acad Sci U S A.* Aug 11;106(32):13219-24.

Kizana E, Cingolani E, Marbán E. Non-cell-autonomous effects of vector-expressed regulatory RNAs in mammalian heart cells. *Gene Ther.* Sep;16(9):1163-8.

Mahairaki V, Xu L, Farah MH, Hatfield G, Kizana E, Marbán E, Koliatsos VE. Targeted knock-down of neuronal nitric oxide synthase expression in basal forebrain with RNA interference. *J Neurosci Methods.* May 15;179(2):292-9.

Sekar RB, Kizana E, Cho HC, Molitoris JM, Hesketh GG, Eaton BP, Marbán E, Tung L. IK1 heterogeneity affects genesis and stability of spiral waves in cardiac myocyte monolayers. *Circ Res.* Feb;104(3):355-64.

Schmidt EJ, Mallozzi RP, Thiagalingam A, Holmvang G, d'Avila A, Guhde R, Darrow R, Slavin GS, Fung MM, Dando J, Foley L, Dumoulin CL, Reddy VY. Electroanatomic mapping and radiofrequency ablation of porcine left atria and atrioventricular nodes using magnetic resonance catheter tracking. *Circ Arrhythm Electrophysiol.* Dec;2(6):695-704.

Thiagalingam A, Reddy VY, Cury RC, Abbara S, Holmvang G, Thangaroopan M, Ruskin JN, d'Avila A. Pulmonary vein contraction: characterization of dynamic changes in pulmonary vein morphology using multiphase multislice computed tomography scanning. *Heart Rhythm.* 2008 Dec;5(12):1645-50.

Lim TW, Clout R, Barry MA, Lu J, Huang K, Thomas SP. Percutaneous Microwave Ablation with a Long Side-Firing Antenna Array Can Successfully Treat a Nonsurgical Chronic Ovine Atrial Flutter Model. *J Cardiovasc Electrophysiol.* Jul 13.

McCall R, Thomas SP. Esophageal hematoma complicating catheter ablation for atrial fibrillation. *J Cardiovasc Electrophysiol.* Feb;20(2):221-3.

Eshoo S, Ross DL, Thomas L. Impact of mild hypertension on left atrial size and function. *Circ Cardiovasc Imaging.* Mar;2(2):93-9.

Eshoo S, Boyd AC, Ross DL, Marwick TH, Thomas L. Strain rate evaluation of phasic atrial function in hypertension. *Heart.* Jul;95(14):1184-91.

Boyd AC, Schiller NB, Ross DL, Thomas L. Differential recovery of regional atrial contraction after restoration of sinus rhythm after intraoperative linear radiofrequency ablation for atrial fibrillation. *Am J Cardiol.* Feb 15;103(4):528-34.

Barile L, F. Cerisoli, G. Frati, R. Gaetani, I. Chimenti, E. Forte, L. Cassinelli, L. Spinardi, C. Altomare, E. Kizana, A. Giacomello, E. Messina, S. Ottolenghi and M. C. Magli (). "Bone marrow-derived cells can acquire cardiac stem cells properties in damaged heart." *J Cell Mol Med.*

Kizana, E., E. Cingolani and E. Marban (). "Non-cell-autonomous effects of vector-expressed regulatory RNAs in mammalian heart cells." *Gene Ther* 16(9): 1163-1168.

Mahairaki, V., L. Xu, M. H. Farah, G. Hatfield, E. Kizana, E. Marban and V. E. Koliatsos (). "Targeted knock-down of neuronal nitric oxide synthase expression in basal forebrain with RNA interference." *J Neurosci Methods* 179(2): 292-299.

Rossello, R. A., Z. Wang, E. Kizana, P. H. Krebsbach and D. H. Kohn (). "Connexin 43 as a signaling platform for increasing the volume and spatial distribution of regenerated tissue." *Proc Natl Acad Sci U S A* 106(32): 13219-13224.

Sekar, R. B., E. Kizana, H. C. Cho, J. M. Molitoris, G. G. Hesketh, B. P. Eaton, E. Marban and L. Tung (). "IK1 heterogeneity affects genesis and stability of spiral waves in cardiac myocyte monolayers." *Circ Res* 104(3): 355-364.

#### CENTRE FOR INFECTIOUS DISEASES AND MICROBIOLOGY

Vanhal S, Marriott D, Chen SCS, Nguyen Q, Sorrell TC, Ellis DH, Slavin M and the Australian Candidemia Study Group. Candidemia following solid organ transplantation in the era of antifungal prophylaxis- the Australian experience. *Transpl Infect Dis.* 11:122-7.

Gordon-Thomson C, Kumari A, Tomkins L, Holford, P, Wright LC, Djordjevic J, Sorrell TC, and Moore GPM. Chitotriosidase and gene therapy for fungal infections. *Cell Molecular Life Sci.* 66 (6):1116-25

Heath CH, Slavin MA, Handke R, Sorrell TC, Meyer M, Phillips M, Ellis D, Harun A, Nguyen Q, Chen SCA and the Australian Scedosporium (AUSCEDO) Study Group. Population-based surveillance for Scedosporiosis in Australia: clinical epidemiology, disease manifestations and emergence of Scedosporium aurantiacum. *Clinical Microbiology and Infection.* 1469-0691

Ferguson PE, Sorrell TC, Bradstock KF, Carr P, Gilroy NM. Parainfluenza virus 3 pneumonia in bone marrow transplant recipients – Multiple small nodules in high resolution computed tomographic lung scans provide a radiological clue to diagnosis. *Clin Infect Dis,* 48: 905-9

Blyth CC, Chen SC, Slavin MA, Serena C, Nguyen Q, Marriott D, Ellis D, Meyer W, Sorrell TC. Not just little adults: Candidemia epidemiology, molecular characterization, and antifungal susceptibility in neonatal and pediatric patients. *Pediatrics.* 123; 1360-68

Kesson AM, Bellemore MC, O'Mara TJ, Ellis DH, Sorrell TC. Scedosporium prolificans osteomyelitis in an immunocompetent child treated with a novel agent, hexadecylphosphocholine (miltefosine), in combination with terbinafine and voriconazole: a case report. *Clin Infect Dis.* 48:1257-61

Himmelreich U, Malik R, Kuhn T, Daniel H-M, Somorjai RL, Dolenko B, Sorrell TC. Rapid etiological classification of meningitis based on metabolite profiles and host-response by NMR spectroscopy. *PLoS One* 4 (4):e532.

Brown GV, Sorrell TC. Clinical research in crisis – setting the stage. *Med J Aust* Accepted 20/1/09

Chen S, Marriott D, Playford EG, Nguyen Q, Ellis D, Meyer W, Sorrell T, Slavin M. Candidaemia with uncommon Candida species: predisposing factors, outcome, antifungal susceptibility and implications for management. *Clin Microbiol Infect* Accepted for publication 9/1/09

Marriott D, Playford EG, Chen S, Slavin M, Nguyen Q, Ellis D, Sorrell TC. Determinants of mortality in non-neutropenic ICU patients with candidemia. *Critical Care*, 13:R115

Kong FR, Chen SCA, Chen XY, Sintchenko V, Halliady C, Cai L, Tong AS, Lee KC, Sorrell TC. Assignment of reference 5'-end 16S rDNA sequences and species-specific sequence polymorphisms improves species identification of Nocardia. *The Open Microbiol J*; 3: 97-105.

Obando D, Pantarat N, Handke R, Koda Y, Widmer F, Djordjevic J, Ellis DH, Sorrell TC, Jolliffe KA. Synthesis, Antifungal, Haemolytic and Cytotoxic activities of a series of bis(alkylpyridinium)alkanes. *Biorg Med Chem.*

Tsafnat G, Coiera E, Partridge SR, Schaeffer J, Iredell JR. Context-driven discovery of gene cassettes in mobile integrons using a computational grammar. *BMC Bioinformatics.* Sep 8;10:281.

Chatterjee, I., Dulhunty, J.M., Iredell, J.R., Gallagher, J.E., Sud, A., Woods, M., Lipman, J. Predictors and outcome associated with an Enterococcus positive isolate during an Intensive Care admission. *Anaesthesia and Intensive Care.* ; 37:976-982

The ANZIC Influenza Investigators. Critical Care Services and H1N1 Influenza in Australia and New Zealand. *N Engl J Med.* Oct 8.

Kok J, Blyth CC, Foo H, Patterson J, Taylor J, McPhie K, Ratnamohan VM, Iredell, J.R., Dwyer, D.E. Comparison of a Rapid Antigen Test with Nucleic Acid Testing During Co-circulation of Pandemic Influenza A/H1N1 and Seasonal Influenza A/H3N2. *J Clin Microbiol Nov 4.*

#### CENTRE FOR TRANSPLANT AND RENAL RESEARCH

Ahluwalia TS, Ahuja M, Rai T, Kohli HS, Bhansali A, Sud K, Khullar M. ACE variants interact with the RAS pathway to confer risk and protection against type 2 diabetic nephropathy. *DNA and Cell Biology* 28(3), 141-50

Markan S, Kohli HS, Joshi K, Minz RW, Sud K, Ahuja M, Anand S, Khullar M. Up regulation of the GRP-78 and GADD-153 and down regulation of Bcl-2 proteins in primary glomerular diseases: a possible involvement of the ER stress pathway in glomerulonephritis. *Mol Cell Biochem* 324(1-2):131-8, .

Ahluwalia TS, Khullar M, Ahuja M, Kohli HS, Bhansali A, Mohan V, Venkatesan R, Rai TS, Sud K, Singal PK. Common Variants of Inflammatory Cytokine Genes are associated with risk of nephropathy in Type 2 Diabetes among Asian Indians. *Plos One* 4(4):e5168, .

Phoon RK, Kitching AR, Jones LK, Holdsworth SR. Atorvastatin enhances humoral immune responses but does not alter renal injury in experimental crescentic glomerulonephritis. *Nephrology (Carlton).* Oct; 14 (7): 650-7

O'Connor K, Fulcher D, Phoon RK. Development of Anti-Glomerular Basement Membrane Disease After Remission From Perinuclear ANCA-Associated Glomerulonephritis in a Patient With HLA Susceptibility. *Am J Kidney Dis.* Sep 4.

Ooi JD, Phoon RK, Holdsworth SR, Kitching AR. Endogenous IL-23, but not IL-12, directs autoimmunity to the Goodpasture antigen. *J Am Soc Nephrol.* May; 20 (5): 980-9

Summers SA, Phoon R, Holdsworth S, Kitching RA. The IL-27 Receptor Promotes Early Immune Injury but Later Limits Disease in Experimental Crescentic Glomerulonephritis. Abstracts from the 45th Annual Scientific Meeting of the Australian and New Zealand Society of Nephrology in *J Am Soc Nephrol*, November

Summers SA, Phoon RKS, Holdsworth SR, Kitching AR. The IL-27 Receptor Promotes Early Immune Injury but Later Limits Disease in Experimental Crescentic Glomerulonephritis. Abstracts from the 45th Annual Scientific Meeting of the Australian and New Zealand Society of Nephrology in *Nephrology (Carlton)*, September

Vilayur E, Lin MW, Stewart G, Gottlieb D, Taper J, Thomas L, Phoon RKS. Two Year's Experience of the Westmead Amyloidosis Clinic. Abstracts from the 45th Annual Scientific Meeting of the Australian and New Zealand Society of Nephrology in *Nephrology (Carlton)*, September

Phoon RKS, Atai E. The Healthy Kidney Clinic – An Early Chronic Kidney Disease Model of Care. Abstracts from the 45th Annual Scientific Meeting of the Australian and New Zealand Society of Nephrology in *Nephrology (Carlton)*, September

Field MJ, Pollock CA, Harris DCH. *Systems of the Body. The Renal System*. Ed., Churchill-Livingstone, London, 2nd edition .

Harris DCH, Collins JK, Becker G. *Global considerations in kidney disease*, Oceania and Australia. *The Kidney*. Brenner & Rector, 9th Edition

Tong A, Sainsbury P, Chadban S, Walker RG, Harris DC, Carter SM, Hall B, Hawley C, Craig JC. Patients' experiences and perspectives of living with CKD. *American Journal of Kidney Diseases* ; 53: 689-700.

Zheng G, Lyons J, Tan TK, Wang Y, Hsu TT, Min D, Succar L, Rangan GK, Hu M, Henderson BR, Alexander SI, Harris DC: Disruption of E-cadherin by matrix metalloproteinase directly mediates epithelial-mesenchymal transition downstream of TGF- 1 in renal tubular epithelial cells. *Am J Pathol* ; 175: 580-591.

Prodjosudjadi W, Suhardjono, Suwitra K, Pranawa, Widiana IGR, Loekman JS, Nainggolan G, Prasanto H, Wijayanti Y, Dharmeizar, Sja'bani M, Nasution MY, Basuki W, Aditiawardana, Harris DCH, Pugsley DJ. Detection and prevention of chronic kidney disease in Indonesia: initial community screening. *Nephrology* ; 14(7): 669-74.

Tsukamoto Y, Wang HY, Becker G, Chen H-C, Han D-S, Harris DC, Imai E, Jha V, Li PKT, Lee EJC, Matsuo S, Tomino Y, Tungsanga K, Yamagata K, Hishida A. Report of the Asian Forum of Chronic Kidney Disease Initiative (AFCKDI) 2007. "Current status and perspective of CKD in Asia": diversity and specificity among Asian countries. *Clin. Exp. Nephrol* ; (Online - Epub 14 Mar ).

Martincic, G. Cyclodextrins as potential human anti-atherosclerotic agents. A comparative study to determine the optimum route of administration of Hydroxy-propyl-beta-cyclodextrin (HP-B-CD) in the apolipoprotein-E deficient 'knockout' mouse. II. Comparison of water, feed and intra-peritoneal delivery routes. *Animal Welfare & Technology*

Martincic, G. Refurbishing research laboratories in hospitals. A case study of the Centre for Transplant & Renal Research (CTRR) - notes on project management 'from concept to completion', with emphasis on improving operational management and laboratory functionality.

Lee VW, Qin X, Wang Y, Zheng G, Wang Y, Wang Y, Ince J, Tan TK, Kairaitis LK, Alexander SI, Harris DC. The CD40-CD154 co-stimulation pathway mediates innate immune injury in adriamycin nephrosis. *Nephrology Dialysis Transplantation* Nov 4 (Epub).

Tan TK, Zheng G, Wang Y, Hsu TT, Lee V, Wang Y, Harris DCH. Macrophage matrix metalloproteinase-9 mediates epithelial-mesenchymal transition in renal tubular cells. *Am J Pathol.*

Rangan G, Wang Y-P, Harris DCH. NF- B signalling in chronic kidney disease. *Frontiers in Bioscience* ; 14: 3496-3522.

Vilayur E, Harris DCH. Emerging therapies for chronic kidney disease: What is their role? *Nature Reviews Nephrol* ; 5: 375-383.

Rangan GK, Burgess JS, Schwensen KG, Chaudhry R, O'Brien K, Harris DC. Autosomal Dominant Polycystic Kidney Disease. *Medical Observer.*

Rangan G, Wang Y-P, Harris DCH. NF- B signalling in chronic kidney disease. *Frontiers in Bioscience* ; 14: 3496-3522.

Wang YM, Kemmler J, Zhang GY, Hu M, Polhill T, Winlaw D, Henwood T, Harris DCH, Alexander SI. Expression and Localisation of Renal Antigens in the Human Thymus. *Transplant Society ANZ, .*

Lee VWS, Zheng D, Wang Y, Harris DC. Regulatory Macrophages, but not regulatory T lymphocytes, protect against renal injury in diabetic endothelial nitric oxide synthase knockout mice. *World Congress of Nephrology .*

Lee VWS, Zheng D, Wang Y, Harris DC. Regulatory Macrophages, but not regulatory T lymphocytes, protect against renal injury in diabetic endothelial nitric oxide synthase knockout mice. *Nephrology* ; 14 (SI) A36.

Polhill T, Wang YM, Kemmler J, Zhang GY, Hu M, Winlaw D, Henwood T, Harris DCH, Alexander SI. Human thymic expression and localisation of renal antigens to e-cadherin positive medullary thymic epithelial cells (MTEC). *ANZSN, . Nephrology* ; 14 (SI) A17.

Succar L, Nikolic-Paterson DJ, Harris DC, Rangan GK. Early expression of phospho-S6 ribosomal protein is associated with proliferation in experimental crescentic glomerulonephritis. *ANZSN, . Nephrology* ; 14 (SI) A19.

Tong A, Sainsbury P, Chadban S, Walker RG, Harris DC, Carter SM, Hall B, Hawley C, Craig JC. Patients' experiences and perspectives of living with chronic kidney disease. *Nephrology* ; 14 (SI) A3.

Cao Q, Zheng D, Sun Y, Wang Y, Lee VWS, Zheng G, Tan TK, Ince J, Alexander SI, Harris DCH, Wang Y. Discrete functions of protective macrophages determine their relative therapeutic efficacy in chronic kidney disease. *Nephrology* ; 14 (SI) A16.

Cao Q, Zheng D, Sun Y, Wang Y, Lee VWS, Zheng G, Tan TK, Ince J, Alexander SI, Harris DCH, Wang Y. The failure of wound healing macrophages from bone marrow in treatment of CKD explained by their proliferation in inflamed kidney. *Nephrology* ; 14 (SI) A16.

Zheng D, Cao Q, Sun Y, Wang Y, Lee VWS, Zheng G, Tan TK, Ince J, Alexander SI, Harris DCH, Wang Y. Regulatory plasmacytoid dendritic cells reduce renal injury in murine adriamycin nephropathy. *Nephrology* ; 14 (SI) A17.

Tan TK, Zheng GP, Hsu TT, Wang Y, Lee V, Wang YP, Harris DCH. Macrophage matrix metalloproteinase-9 contributes to renal fibrosis via tubular cell epithelial-mesenchymal transition. *Nephrology* ; 14 (SI) A32.

Cao Q, Zheng D, Sun Y, Wang Y, Lee VWS, Zheng G, Tan TK, Ince J, Alexander SI, Harris DCH, Wang Y. Impaired alternatively activated macrophages from bone marrow in treatment of CKD: Associations with their proliferation in inflamed kidney. *ASN* .

Cao Q, Zheng D, Sun Y, Wang Y, Lee VWS, Zheng G, Tan TK, Ince J, Alexander SI, Harris DCH, Wang Y. IL-25 protects against renal injury in adriamycin nephropathy. *ASN* .

Zheng D, Cao Q, Wang Y, Lee VWS, Zheng G, Alexander SI, Harris DCH, Wang YP. Regulatory plasmacytoid dendritic cells reduce renal injury of adriamycin nephropathy. *ASN* .

Lee VWS, Zheng D, Wang Y, Alexander S, Harris DC. Alternatively-activated macrophages, but not regulatory T lymphocytes, ameliorate renal injury in diabetic endothelial nitric oxide synthase knockout mice. *ASN* .

Tan TK, Zheng GP, Hsu TT, Wang Y, Lee V, Wang YP, Cao Q, Harris DC. A direct role of matrix metalloproteinase-9 in renal fibrosis via tubular cell epithelial-mesenchymal transition. *ASN* .

Wong G, Howard K, Craig JC. Economic evaluation in clinical nephrology: Part 1. An introduction to conducting an economic evaluation in clinical practice. *Nephrology (in-press)*

Wong G, A. Hayden A, Chapman JR, Webster AC, Wang JJ., Mitchell P, Craig JC. Chronic kidney disease and cancer risk in older people *Journal of the American Society of Nephrology (accepted 21st Jan, , In-press)*

Wong G, Webster AC, JR. Chapman JR, Craig JC. Reported cancer screening practices in nephrologists: results of a national survey. *Nephrology, Dialysis, Transplantation*

Morton RL, Moustakas J, Howard K, Webster AC, Snelling P. A National Audit of Information Provided to new CKD Stage 4 & 5 patients - results from a pilot study. *Renal Society of Australasia Journal* ; 5:138-146.

Stewart JH, Vajdic CM, van Leeuwen MT, Amin J, Webster AC, Chapman JR, McDonald SP, Grulich AE, McCredie MRE. The pattern of excess cancer in dialysis and transplantation. *Nephrology Dialysis Transplantation* ; 24: 3225-3231

Masson P, Matheson S, Webster AC, Craig JC. Meta-analyses on the prevention and treatment of urinary tract infections. *Infectious Disease Clinics of North America* ; 23(2):355-85

Cross NB, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensive treatment for kidney transplant recipients. *Cochrane Database of Systematic Reviews* , Issue 3.CD003598

Vajdic CM, van Leeuwen MT, Webster AC, McCredie MRE, Stewart JH, Chapman JR, Amin J, McDonald SP, Grulich AE. Grulich. Cutaneous Melanoma is Related to Immune Suppression in Kidney Transplant Recipients. *Cancer Epidemiology, Biomarkers and Prevention* ;18:2297-2303

van Leeuwen MT, Grulich AE, Webster AC, McCredie MRE, Stewart JH, McDonald SP, Amin J, Kaldor JM, Chapman JR, Vajdic CM. Immunosuppression and other risk factors for early and late non-Hodgkin lymphoma after kidney transplantation. *Blood* ; 114(3):630-7

Cross NB, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensives for kidney transplant recipients: systematic review and meta-analysis of randomised controlled trials. *Transplantation* ; 88(1):7-18

Morton RL, Howard K, Webster AC, Wong G, Craig JC. The Cost-effectiveness of Induction Immunosuppression in Kidney Transplantation. *Nephrology Dialysis Transplantation* ; 24: 2258-2269

Cross NB, Webster AC, O'Connell PJ, Jeffreys N, Dwyer DE, Craig JC. Diagnostic accuracy of blood qualitative nucleic acid testing for polyomavirus-associated nephropathy in kidney recipients. *Nephrology* ;14(3):350-6

Craig JC, Webster A, McDonald SP. The case of Azathioprine versus Mycophenolate. Do different drugs really cause different transplant outcomes? *Transplantation* ; 87(6): 803-804

Wong G, Webster AC, Chapman JR, Craig JC. Reported cancer screening practices of nephrologists: results from a national survey. *Nephrology Dialysis Transplantation* ; 24: 2136-2143

Conway B, Webster AC, Ramsay G, Morgan N, Neary J, Whitworth CE, Harty J. Predicting mortality and uptake of renal replacement therapy in patients with stage 4 chronic kidney disease. *Nephrology Dialysis Transplantation* . ; 24(6):1930-1937

van Leeuwen MT, Grulich AE., McDonald SP., McCredie MRE, Amin J, Stewart JH., Webster AC, Chapman JR, Vajdic CM. Immunosuppression and other risk factors for lip cancer after

kidney transplantation. *Cancer Epidemiology, Biomarkers and Prevention* 18(2):561-569

Wong G, Hayden A, Chapman JR, Webster AC, Wang JJ, Mitchell P, Craig JC. Chronic kidney disease and risk of cancer in older people. *J Am Soc Nephrol* ; 20(6):1341-50

Wong G, Howard K, Webster AC, Chapman JR, Craig JC. The health and economic impact of cervical cancer screening and HPV vaccination in kidney transplant recipients. *Transplantation* ;87(7):1078-91

Rangan GK, Wang Y, Harris DCH. NF- $\kappa$ B signalling in chronic kidney disease. *Front Biosc* 14: 3496-3522,

Rangan GK, Nguyen T, Mainra R, Succar L, Schwensen K, Burgess J, Ho K. Role of sirolimus in non-transplant kidney disease. *Pharmacol Ther* 123: 187-206, Impact Factor 7.968

Zheng G, Lyons G, Tan T, Wang y, Succar L, Rangan GK, Henderson B, Alexander S, Harris DCH. Disruption of E-cadherin by matrix metalloproteinase directly mediates epithelial-mesenchymal transition downstream of TGF- $\beta$ 1 in renal tubular epithelial cells. *Am J Pathol* 175: 580-91

Lee VW, Qin X, Wang Y, Zheng G, Wang Y, Wang Y, Ince J, Tan TK, Kairaitis LK, Alexander SI, Harris DC. The CD40-CD154 co-stimulation pathway mediates innate immune injury in adriamycin nephrosis. *Nephrol Dial Transplant*. Nov 4

Lee, VWS, Qin X, Wang Y, Zheng G, Wang Y, Wang Y, Ince J, Tan TK, Kairaitis LK, Alexander SI, Harris DCH. The CD40-CD154 costimulation pathway mediates innate immune injury in adriamycin nephrosis. *Nephrol Dial Transplant* 10.1093

Londrigan SL, Brady JL, Sutherland RM, Cowan PJ, d'Apice AJ, Hawthorne WJ, O'Connell PJ, Lew AM. Optimizing transduction of pig islet cell clusters for xenotransplantation. *Xenotransplantation*., 16; 45-6.

Chapman J, O'Connell P. XXII International Congress of The Transplantation Society. *Transplant Proc*. Jan-Feb;41(1):13.

- Suh N, Ryan B, Allen R, O'Connell P, Pleass H. Simultaneous pancreas and kidney transplantation from organ donation after cardiac death. *ANZ J Surg.* ; 79; 245-246.
- Cross NB, Webster AC, O'Connell PJ, Jeoffreys N, Dwyer DE, Craig JC. Diagnostic accuracy of blood qualitative nucleic acid testing for polyomavirus-associated nephropathy in kidney recipients *Nephrology* ;14:350-356
- Akima S, Hawthorne WJ, Favaloro E, Patel A, Blyth K, Mudaliar Y, Chapman JR, O'Connell PJ. Tirofiban and activated Protein C synergistically inhibit the instant blood mediated inflammatory reaction (IBMIR) from allogeneic islet cells exposure to human blood. *Am. J. Transplant.* ; 9; 1533-1540.
- Cross NB, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensives for kidney transplant recipients: systematic review and meta-analysis of randomized controlled trials. *Transplantation* , 88; 7-18.
- Cross NB, Webster AC, Masson P, O'Connell PJ, Craig JC. Antihypertensive treatment for kidney transplant recipients. *Cochrane Database Syst Rev.* Jul 8;(3):CD003598
- O'Connell PJ. The International Xenotransplantation Association consensus statement on conditions for undertaking clinical trials of porcine islet products in type 1 diabetes— Chapter 6: Patient selection for pilot clinical trials of islet xenotransplantation. *Xenotransplantation* , 16; 249-254.
- Hering BJ, Cooper DK, Cozzi E, Schuurman HJ, Korbitt GS, Denner J, O'Connell PJ, Vanderpool HY, Pierson RN 3rd. The International Xenotransplantation Association consensus statement on conditions for undertaking clinical trials of porcine islet products in type 1 diabetes-- executive summary. *Xenotransplantation.* Jul;16(4):196-202.
- Lam V, Laurence JM, Hawthorne W, Robertson P, Lau H, Ryan B, Allen RDM, Pleass HCC, En bloc paediatric kidney donors: is this the best use of a scarce resource? *ANZ J. Surg* 79(027)-32
- Suh, N, Ryan, B, Allen, R, O'Connell, P & Pleass, H: Simultaneous pancreas and kidney transplantation from organ donation after cardiac death. *ANZ J Surg.* 79: 245-6, .
- Sandroussi, C, Crawford, M, Lockwood, DS, Tang, P, Gallagher, JP, Pleass, H, Strasser, SI, Shackel, NA, McCaughan, GW & Verran, DJ: Donor and recipient selection leads to good patient and graft outcomes for right lobe split transplantation versus whole graft liver transplantation in adult recipients. *Liver Transpl.* 15: 1586-93
- Toussaint ND, Elder GJ, Kerr PG: Bisphosphonates in Chronic Kidney Disease; Balancing Potential Benefits and Adverse Effects on Bone and Soft Tissue. *Clin J Am Soc Nephrol.* Jan;4(1):221-33
- Mainra R, Elder G. Managing bone complications after kidney transplantation. *Nephrology.* Jun;14(4):437-42
- O'Shaughnessy D, Elder G. Patient Level Outcomes - the Missing Link. *Nephrology.* Jun;14(4):443-51.
- Palmer SC, McGregor DO, Craig JC, Elder G, Macaskill P, Strippoli GFM. Vitamin D compounds for people with chronic kidney disease requiring dialysis. *Cochrane Database of Systematic Reviews* , Issue 4. Art. No.: CD005633.
- Palmer SC, McGregor DO, Craig JC, Elder G, Macaskill P, Strippoli GFM. Vitamin D compounds for people with chronic kidney disease not requiring dialysis. *Cochrane Database of Systematic Reviews* , Issue 4. Art. No.: CD008175.
- Navaneethan S, Craig J, Elder G, Strippoli G. Benefits and harms of phosphate binders in chronic kidney disease: a systematic review of randomized, controlled trials. *Am J Kid Dis* Vol 54, No 4 (October), : pp 619-637
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease—mineral and bone disorder (CKD-MBD). *Kidney International* ; 76 (Suppl 113): S1-S130.
- Mainra R, Elder G. Individualized therapy to prevent BMD loss after kidney and kidney-pancreas transplantation. *Clin J Am Soc Nephrol* ; epub December : 0: CJN.03770609v1-CJN.03770609
- Horton PJ, Hawthorne WJ, Walters S, Patel T, Stewart GJ, Allen RD, Chapman JR. Tolerance induction in a large-animal model using total lymphoid irradiation and intrathymic bone marrow. *Transplant Proc.* Jan-Feb; 41(1): 13.
- Chapman J, O'Connell P. XXII International Congress of The Transplantation Society. *Transplant Proc.* Jan-Feb;41(1):13. PubMed PMID: 19249462.
- Van Leeuwen MT, Grulich AE, McDonald SP, McCredie MR, Amin J, Stewart JH, Webster AC, Chapman JR, Vajdic CM. Immunosuppression and other risk factors for lip cancer after kidney transplantation. *Cancer Epidemiol Biomarkers Prev.* Feb; 18(2):561-9.
- Wong G, Howard K, Webster A, Chapman JR, Craig JC. The health and economic impact of cervical cancer screening and human papillomavirus vaccination in kidney transplant recipients. *Transplantation.* Apr 15;87(7):1078-91.
- Kliem V, Michel U, Burg M, Bock A, Chapman J, Dussol B, Fritsche L, Lebranchu Y, Oppenheimer F, Pohanka E, Salvadori M, Tufveson G. Geographical prevalence, risk factors and impact of hepatitis B and C after renal transplantation. *Clin Nephrol.* Apr;71(4):423-9. PubMed PMID: 19356375.
- Wong G, Hayen A, Chapman JR, Webster AC, Wang JJ, Mitchell P, Craig JC. Association of CKD and cancer risk in older people. *JASN.* Jun20(6):1341-50.
- Wong G, Webster AC, Chapman JR, Craig JC. Reported cancer screening practices of nephrologist: results from a national survey. *Nephrol Dial Transplant.* Jul;24 (7) 2136-43
- Akima, S., Hawthorne, W., Favaloro, E., Patel, A., Blyth, K., Mudaliar, Y., Chapman, J., O'Connell, P. Tirofiban and Activated Protein C Synergistically Inhibit the Instant Blood Mediated Inflammatory Reaction (IBMIR) from Allogeneic Islet Cells Exposure to Human Blood. *AJT.* ; 9:1533-40.
- Stewart JH, Vajdic CM, van Leeuwen MT, Amin J, Webster AC, Chapman JR, McDonald SP, Grulich AE, McCredie MR. The pattern of excess cancer in dialysis and transplantation. *Nephrol Dial Transplant.* Jul 8.
- Van Leeuwen MT, Grulich AE, Webster AC, McCredie MR, Stewart JH, McDonald SP, Amin J, Kaldor JM, Chapman JR, Vajdic CM. Immunosuppression and other risk factors for early and late non-Hodgkin lymphoma after kidney transplantation. *Blood.* Jul 16;114(3):630-7.
- Vajdic, C., van Leeuwen, M., Webster, A., McCredie, M., Stewart, J., Chapman, J., Amin, J., McDonald, S., Grulich, A. Cutaneous Melanoma Is Related to Immune Suppression in Kidney Transplant Recipients. *Cancer epidemiology, biomarkers & prevention* : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology. ; 18:2297-303.
- Campistol JM, Boletis IN, Dantal J, de Fijter JW, Hertig A, Neumayer HH, Oyen O, Pascual J, Pohanka E, Ruiz JC, Scolari MP, Stefoni S, Serón D, Sparacino V, Arns W, Chapman JR. Chronic allograft nephropathy - a clinical syndrome: early detection and the potential role of proliferation signal inhibitors. *Clin Transplant.* Aug 27. 19719730.
- Kasike BL, Zeier MG, Chapman JR, Craig JC, Ekberg H, Garvey CA, Green MD, Jha V, Josephson MA, Kiberd BA, Kreis HA, McDonald RA, Newmann JM, Obrador GT, Vincenti FG, Cheung M, Earley A, Raman G, Abariga S, Wagner M, Balk EM. KDIGO clinical practice guideline for the care of kidney transplant recipients: a summary. *Kidney Int* Oct 21.
- Chapman JR. Commentary - Not that day... *MJA.* Dec . 191:613

## CENTRE FOR VISION RESEARCH

Liew G, Wong TY, Mitchell P, Cheung N, Wang JJ. Retinopathy predicts coronary heart disease mortality. *Heart* 95(5):391-4,

- Cheung N, Donaghue K, Liew G, Rogers S, Wang JJ, Lim SW, Jenkins A, Hsu W, Lee M, Wong TY. Quantitative assessment of early diabetic retinopathy using fractal analysis. *Diabetes Care* 32(1):106-10,
- Lavanya R, Wong TY, Aung T, Tan DT, Saw SM, Tay WT, Wang JJ. Prevalence of cataract surgery and post surgery visual outcomes in an urban Asian population: the Singapore Malay Eye Study. *British Journal of Ophthalmology* 93(3):299-304,
- Kaushik S, Wang JJ, Wong TY, Flood V, Barclay A, Brand-Miller J, Mitchell P. Glycemic index, retinal vascular caliber, and stroke mortality. *Stroke* 40(1):206-12,
- [Kaushik S, Wang JJ, Flood V, Barclay A, Brand-Miller J, Mitchell P. Does diet influence the retinal microvasculature in children? (response to Lim et al) *Stroke* 40(6):e475-6, ]
- Kreis AJ, Nguyen TT, Wang JJ, Rogers S, Al-Fiadh A, Freeman M, Wong TY, Farouque HM. Are retinal microvascular caliber changes associated with severity of coronary artery disease in symptomatic cardiac patients? *Microcirculation* 16(2):177-81,
- Wang JJ, Rochtchina E, Smith W, Klein R, Klein BE, Joshi T, Sivakumaran TA, Iyengar S, Mitchell P. Combined effects of complement factor H genotypes, fish consumption and inflammatory markers on long-term risk for age-related macular degeneration in a cohort. *American Journal of Epidemiology* 169(5):633-41,
- Duan XR, Liang YB, Friedman DS, Sun LP, Wei WB, Wang JJ, Wang GL, Liu W, Tao QS, Wang NL, Wong TY. Prevalence and associations of epiretinal membranes in a rural Chinese adult population: the Handan Eye Study. *Investigative Ophthalmology and Visual Science* 50(5):2018-23
- Mehta P, Mellick GD, Rowe DB, Halliday GM, Jones MM, Manwaring N, Vandebona H, Silburn PA, Wang JJ, Mitchell P, Sue CM. Mitochondrial DNA haplogroups J and K are not protective for Parkinson's disease in the Australian community. *Movement Disorders* 24(2):290-2
- Wong N, Wang SS, Lamoureux E, Wong TY, Tikellis G, Harper A, Wang JJ. Blood pressure control and awareness among patients with diabetes and hypertension attending a tertiary ophthalmic clinic. *Diabetic Medicine* 26(1):34-9
- Kreis AJ, Wong TY, Islam FM, Klein R, Klein BE, Cotch MF, Jenkins AJ, Shea S, Wang JJ. Is nuclear magnetic resonance lipoprotein subclass related to diabetic retinopathy? The Multi-Ethnic Study of Atherosclerosis (MESA). *Diabetes and Vascular Disease Research* 6(1):40-2,
- Wang FH, Liang YB, Zhang F, Wang JJ, Wei WB, Tao QS, Sun LP, Friedman DS, Wang NL, Wong TY. Prevalence of diabetic retinopathy in rural China: The Handan Eye Study. *Ophthalmology* 116(3):461-7
- Sun C, Wang JJ, Mackey DA, Wong TY. Retinal vascular caliber: systemic, environmental and genetic associations. *Survey of Ophthalmology* 54(1):74-95
- Tong L, Saw SM, Lamoureux EL, Wang JJ, Rosman M, Tan DT, Wong TY. A questionnaire-based assessment of symptoms associated with tear film dysfunction and lid margin disease in an Asian population. *Ophthalmic Epidemiology* 16(1):31-7
- Samarawickrama C, Fotedar R, Mitchell P, Rose KA. Refractive error, strabismus, and amblyopia [letter]. *Ophthalmology* 116(2):364-5
- Vandebona H, Mitchell P, Manwaring N, Griffiths K, Gopinath B, Wang JJ, Sue CM. Prevalence of mitochondrial 1555 A->G mutation in adults of European descent. *New England Journal of Medicine* 360(6):642-4
- Liew G, Mitchell P, Wong TY. Systemic management of diabetic retinopathy: ADVANCES and DIRECT implications of new trials [editorial] *British Medical Journal* 338:b441
- Roberts TV, Hodge C, Graham SL, Burlutsky G, Mitchell P. Prevalence of nocturnal oxygen desaturation and self-reported sleep-disordered breathing in glaucoma. *Journal of Glaucoma* 18(2):114-8
- Samarawickrama C, Mitchell P. Ocular dominance and myopia [letter] *Investigative Ophthalmology and Visual Science eLetter*, published online 10 February,
- Gopinath B, Rochtchina E, Wang JJ, Schneider J, Leeder SR, Mitchell P. Prevalence of age-related hearing loss in older adults: Blue Mountains Study. *Archives of Internal Medicine* 169(4):415-6
- Wang JJ, Rochtchina E, Tan AG, Cumming RG, Leeder SR, Mitchell P. Use of inhaled and oral corticosteroids and the long-term risk of cataract. *Ophthalmology* 116(4):652-7
- Gopinath B, Schneider J, Rochtchina E, Leeder SR, Mitchell P. The association between age-related hearing loss and stroke in an older population. *Stroke* 40(4):1496-8
- Martinez AA, Sankaridurg, PR, Naduvilath TJ, Mitchell P. Monochromatic aberrations in hyperopic and emmetropic children. *Journal of Vision* 9(1):23.1-14
- Ng CH, Wang JJ, Mitchell P, Amirul Islam FM, Wong TY. Prevalence and characteristics of choroidal nevi in an Asian vs white population. *Archives of Ophthalmology* 127(3):314-9
- Pham TQ, Rochtchina E, Mitchell P, Smith W, Wang JJ. Sunlight-related factors and the 10-year incidence of age-related maculopathy. *Ophthalmic Epidemiology* 16(2):136-41
- Schäche M, Chen CY, Pertile KK, Richardson AJ, Dirani M, Mitchell P, Baird PN. Fine mapping linkage analysis identifies a novel susceptibility locus for myopia on chromosome 2q37 adjacent to but not overlapping MYP12. *Molecular Vision* 15:722-30
- Samarawickrama C, Wang JJ, Mitchell P. Association between ocular dominance and refraction – uncertain dominance [letter]. *Journal of Refractive Surgery* 25(3):249
- Samarawickrama C, Wang JJ, Huynh SC, Wang XY, Burlutsky G, Stapleton F, Mitchell P. Macular thickness, retinal thickness and optic disk parameters in dominant compared with nondominant eyes. *Journal of the American Association for Pediatric Ophthalmology and Strabismus* 13(2):142-7
- SanGiovanni JP, Arking DE, Iyengar SK, Elashoff M, Clemons TE, Reed GF, Henning AK, Sivakumaran TA, Xu X, DeWan A, Agron E, Rochtchina E, Sue CM, Wang JJ, Mitchell P, Hoh J, Francis PJ, Klein ML, Chew EY, Chakravarti A. Mitochondrial DNA variants of respiratory complex I that uniquely characterize haplogroup T2 are associated with increased risk of age-related macular degeneration. *PLoS One* 4(5):e5508
- Tan JSL, Wang JJ, Flood V, Mitchell P. Dietary fatty acids and the 10-year incidence of age-related macular degeneration: the Blue Mountains Eye Study. *Archives of Ophthalmology* 127(5):656-65
- Larsson J, Kifley A, Zhu M, Wang JJ, Mitchell P, Sutter FK, Gillies MC. Rapid reduction of hard exudates in eyes with diabetic retinopathy after intravitreal triamcinolone: data from a randomized, placebo controlled, clinical trial. *Acta Ophthalmologica* 87(3):275-80
- Swamy BN, Chia E-M, Wang JJ, Rochtchina E, Mitchell P. Correlation between vision and health-related quality of life scores. *Acta Ophthalmologica* 87(3):335-9
- Gopinath B, Rochtchina E, Flood VM, Mitchell P. Association of elevated homocysteine level and vitamin B12 deficiency with anemia in older adults. *Archives of Internal Medicine* 169(9):901-2
- Mitchell P, Gopinath B, McMahon C, Rochtchina E, Wang JJ, Boyages SC, Leeder SR. Relationship of type 2 diabetes to the prevalence, incidence and progression of age-related hearing loss. *Diabetic Medicine* 26(5):483-8
- Liew G, Klein R, Wong TY. The role of genetics in susceptibility to diabetic retinopathy. *International Ophthalmology Clinics* 49(2):35-52
- Liew G, Mitchell P, Wong TY. Geographic atrophy in age-related macular degeneration and TLR3 [letter]. *New England Journal of Medicine* 360(21):2252
- Kawasaki R, Wang JJ, Sato H, Mitchell P, Kato T, Kawata S, Kayama T, Yamashita H, Wong TY. Prevalence and associations of epiretinal membranes in an adult Japanese population: the Funagata Study. *Eye* 23(5):1045-51

- Baker ML, Wang JJ, Rogers S, Klein R, Kuller LH, Larsen EK, Wong TY. Early age-related macular degeneration, cognitive function and dementia: The Cardiovascular Health Study Archives of Ophthalmology 127(5):667-73
- Loon SC, Tay WT, Saw SM, Wang JJ, Wong TY. Prevalence and risk factors of ocular trauma in an urban south-east Asian population: the Singapore Malay Eye Study. Clinical and Experimental Ophthalmology 37(4):362-7
- Dirani M, Tong L, Gazzard G, Zhang X, Chia A, Young TL, Rose KA, Mitchell P, Saw SM. Outdoor activity and myopia in Singapore teenage children. British Journal of Ophthalmology 93(8):997-1000
- Zheng Y, Cheung N, Aung T, Mitchell P, He M, Wong TY. Relationship of retinal vascular caliber with retinal nerve fiber layer thickness: the Singapore Malay Eye Study. Investigative Ophthalmology and Visual Science 50(9):4091-6
- Lamoureux EL, Saw SM, Thumboo J, Wee HL, Aung T, Mitchell P, Wong TY. The impact of corrected and uncorrected refractive error on visual function: the Singapore Malay Eye Study. Investigative Ophthalmology and Visual Science 50(6):2614-20
- Samarawickrama C, Huynh SC, Liew G, Burlutsky G, Mitchell P. Birth weight and optic nerve head parameters. Ophthalmology 116(6):1112-8
- Wong G, Hayden A, Chapman JR, Webster AC, Wang JJ, Mitchell P, Craig JC. Association of CKD and cancer risk in older people. Journal of the American Society of Nephrology 20(6):1341-50
- Gopinath B, Wang JJ, Schneider J, Burlutsky G, Snowdon J, McMahon CM, Leeder SR, Mitchell P. Depressive symptoms in older adults with hearing impairments: the Blue Mountains Study. Journal of the American Geriatrics Society 57(7):1306-8
- Samarawickrama C, Mitchell P. Influence of signal strength on OCT measurements [letter]. Journal of Glaucoma 18(6):499-500
- Flood VM, Gopinath B, Rochtchina E, Smith W, Mitchell P. Re: 'Red meat and chicken consumption and its association with age-related macular degeneration' [letter]. American Journal of Epidemiology 170(4):531-2
- Veerappan S, Schäche M, Pertile KK, Islam FM, Chen CY, Mitchell P, Dirani M, Baird P. The retinoic acid receptor alpha (RARA) gene is not associated with myopia, hypermetropia, and ocular biometric measures. Molecular Vision 15:1390-7
- Jun G, Guo H, Klein BEK, Klein R, Wang JJ, Mitchell P, Miao H, Lee KE, Joshi T, Buck M, Chugha P, Bardenstein D, Klein AP, Bailey-Wilson JE, Gong X, Spector TD, Andrew T, Hammond CJ, RC Elston, Iyengar SK, Wang B. EPHA2 is associated with age-related cataract in mice and humans. PLoS Genetics 5(7):e1000584
- Swamy B, Cumming RG, Ivers R, Clemson L, Cullen J, Hayes MF, Tanzer M, Mitchell P. Vision screening for frail older people: a randomized trial. British Journal of Ophthalmology 93(6):736-41
- Kanthan GL, Wang JJ, Rochtchina E, Mitchell P. Use of antihypertensive medications and topical beta-blockers and the long-term incidence of cataract and cataract surgery. British Journal of Ophthalmology 93(9):1210-4
- Lim LS, Saw SM, Cheung N, Mitchell P, Wong TY. Relationship of retinal vascular caliber with optic disc and macular structure. American Journal of Ophthalmology 148(3):368-75
- Lindley RI, Wang JJ, Wong MC, Mitchell P, Liew G, Hand P, Wardlaw J, De Silva DA, Baker M, Rochtchina E, Chen C, Hankey GM, Chang HM, Fung VS, Gomes L, Wong TY. Retinal microvasculature in acute lacunar stroke: a cross-sectional study. Lancet Neurology 8(7):628-34,
- Hong T, Mitchell P, de Loryn T, Rochtchina E, Cugati S, Wang JJ. Development and progression of diabetic retinopathy 12 months after phacoemulsification cataract surgery. Ophthalmology 116(8):1510-4
- Huynh SC, Samarawickrama C, Wang XY, Rochtchina E, Wong TY, Gole GA, Rose KA, Mitchell P. Macular and nerve fiber layer thickness in amblyopia: the Sydney Childhood Eye Study. Ophthalmology 116(9):1604-9
- Islam FMA, Nguyen TT, Wang JJ, Tai ES, Shankar A, Saw SM, Aung T, Lim SC, Mitchell P, Wong TY. Quantitative retinal vascular calibre changes in diabetes and retinopathy: the Singapore Malay Eye Study. Eye 23(8):1719-24
- Fong CS, Wang JJ, Rochtchina E, Schneider J, Jakobsen KB, Smith W, Mitchell P. Survey effect on use of eye care by older persons with correctable visual impairment. Ophthalmic Epidemiology 16(4):249-53
- McGeechan K, Liew G, Macaskill P, Irwig L, Klein R, Klein BEK, Wang JJ, Mitchell P, Vingerling JR, de Jong PTM, Witteman JCM, Breteler MMB, Shaw JE, Zimmet P, Wong TY. Meta-analysis: Retinal vessel caliber and risk of coronary heart disease. Annals of Internal Medicine 151(6):404-13
- Tariq Y, Samarawickrama C, Mitchell P. Visual morbidity due to inaccurate spectacles among school children in rural China [letter]. Investigative Ophthalmology and Visual Science eLetter published online, 3 September
- Sun C, Wang JJ, Islam FMA, Heckbert SR, Klein R, Siscovick DS, Klein BE, Wong TY. Hypertension genes and retinal vascular calibre: The Cardiovascular Health Study. Journal of Human Hypertension 23(9):578-84
- Ross LA, Anstey KJ, Kiely KM, Windsor TD, Byles JE, Luszcz MA, Mitchell P. Older drivers in Australia: Trends in driving status and cognitive and visual impairment. Journal of the American Geriatrics Society 57(10):1868-73
- Liew G, Mitchell P, Wong TY, Lindley RI, Cheung N, Kaushik S, Gopinath B, Wang JJ. Retinal microvascular signs and cognitive impairment. Journal of the American Geriatrics Society 57(10):1892-6
- Samarawickrama C, Huynh SC, Mitchell P. Retinal structure in amblyopia [letter]. Ophthalmology 116(10):2041
- Pai AS, Mitchell P, Rochtchina E, Iyengar S, Wang JJ. Complement factor H and the bilaterality of age-related macular degeneration: the Blue Mountains Eye Study. Archives of Ophthalmology 127(10):1339-44
- Karpa MJ, Mitchell P, Beath K, Rochtchina E, Cumming RG, Wang JJ. Direct and indirect effects of visual impairment on mortality risk in older persons: the Blue Mountains Eye Study. Archives of Ophthalmology 127(10):1347-53
- Samarawickrama C, Pai A, Huynh SC, Burlutsky G, Jonas JB, Mitchell P. Measurement of optic nerve head parameters: comparison of optical coherence tomography with digital planimetry. Journal of Glaucoma 18(8):571-5
- van Koolwijk LM, Healey PR, Hitchings RA, Mitchell P, Sham PC, McGuffin P, Viswanathan AC. Major genetic effects in glaucoma: a commingling analysis of optic disk parameters in an older Australian population. Investigative Ophthalmology and Visual Science 50(11):5275-80
- Nguyen TT, Kawasaki R, Wang JJ, Kreis AJ, Shaw J, Vilser W, Wong TY. Flicker-light induced retinal vasodilation in diabetes and diabetic retinopathy. Diabetes Care 32(11):2075-80
- Lim SW, Cheung N, Wang JJ, Donaghue KC, Liew G, Islam F, Jenkins AJ, Wong TY. Retinal vascular fractal dimension and risk of early diabetic retinopathy: a prospective study of children and adolescents with type 1 diabetes. Diabetes Care 32(11):2081-3
- Liang YB, Wong TY, Sun L, Tao Q, Wang JJ, Yang X, Xiong Y, Wang N, Friedman D. Refractive errors in a rural adult Chinese population: The Handan Eye Study. Ophthalmology 116(11):2119-27
- Kawasaki R, Cheung N, Wang JJ, Klein R, Klein BE, Cotch MF, Sharrett AR, Shea S, Islam FA, Wong TY. Retinal vessel diameters and risk of hypertension: the Multi-Ethnic Study of Atherosclerosis (MESA). Journal of Hypertension 27(12):2386-93

- Tanabe Y, Kawasaki R, Wang JJ, Wong TY, Mitchell P, Daimon M, Oizummi T, Kato T, Kawata S, Kayama T, Yamashita H. Angiotensin-converting enzyme gene and retinal arteriolar narrowing: the Funagata Study. *Journal of Human Hypertension* 23(12):788-93
- De Silva DA, Liew G, Wong MC, Chang HM, Chen C, Wang JJ, Baker ML, Hand PJ, Rochtchina E, Liu EY, Mitchell P, Lindley RI, Wong TY. Retinal vascular caliber and extracranial carotid disease in acute ischemic stroke patients: the Multi-Centre Retinal Stroke (MCRS) Study. *Stroke* 40(12):3695-9
- McGeechan K, Liew G, Macaskill P, Irwig L, Klein R, Klein BE, Wang JJ, Mitchell P, Vingerling JR, de Jong PT, Wittman JC, Breteler MM, Shaw J, Zimmet P, Wong TY. Prediction of incident stroke events based on retinal vessel caliber: A systematic review and individual-participant meta-analysis. *American Journal of Epidemiology* 170(11):1323-32
- Samarawickrama C, Huynh SC, Mitchell P. Thickness of the retinal nerve fiber layer in amblyopia [letter]. *American Journal of Ophthalmology* 148(6):951
- Pai AS, Samarawickrama C, Tariq Y, Mitchell P. Low vision among preschool children in the Beijing Study of Visual Impairment [letter]. *American Journal of Ophthalmology* 148(6):953-4
- Gopinath B, Wang JJ, Flood VM, Burlutsky G, Wong TY, Mitchell P. The associations between blood levels of homocysteine, folate, vitamin B12 and retinal vascular caliber. *American Journal of Ophthalmology* 148(6):902-9
- Wong TY, Mwamburi M, Klein R, Larsen M, Flynn H, Hernandez-Medina M, Ranganathan G, Wirostko B, Pleil A, Mitchell P. Rates of progression in diabetic retinopathy during different time periods: a systematic review and meta-analysis. *Diabetes Care* 32(12):2307-13
- Nguyen T, Kawasaki R, Kreis AJ, Wang JJ, Shaw J, Vilser W, Wong TY. Correlation of flicker-light induced retinal vasodilation and retinal vascular caliber measurement in diabetes. *Investigative Ophthalmology and Visual Science* 50(12):5609-13
- Cho Y, Wang JJ, Chew EY, Ferris FL, Mitchell P, Chan C, Tuo J. Toll-like receptor polymorphisms and age-related macular degeneration: replication in three case-control samples. *Investigative Ophthalmology and Visual Science* 50(12):5614-8
- Samarawickrama C, Huynh SC, Wang JJ, Pai A, Joachim N, Burlutsky G, Wong TY, Mitchell P. Relationship between retinal structures and retinal vessel caliber in normal adolescents. *Investigative Ophthalmology and Visual Science* 50(12):5619-24
- Nguyen TT, Kreis AJ, Kawasaki R, Wang JJ, Seifert BU, Vilser W, Nagel E, Shaw J, Wong TY. Reproducibility of the retinal vascular response to flicker light in Asians. *Current Eye Research* 34(12):1082-8
- Anstey KJ, Byles JE, Luszcz MA, Mitchell P, Steel D, Booth H, Browning C, Butterworth P, Cumming RG, Healy J, Windsor TD, Ross L, Bartsch L, Burns RA, Kiely K, Birrell CL, Broe GA, Shaw J, Kendig H. Cohort profile: The Dynamic Analyses to Optimise Ageing (DYNOPTA) project. *International Journal of Epidemiology* 57(10):1868-73
- Lavanya R, Jeganathan VSE, Zheng Y, Raju P, Cheung N, Tai ES, Wang JJ, Lamoureux E, Mitchell P, Young TL, Cajucom-Uy H, Foster PJ, Aung T, Saw SM, Wong TY. Methodology of the Singapore Indian Chinese Cohort (SICC) eye study: Quantifying ethnic variations in the epidemiology of eye diseases in Asians. *Ophthalmic Epidemiology* 16(6):325-36
- Fong CS, Gopinath B, Wang JJ, Mitchell P. Mitochondrial DNA variations and advanced age-related macular degeneration: 2 recent studies [letter]. *Investigative Ophthalmology and Visual Science eLetter*, published online 31 December
- Mitchell P, Korobelnik JF, Lanzetta P, Holz FG, Pruenke C, Schmidt-Erfurth UM, Tano Y, Wolf S. Ranibizumab (Lucentis) in neovascular age-related macular degeneration: Evidence from clinical trials. *British Journal of Ophthalmology* 20 May
- Kanthan GL, Wang JJ, Burlutsky G, Cumming RG, Mitchell P. Exogenous oestrogen exposure, female reproductive factors and the long-term incidence of cataract – the Blue Mountains Eye Study. *Acta Ophthalmologica* 1 June
- Dimasi DP, Chen JY, Hewitt AW, Klebe S, Davey R, Stirling J, Thompson E, Forbes R, Tan TY, Savarirayan R, Mackey DA, Healey PR, Mitchell P, Burdon KP, Craig JE. Novel quantitative trait loci for central corneal thickness identified by candidate gene analysis of osteogenesis imperfecta genes. *Journal of Human Genetics* 28 August
- Chen L, Tonkin AM, Moon L, Mitchell P, Dobson A, Giles G, Hobbs M, Phillips PJ, Shaw JE, Simmons D, Simons LA, Fitzgerald AP, Backer GD, Backer DD. Recalibration and validation of the SCORE risk chart in the Australian population: the AusSCORE chart. *European Journal of Cardiovascular Prevention and Rehabilitation* 8 September
- Samarawickrama C, Wang JJ, Huynh SC, Pai A, Burlutsky G, Rose K, Mitchell P. Ethnic differences in optic nerve head and retinal nerve fibre layer thickness parameters. *British Journal of Ophthalmology* 12 October
- Leone JF, Kifley A, Morgan IG, Wang JJ, Cornall E, Mitchell P, Rose KA. Prevalence of heterophoria and associations with refractive error, heterotropia and ethnicity in Australian school children. *British Journal of Ophthalmology* 22 October
- Boey PY, Tay WT, Lamoureux EL, Tai ES, Mitchell P, Wang JJ, Saw SM, Wong TY. C-reactive protein and age-related macular degeneration and cataract: the Singapore Malay Eye Study. *Investigative Ophthalmology and Visual Science* 20 November
- Dirani M, Chan YH, Gazzard G, Hornbeak DM, Leo S, Selvaraj P, Zhou B, Young TL, Mitchell P, Varma R, Wong TY, Saw SM. Prevalence of refractive error in Singapore Chinese children: The Strabismus, Amblyopia and Refractive error in Young Singaporean Children (STARS) study. *Investigative Ophthalmology and Visual Science* 20 November
- Veerappan S, Pertile KK, Islam AF, Schäche M, Chen CY, Mitchell P, Dirani M, Baird PN. Role of the Hepatocyte Growth Factor gene in refraction. *Ophthalmology* 14 December
- Zheng Y, Wong TY, Lamoureux E, Mitchell P, Loon SC, Saw SM, Aung T. Diagnostic ability of Heidelberg Retina Tomography in detecting glaucoma in a population setting: the Singapore Malay Eye Study. *Ophthalmology* 14 December
- Rogers S, McIntosh RL, Cheung N, Lim L, Wang JJ, Mitchell P, Kowalski JW, Nguyen H, Wong TY, International Eye Disease Consortium. The prevalence of retinal vein occlusion: Pooled data from population studies from the US, Europe, Asia and Australia. *Ophthalmology* 16 December [Epub ahead of print].
- Fotedar R, Wang JJ, Burlutsky G, Morgan IG, Rose K, Wong TY, Mitchell P. Distribution of axial length and ocular biometry measured using partial coherence laser interferometry (IOL Master) in an older white population. *Ophthalmology* 22 December [Epub ahead of print].
- Lim LS, Lamoureux E, Saw SM, Tay WT, Mitchell P, Wong TY. Are myopic eyes less likely to have diabetic retinopathy? *Ophthalmology* 22 December [Epub ahead of print].

#### CENTRE FOR VIRUS RESEARCH

- Blyth, C. C., R. Booy and D. Dwyer (). Point of Care Testing: Diagnosis outside the virology laboratory. *Diagnostic Virology Protocols*. United Kingdom.
- Blyth, C. C., J. R. Iredell and D. E. Dwyer (). "Rapid-test sensitivity for novel swine-origin influenza A (H1N1) virus in humans." *N Engl J Med* 361(25): 2493.
- Carey, D., D. Baker, K. Petoumenos, J. Chuah, G. D. Rogers, J. Watson, D. A. Cooper, S. Emery and A. Carr (). "Poly-l-lactic acid for HIV-1 facial lipoatrophy: 48-week follow-up." *HIV Med* 10(3): 163-172.
- Cheng, A. C., D. E. Dwyer, A. T. Kotsimpos, M. Starr, T. M. Korman, J. P. Buttery, C. R. Jenkins, V. L. Krause and P. D. Johnson (). "Summary of the Australasian

- Society for Infectious Diseases and the Thoracic Society of Australia and New Zealand guidelines: treatment and prevention of H1N1 influenza 09 (human swine influenza) with antiviral agents." *Med J Aust* 191(3): 142-145.
- Cheung, A. K., D. J. Gottlieb, B. Plachter, S. Pepperl-Klindworth, S. Avdic, A. L. Cunningham, A. Abendroth and B. Slobedman (). "The role of the human cytomegalovirus UL111A gene in down-regulating CD4+ T-cell recognition of latently infected cells: implications for virus elimination during latency." *Blood* 114(19): 4128-4137.
- Cross, N. B., A. C. Webster, P. J. O'Connell, N. Jeoffreys, D. E. Dwyer and J. C. Craig (). "Diagnostic accuracy of blood qualitative nucleic acid testing for polyomavirus-associated nephropathy in kidney recipients." *Nephrology (Carlton)* 14(3): 350-356.
- Donaghy, H., L. Bosnjak, A. N. Harman, V. Marsden, S. K. Tyring, T. C. Meng and A. L. Cunningham (). "Role for plasmacytoid dendritic cells in the immune control of recurrent human herpes simplex virus infection." *J Virol* 83(4): 1952-1961.
- Dwyer, D. E. (). *Influenza. Infectious Diseases: A Clinical Approach*. A. Yung, M. McDonald, D. Spelman et al. Victoria, IP Communications.
- Foo, H., C. C. Blyth, S. van Hal, K. McPhie, M. Ratnamohan, M. Fennell, F. Ba Alawi, W. Rawlinson, S. Adamson, P. Armstrong and D. E. Dwyer (). "Laboratory test performance in young adults during influenza outbreaks at World Youth Day 2008." *J Clin Virol* 46(4): 384-386.
- Gray, L., M. Roche, M. J. Churchill, J. Sterjovski, A. Ellett, P. Pombourios, S. Sherieff, B. Wang, N. Saksena, D. F. Purcell, S. Wesselingh, A. L. Cunningham, B. J. Brew, D. Gabuzda and P. R. Gorry (). "Tissue-specific sequence alterations in the human immunodeficiency virus type 1 envelope favoring CCR5 usage contribute to persistence of dual-tropic virus in the brain." *J Virol* 83(11): 5430-5441.
- Harman, A. N., M. Kraus, C. R. Bye, K. Byth, S. G. Turville, O. Tang, S. K. Mercier, N. Nasr, J. L. Stern, B. Slobedman, C. Driessen and A. L. Cunningham (). "HIV-1-infected dendritic cells show 2 phases of gene expression changes, with lysosomal enzyme activity decreased during the second phase." *Blood* 114(1): 85-94.
- Hurt, A. C., J. Ernest, Y. M. Deng, P. Iannello, T. G. Besselaar, C. Birch, P. Buchy, M. Chittaganpitch, S. C. Chiu, D. Dwyer, A. Guigon, B. Harrower, I. P. Kei, T. Kok, C. Lin, K. McPhie, A. Mohd, R. Olveda, T. Panayotou, W. Rawlinson, L. Scott, D. Smith, H. D'Souza, N. Komadina, R. Shaw, A. Kelso and I. G. Barr (). "Emergence and spread of oseltamivir-resistant A(H1N1) influenza viruses in Oceania, South East Asia and South Africa." *Antiviral Res* 83(1): 90-93.
- Iskander, M., A. Kesson, D. Dwyer, L. Rost, M. Pym, H. Wang, M. McCaskill and R. Booy (). "The burden of influenza in children under 5 years admitted to the Children's Hospital at Westmead in the winter of 2006." *J Paediatr Child Health*.
- Italiano, C. M., C. S. Toi, S. P. Chan and D. E. Dwyer (). "Prolonged varicella viraemia and streptococcal toxic shock syndrome following varicella vaccination of a health care worker." *Med J Aust* 190(8): 451-453.
- Jaworowski, A., W. J. Cheng, C. L. Westhorpe, A. Abendroth, S. M. Crowe and B. Slobedman (). "Enhanced monocyte Fc phagocytosis by a homologue of interleukin-10 encoded by human cytomegalovirus." *Virology* 391(1): 20-24.
- Kelly, B. J., C. Fraefel, A. L. Cunningham and R. J. Diefenbach (). "Functional roles of the tegument proteins of herpes simplex virus type 1." *Virus Res* 145(2): 173-186.
- Lai, J., O. K. Bernhard, S. G. Turville, A. N. Harman, J. Wilkinson and A. L. Cunningham (). "Oligomerization of the macrophage mannose receptor enhances gp120-mediated binding of HIV-1." *J Biol Chem* 284(17): 11027-11038.
- MacIntyre, C. R., S. Cauchemez, D. E. Dwyer, H. Seale, P. Cheung, G. Browne, M. Fasher, J. Wood, Z. Gao, R. Booy and N. Ferguson (). "Face mask use and control of respiratory virus transmission in households." *Emerg Infect Dis* 15(2): 233-241.
- Maddocks, S., G. M. Scandurra, C. Nourse, C. Bye, R. B. Williams, B. Slobedman, A. L. Cunningham and W. J. Britton (). "Gene expression in HIV-1/Mycobacterium tuberculosis co-infected macrophages is dominated by M. tuberculosis." *Tuberculosis (Edinb)* 89(4): 285-293.
- Martin, A., M. Bloch, J. Amin, D. Baker, D. A. Cooper, S. Emery and A. Carr (). "Simplification of antiretroviral therapy with tenofovir-emtricitabine or abacavir-Lamivudine: a randomized, 96-week trial." *Clin Infect Dis* 49(10): 1591-1601.
- Mills, A. M., M. Nelson, D. Jayaweera, K. Ruxrungtham, I. Cassetti, P. M. Girard, C. Workman, I. Dierynck, V. Sekar, C. V. Abeele and L. Lavreys (). "Once-daily darunavir/ritonavir vs. lopinavir/ritonavir in treatment-naive, HIV-1-infected patients: 96-week analysis." *AIDS* 23(13): 1679-1688.
- Miranda-Saksena, M., R. A. Boadle, A. Aggarwal, B. Tijono, F. J. Rixon, R. J. Diefenbach and A. L. Cunningham (). "Herpes simplex virus utilizes the large secretory vesicle pathway for anterograde transport of tegument and envelope proteins and for viral exocytosis from growth cones of human fetal axons." *J Virol* 83(7): 3187-3199.
- Mocroft, A., C. Wyatt, L. Szczech, J. Neuhaus, W. El-Sadr, R. Tracy, L. Kuller, M. Shlipak, B. Angus, H. Klinker and M. Ross (). "Interruption of antiretroviral therapy is associated with increased plasma cystatin C." *AIDS* 23(1): 71-82.
- Osbourne, M., K. A. McPhie, V. M. Ratnamohan, D. E. Dwyer and D. N. Durrheim (). "Outbreak of human metapneumovirus infection in a residential aged care facility." *Commun Dis Intell* 33(1): 38-40.
- Page, A., R. Taylor, J. Richters, J. Shaw, J. Taylor, A. Cunningham and A. Mindel (). "Upstairs and downstairs: socio-economic and gender interactions in herpes simplex virus type 2 seroprevalence in Australia." *Sex Transm Dis* 36(6): 344-349.
- Rodger, A. J., Z. Fox, J. D. Lundgren, L. H. Kuller, C. Boesecke, D. Gey, A. Skoutelis, M. B. Goetz and A. N. Phillips (). "Activation and coagulation biomarkers are independent predictors of the development of opportunistic disease in patients with HIV infection." *J Infect Dis* 200(6): 973-983.
- Rosewell, A., C. Chiu, R. Lindley, D. E. Dwyer, C. R. Moffatt, C. Shineberg, E. Clarke, R. Booy and C. R. Macintyre (). "Surveillance for outbreaks of influenza-like illness in the institutionalized elderly." *Epidemiol Infect*: 1-9.
- Rosewell, A., B. Wang, N. Saksena, C. R. Macintyre, R. Lindley, C. Chiu, C. Shineberg, E. Clarke, K. McPhie, V. M. Ratnamohan, R. Booy and D. Dwyer (). "Failure to detect oseltamivir resistance by rolling circle amplification and sequencing following use in an influenza A (H3N2) outbreak at an aged care facility." *Journal of Antivirals and Antiretrovirals*.
- Saksena, N., J. Q. Wu, K. A. Lau, L. Zhou, M. Soedjono and B. Wang (). *CD8 Antiviral Soluble Factors and Human Immunodeficiency Virus (HIV) Control*. M. A. Ph.D. Bentham Science Publishers: 11-34.
- Seale, H., S. Corbett, D. E. Dwyer and C. R. MacIntyre (). "Feasibility exercise to evaluate the use of particulate respirators by emergency department staff during the 2007 influenza season." *Infect Control Hosp Epidemiol* 30(7): 710-712.
- Seale, H., D. E. Dwyer, B. J. Cowling, Q. Wang, P. Yang and C. R. Macintyre (). "A review of medical masks and respirators for use during an influenza pandemic." *Influenza Other Respi Viruses* 3(5): 205-206.
- Seale, H., K. M. Weston, D. E. Dwyer, M. Zhu, L. Allchin, R. Booy and C. R. MacIntyre (). "The use of oseltamivir during an influenza B outbreak in a chronic care hospital." *Influenza Other Respi Viruses* 3(1): 15-20.
- Sheppard, V., B. Forssman, M. J. Ferson, C. Moreira, S. Campbell-Lloyd, D. E. Dwyer and J. M. McNulty (). "The effectiveness of prophylaxis for measles contacts in NSW." *N S W Public Health Bull* 20(5-6): 81-85.

- Sheppard, V., B. Forssman, M. J. Ferson, C. Moreira, S. Campbell-Lloyd, D. E. Dwyer and J. M. McAnulty (). "Vaccine failures and vaccine effectiveness in children during measles outbreaks in New South Wales, March-May 2006." *Commun Dis Intell* 33(1): 21-26.
- Slobedman, B., P. A. Barry, J. V. Spencer, S. Avdic and A. Abendroth (). "Virus-encoded homologs of cellular interleukin-10 and their control of host immune function." *J Virol* 83(19): 9618-9629.
- Steain, M. C., D. E. Dwyer, A. C. Hurt, C. Kol, N. K. Saksena, A. L. Cunningham and B. Wang (). "Detection of influenza A H1N1 and H3N2 mutations conferring resistance to oseltamivir using rolling circle amplification." *Antiviral Res* 84(3): 242-248.
- Stein, A. N., H. Britt, C. Harrison, E. L. Conway, A. Cunningham and C. R. Macintyre (). "Herpes zoster burden of illness and health care resource utilisation in the Australian population aged 50 years and older." *Vaccine* 27(4): 520-529.
- Su, B., S. Wurtzer, M. A. Rameix-Welti, D. Dwyer, S. van der Werf, N. Naffakh, F. Clavel and B. Labrosse (). "Enhancement of the influenza A hemagglutinin (HA)-mediated cell-cell fusion and virus entry by the viral neuraminidase (NA)." *PLoS One* 4(12): e8495.
- Taylor, J., K. McPhie, J. Druce, C. Birch and D. E. Dwyer (). "Evaluation of twenty rapid antigen tests for the detection of human influenza A H5N1, H3N2, H1N1, and B viruses." *J Med Virol* 81(11): 1918-1922.
- Templeton, D. J., F. Jin, G. P. Prestage, B. Donovan, J. C. Imrie, S. C. Kippax, P. H. Cunningham, J. M. Kaldor, A. Mindel, A. L. Cunningham and A. E. Grulich (). "Circumcision and risk of sexually transmissible infections in a community-based cohort of HIV-negative homosexual men in Sydney, Australia." *J Infect Dis* 200(12): 1813-1819.
- Trapp, S., N. R. Derby, R. Singer, A. Shaw, V. G. Williams, S. G. Turville, J. W. Bess, Jr., J. D. Lifson and M. Robbiani (). "Double-stranded RNA analog poly(I:C) inhibits human immunodeficiency virus amplification in dendritic cells via type I interferon-mediated activation of APOBEC3G." *J Virol* 83(2): 884-895.
- van Hal, S. J., H. Foo, C. C. Blyth, K. McPhie, P. Armstrong, V. Sintchenko and D. E. Dwyer (). "Influenza outbreak during Sydney World Youth Day 2008: the utility of laboratory testing and case definitions on mass gathering outbreak containment." *PLoS One* 4(9): e6620.
- van Hal, S. J., B. Herring, Z. Deris, B. Wang, N. K. Saksena and D. E. Dwyer (). "HIV-1 integrase polymorphisms are associated with prior antiretroviral drug exposure." *Retrovirology* 6: 12.
- Wade, J., J. Sterjovski, L. Gray, M. Roche, L. Chiavaroli, A. Ellett, M. R. Jakobsen, D. Cowley, F. Pereira Cda, N. Saksena, B. Wang, D. F. Purcell, I. Karlsson, E. M. Fenyo, M. Churchill and P. R. Gorry (2010). "Enhanced CD4+ cellular apoptosis by CCR5-restricted HIV-1 envelope glycoprotein variants from patients with progressive HIV-1 infection." *Virology* 396(2): 246-255.
- Wang, B., D. E. Dwyer, C. B. Chew, C. Kol, Z. P. He, H. Joshi, M. C. Steain, A. L. Cunningham and N. K. Saksena (). "Sensitive detection of the K103N non-nucleoside reverse transcriptase inhibitor resistance mutation in treatment-naive HIV-1 infected individuals by rolling circle amplification." *J Virol Methods* 161(1): 128-135.
- Wang, H., F. Kong, T. C. Sorrell, B. Wang, P. McNicholas, N. Pantarat, D. Ellis, M. Xiao, F. Widmer and S. C. Chen (). "Rapid detection of ERG11 gene mutations in clinical *Candida albicans* isolates with reduced susceptibility to fluconazole by rolling circle amplification and DNA sequencing." *BMC Microbiol* 9: 167.
- Zaunders, J. J., M. L. Munier, N. Seddiki, S. Pett, S. Ip, M. Bailey, Y. Xu, K. Brown, W. B. Dyer, M. Kim, R. de Rose, S. J. Kent, L. Jiang, S. N. Breit, S. Emery, A. L. Cunningham, D. A. Cooper and A. D. Kelleher (). "High levels of human antigen-specific CD4+ T cells in peripheral blood revealed by stimulated coexpression of CD25 and CD134 (OX40)." *J Immunol* 183(4): 2827-2836.
- Zhou, F., F. Kong, K. McPhie, M. Ratnamohan, L. Donovan, F. Zeng, G. L. Gilbert and D. E. Dwyer (). "Identification of 20 common human enterovirus serotypes by use of a reverse transcription-PCR-based reverse line blot hybridization assay." *J Clin Microbiol* 47(9): 2737-2743.
- a novel marsupial cathelicidin from the tammar wallaby (*Macropus eugenii*). *Vet Immunol Immunopathol.* Feb 15;127(3-4):269-76.
- Yap, BCM, Simpkins, G L, Collyer, C A, Hunter, N, Crossley, M J , Porphyrin-linked nitroimidazole antibiotics targeting *Prophyromonas gingivalis*. *Organic & Biomolecular Chemistry*,7(Online: DOI: 10.1039/b904340c), 2855-2863
- Nguyen, K-A, Zyllicz, J, Szczesny, P, Sroka, A, Hunter, N, Potempa, J , Verification of a topology model of PorT as an integral outer-membrane protein in *Prophyromonas gingivalis*. *Microbiology*,155, 328-337
- Monteiro AC, Scovino A, Raposo S, Gaze VM, Cruz C, Svensjo E, Narciso MS, Colombo AP, Pesquero JB, Feres-Filho E, Nguyen KA, Sroka A, Potempa J, Scharfstein J , Kinin danger signals proteolytically released by gingipains induce fimriae-specific IFN- $\gamma$ - and IL-17-producing T Cells in mice infected intramuscularly with *prophyromonas gingivalis*. *The Journal of Immunology*, 183: 3700-3711.
- Nadkarni MA, Chhour KL, Browne G, Jacques NA, Hunter N , Lysine gingipains (kgp) biovars of *Prophyromonas gingivalis* exhibit differential distribution on oral mucosal sites. *Journal of Clinical Microbiology* 47: 3350-3352
- Nadkarni MA, Martin FE, Jacques NA and Hunter N. . Caries, p.279-280. In *Encyclopedia of Molecular Mechanisms of Disease*. Springer-Verlag, Heidelberg.

#### INSTITUTE OF DENTAL RESEARCH

Nadkarni MA, FE Martin, N Hunter and NA Jacques. Methods for optimizing DNA extraction before quantifying oral bacterial numbers by real-time PCR. *FEMS Microbiol Lett* .

Potempa M, Potempa J, Kantyka T, Nguyen KA, Wawrzonek K, Manandhar SP, Popadiak K, Riesbeck K, Eick S and Blom AM. Interpain A, Cysteine Proteinase from *Prevotella intermedia* Inhibits Complement by Degrading Complement Factor C3. *PLoS Pathogens* ; 5(2): e1000316. doi:10.1371/journal.ppat.1000316

Zou W, Gao J, Jones AS, Hunter N, Swain MV. Characterization of a novel calibration method for mineral density determination of dentine by X-ray microtomography. *Analyst*. Jan;134(1):72-9. Epub 2008 Oct 18.

Ye P, Nadkarni MA, Simonian M, Hunter N. CD24 regulated gene expression and distribution of tight junction proteins is associated with altered barrier function in oral epithelial monolayers. *BMC Cell Biol.* Jan 13;10:2.

Nguyen KA, Zyllicz J, Szczesny P, Sroka A, Hunter N, Potempa J. Verification of a topology model of PorT as an integral outer-membrane protein in *Prophyromonas gingivalis*. *Microbiology.* 155(Pt 2):328-37.

Carman RL, Old JM, Baker M, Jacques NA, Deane EM. Identification and expression of

#### INSTITUTE FOR IMMUNOLOGY AND ALLERGY RESEARCH

Suppiah V, Moldovan M, Ahlenstiel G, Berg T, Weltman M, Abate ML, Bassendine M, Spengler U, Dore GJ, Powell E, Riordan S, Sheridan D, Smedile A, Fragomeli V, Müller T, Bahlo M, Stewart GJ, Booth DR, George J. IL28B is associated with response to chronic hepatitis C interferon-alpha and ribavirin therapy. *Nat Genet*.

ANZgene (incl Booth DR) Genome-wide association study identifies new multiple sclerosis susceptibility loci on chromosomes 12 and 20. *Nat Genetics* 41(7):824-8. IF:26

Stankovich J, Butzkueven H, Marriott M, Chapman C, Tubridy N, Tait BD, Varney MD, Taylor BV, Foote SJ; ANZgene Consortium (incl Booth DR), Kilpatrick TJ, Rubio JPHLA-DRB1 associations with disease susceptibility and clinical course in Australians with multiple sclerosis. *Tissue Antigens*. 74(1):17-21. (IF:2.2)

IMSGC, (incl Booth DR) Replication analysis identifies TYK2 as a multiple sclerosis susceptibility factor. *Eur J Hum Genet*. 1309-13

De Jager P, et al (incl Booth DR) The role of the CD58 locus in multiple sclerosis. *Proc Natl Acad Sci U S A*. 106(13):5264-9.

International Multiple Sclerosis Genetics Consortium (IMSGC) (incl Booth DR). The expanding genetic overlap between multiple sclerosis and type I diabetes. *Genes Immun*. (1):11-4

## LUDWIG ENGEL CENTRE FOR RESPIRATORY RESEARCH

Kairaitis K, Howitt L, Wheatley JR, Amis TC. Mass loading of the upper airway extraluminal tissue space in rabbits: effects on tissue pressure and pharyngeal airway lumen geometry. *J Appl Physiol*. March ;106(3): 887-92.

Kairaitis K, Verma M, Fish V, Wheatley JR, Amis TC. Pharyngeal muscle contraction modifies peri-pharyngeal tissue pressure in rabbits. *Respir Physiol Neurobiol*. April ;166(2): 95-101.

Kairaitis K. Is the pharynx a muscular hydrostat? *Medical Hypotheses*. July

House HH and Middleton PG. Impact of different chloride and glucose concentrations on nasal potential difference. *Ped Pulmonol*. July ; 44(7): 645-48.

Middleton S, Vermeulen W, Byth K, Sullivan CE, Middleton PG. Treatment of Obstructive Sleep Apnoea in Samoa progressively reduces daytime blood pressure over size months. *Respirology*. April ;14: 404-410.

Goubau C, Wilschanski M, Skalická V, Lebecque P, Southern KW, Sermet I, Munck A, Derichs N, Middleton PG, Hjelte L, Padoan R, Vasar M, De Boeck K. Phenotypic characterisation of patients with intermediate sweat chloride values: towards validation of the European diagnostic algorithm for cystic fibrosis. *Thorax*. August ; 64(8):683-91.

## STORR LIVER UNIT

Jonker JW, Stedman CAM, Liddle C, Downes M () Hepatobiliary ABC transporters: physiology, regulation and implications for disease. *Front Biosci* 14:4904-20. (IF:3.308)

Hilmer SN, Seale JP, Le Couter DG, Crampton R Liddle C () Do medical courses adequately prepare interns for safe and effective prescribing in New South Wales public hospitals? *Int Med J* 39:428-34. (IF:2.027)

Phung N, Pera N, Farrell G, Leclercq I, Hou JY, George J. Pro-oxidant-mediated hepatic fibrosis and effects of antioxidant intervention in murine dietary steatohepatitis. *International Journal of Molecular Medicine* ;24:171-80. (IF:1.880)

Bhala N, Usherwood T, George J. Non-alcoholic Fatty Liver Disease: 10 Minute Consultation. *British Medical Journal* ;339:b2474. (IF:12.827)

Matthews G; Hellard M; Haber P; Marks P; Baker D; Sasadeusz J; Bloch M; Crawford D; Rawlinson W; Lloyd A; Kaldor J; Dore G. Characteristics And Treatment Outcomes Amongst Hiv Positive Individuals Within The Australian Trial In Acute Hepatitis C. for the ATAHc Study Group. Second line author. *Clinical Infectious Diseases* ;48:650-658. Author Reply: *Clinical Infectious Diseases* ;49:319. (IF:8.266)

George J, Robotin M. Overview: Hepatocellular Carcinoma – The Future Starts Now. *Cancer Forum* ;33:80-87.

Wang J, Leclercq I, Brymora JM, Ramezani-Moghadam M, London RM, Brigstock D, George J. Kupffer cells: the main player in leptin-induced liver fibrosis. *Gastroenterology* ;137:713-723. (IF:12.716)

Robotin MC, Kansil M, Howard K, George J, Tipper S, Dore GJ, et al. Antiviral therapy for hepatitis B-related liver cancer prevention is more cost-effective than cancer screening. *Journal of Hepatology* ;50:990-998 (IF:7.056)

Sherman M. Prevention of hepatocellular carcinoma: The holy grail of hepatitis B treatment. *Journal of Hepatology* ;50:854-856. (IF:7.056)

Milner K, van der Poorten D, Xu A, Bugianesi E, Kench JG, Lam KSL, Chisholm DJ, George J. Adipocyte Fatty Acid Binding Protein levels relate to inflammation and fibrosis in Non Alcoholic Fatty Liver Disease. *Hepatology* ;49:1926-34. (IF:11.355)

Adipocytokine levels in non-alcoholic fatty liver disease van der Poorten, Milner K, Chisholm D, George J. [Letter] *Hepatology* ;50:327-328. (IF:11.355)

Smith B, George J. Adipocyte-hepatocyte Crosstalk and the Pathogenesis of Nonalcoholic Fatty Liver Disease. *Hepatology* ;49:1765-1767. (IF:11.355)

Booth ML, Dobbins T, Aitken R, Denney-Wilson E, Hardy LL, Okely AD, George J, Sullivan D, Cowell C. Costs of Managing Conditions associated with Obesity Among Australian Teenagers. *Journal of Paediatrics and Child Health* 45:448-56. (IF:1.4)

Johnson NA, Sachinwalla T, Walton DW, Smith K, Armstrong A, Thompson MW, George J. Aerobic exercise training reduces hepatic and visceral lipids in obese individuals without weight loss. *Hepatology* ;50:1105-1112. (IF:11.355)

Brooks M. Reuters Health. Exercise, even without weight loss, reduces obesity-related fatty liver. (Published 17th September )

Regular Aerobic Exercise Reduces Health Concerns Associated with Fatty Liver. Benefits Are Not Dependent On Weight Loss. *Hepatology News Alert*. September .

White PA, Grebely J, Flynn J, Matthews G, Renkin M, Pham ST, Bull RA, Yeung B, Rawlinson W, Kaldor J, Lloyd A, Hellard M, Ffrench M, Dore JG, on behalf of the ATAHc Study Group. Second Line Author. *Hepatitis*

C virus reinfection following treatment-induced clearance of recently acquired infection. *Gastroenterology* (Submitted 26 June ). (IF:12.591)

Dore GJ, Hellard M, Matthews G, Grebely J, Harber PS, Petoumenos K, Yeung B, Marks P, van Beek I, McCaughan G, White P, Ffrench R, Rawlinson W, Lloyd AR, Kaldor JM on behalf of the ATAHc Study Group. Second Line Author. Effective treatment of injecting drug users with recently acquired Hepatitis C virus infection: The ATAHc Study. *Gastroenterology* (Epub ahead of print, accepted September 23). (IF:12.591)

St George A, Bauman A, Johnston A, Farrell G, Chey T, George J. The Independent Effects of Physical Activity in Patients with Non-Alcoholic Fatty Liver Disease. *Hepatology* ;50:68-76. (IF:11.355)

Accepted for Media Release Exercise Helps Patients with Non-Alcoholic Fatty Liver Disease.

St George A, Bauman A, Johnston A, Farrell G, Chey T, George J. Effect of a Lifestyle Intervention in Patients with Abnormal Liver Enzymes and Metabolic Risk Factors. *Journal of Gastroenterology and Hepatology* ;24:399-407. (IF:2.404)

Editorial: Hickman I. Obesity management in liver clinics: What's your style of lifestyle intervention? *Journal of Gastroenterology and Hepatology* ;24:327-328. (IF:2.404)

Douglas MW, George J. Molecular mechanisms of insulin resistance in chronic hepatitis C. *World Journal of Gastroenterology* ;15:4356-4364. (IF:2.081)

Suppiah V, Moldovan M, Ahlenstiel G, Berg T, Weltman M, Abate ML, Bassendine M, Spengler U, Dore GJ, Powell E, Riordan S, Sheridan D, Fragomeli V, Muller T, Bahlo M, Stewart GJ, Booth DR, George J for the Hepatitis C Group. Interferon Lambda 3 Haplotype is Associated with Treatment Response to Interferon-Alpha and Ribavirin Combination Therapy in Chronic Hepatitis C. *Nature Genetics* ;41:1100-1104 (Epub Sep 13) (IF:30.259)

Editorial: O'Brien TR. Interferon-alfa, interferon-lambda and hepatitis C. *Nature Genetics* ;41:(Epub Sep 13).

Poynard T, Colombo M, Bruix J, Schiff E, Terg R, Flamm S, Moreno-Otero R, Carrilho F, Schmidt W, Berg T, McGarrity T, Heathcote EJ, Gonçalves F, Diago M, Craxi A, Silva M, Bedossa P, Mukhopadhyay P, Griffel L, Burroughs M, Brass C, Albrecht J for the EPIC Study Group. Peginterferon alfa-2b and Ribavirin: Effective in Patients With Hepatitis C Who Failed Interferon alfa/Ribavirin Therapy. Second Line Author. *Gastroenterology* ;136:1618-28. (IF:12.591)

van Hazel GA, Pavlakis N, Goldstein D, Olver IN, Tapner MJ, Price D, Bower GD, Briggs GM, Rossleigh MA, Taylor DJ, George J. Treatment of 5-Fluorouracil-Refractory Patients With Liver Metastases From Colorectal Cancer Using Yttrium-90 Resin Microspheres Plus Concomitant Systemic Irinotecan Chemotherapy. *Journal of Clinical Oncology* ;27:4089-4095. (IF:17.157)

Editorial: Kuebler JP. Radioembolization of Liver Metastases in Patients with Colorectal cancer: A Nonsurgical Treatment With Combined Modality Potential. *Journal of Clinical Oncology* ;27:1041-4042. (IF:17.157)

Milner KL, Chisholm D, George J. The Many Faces of Hepatitis C: Liver Disease and Type 2 Diabetes. *Hepatology* ;50:668-670. (IF:11.355)

Roberts S, Weltman MD, Crawford D, McCaughan GW, Sievert W, Cheng WS, Rawlinson W, Desmond PV, Marks PS, Yoshihara M, Rizkalla B, DePamphilis JK, Dore G for the Chariot Study Group. Impact of High-Dose Peginterferon Alfa-2A on Virological Response Rates in Patients with Hepatitis C Genotype 1: a Randomized Controlled Trial. Second Line Author *Hepatology* ;50:1045-1055. (IF:11.355)

Grebely J, Petoumenos K, Matthews GV, Haber P, Marks P, Lloyd AR, Kaldor JM, Dore GJ and Hellard M for the ATAC Study Group. Factors associated with uptake of treatment for recent hepatitis C virus infection in a predominantly injecting drug user cohort: the ATAC Study. Second Line Author *Drug and Alcohol Dependence* (Accepted 23rd September). (IF:3.922)

van der Poorten D, Milner K, George J. Effect of adipokines on liver disease in females. *Female Hepatology: Impact of female sex on progression of liver disease* (ISBN:978-81-308-0361-6).

Pattullo V, George J. Managing the Patient with Chronic Hepatitis receiving Chemotherapy. In *Consultation: When Cancer Crosses Disciplines*. Imperial College Press (Accepted 25 May).

George J, Robotin M Editors. *Hepatocellular Carcinoma*. Cancer Forum. Journal of the Clinical Oncology Society of Australia July ;1-136.

Milner KL, van der Poorten D, Trenell M, Jenkins A, Xu A, Smythe G, Dore G, Zerky A, Weltman M, Fragomeli V, George J\*. Chisholm D\*. Chronic hepatitis CL Associated insulin resistance is predominantly peripheral rather than hepatic. *Gastroenterology*.

#### WESTMEAD INSTITUTE FOR CANCER RESEARCH

Becker TM, Haferkamp S, Dijkstra MK, Scurr LL, Frausto M, Diefenbach E, Scolyer RA, Reisman DN, Mann GJ, Kefford RF, Rizos H () The chromatin remodelling factor BRG1 is a novel binding partner of the tumor suppressor p16INK4a. *Mol Cancer* 8: 4

Bishop DT, Demenais F, Iles MM, Harland M, Taylor JC, Corda E, Randerson-Moor J, Aitken JF, Avril MF, Azizi E, Bakker B, Bianchi-Scarra G, Bressac-de Paillerets B, Calista D, Cannon-Albright LA, Chin AWT, Debnjak T, Galore-Haskel G, Ghiorzo P, Gut I, Hansson J, Hocevar M, Hoiom V, Hopper JL, Ingvar C, Kanetsky PA, Kefford RF, Landi MT, Lang J, Lubinski J, Mackie R, Malvey J, Mann GJ, Martin NG, Montgomery GW, van Nieuwpoort FA, Novakovic S, Olsson H, Puig S, Weiss M, van Workum W, Zelenika D, Brown KM, Goldstein AM, Gillanders

EM, Boland A, Galan P, Elder DE, Gruis NA, Hayward NK, Lathrop GM, Barrett JH, Bishop JA () Genome-wide association study identifies three loci associated with melanoma risk. *Nat Genet* 41: 920-925

Bradstock K, Hertzberg M, Kerridge I, Sventnilson J, George B, McGurgan M, Huang G, Antonenas V, Gottlieb D () Single versus double unrelated umbilical cord blood units for allogeneic transplantation in adults with advanced haematological malignancies: a retrospective comparison of outcomes. *Intern Med J* 39: 744-751

Brooke G, Rossetti T, Pelekanos R, Ilic N, Murray P, Hancock S, Antonenas V, Huang G, Gottlieb D, Bradstock K, Atkinson K () Manufacturing of human placenta-derived mesenchymal stem cells for clinical trials. *Br J Haematol* 144: 571-579

Cheung AK, Gottlieb DJ, Plachter B, Pepperl-Klindworth S, Avdic S, Cunningham AL, Abendroth A, Slobedman B () The role of the human cytomegalovirus UL111A gene in down-regulating CD4+ T-cell recognition of latently infected cells: implications for virus elimination during latency. *Blood* 114: 4128-4137

Crazzolaro R, Bendall L () Emerging treatments in acute lymphoblastic leukemia. *Curr Cancer Drug Targets* 9: 19-31

Crazzolaro R, Bradstock KF, Bendall LJ () RAD001 (Everolimus) induces autophagy in acute lymphoblastic leukemia. *Autophagy* 5: 727-728

Crazzolaro R, Cisterne A, Thien M, Hewson J, Baraz R, Bradstock KF, Bendall LJ () Potentiating effects of RAD001 (Everolimus) on vincristine therapy in childhood acute lymphoblastic leukemia. *Blood* 113: 3297-3306

Cust AE, Schmid H, Maskiell JA, Jetann J, Ferguson M, Holland EA, Agha-Hamilton C, Jenkins MA, Kelly J, Kefford RF, Giles GG, Armstrong BK, Aitken JF, Hopper JL, Mann GJ () Population-based, case-control-family design to investigate genetic and environmental influences on melanoma risk: Australian Melanoma Family Study. *Am J Epidemiol* 170: 1541-1554

Davis ID, Brady B, Kefford RF, Millward M, Cebon J, Skrumsager BK, Mouritzen U, Hansen LT, Skak K, Lundsgaard D, Frederiksen KS, Kristjansen PE, McArthur G () Clinical and biological efficacy of recombinant human interleukin-21 in patients with stage IV malignant melanoma without prior treatment: a phase IIa trial. *Clin Cancer Res* 15: 2123-2129

Etemadmoghadam D, deFazio A, Beroukhi R, Mermel C, George J, Getz G, Tothill R, Okamoto A, Raeder MB, AOCSS Study Group, Harnett P, Lade S, Akslen LA, Tinker AV, Locandro B, Alsop K, Chiew YE, Traficante N, Fereday S, Johnson D, Fox S, Sellers W, Urashima M, Salvesen HB, Meyerson M, Bowtell D () Integrated genome-wide DNA copy number and expression analysis identifies distinct mechanisms of primary chemoresistance in ovarian carcinomas. *Clinical Cancer Research* 15: 1417-1427

Ferguson PE, Sorrell TC, Bradstock KF, Carr P, Gilroy NM () Parainfluenza Virus Type 3 Pneumonia in Bone Marrow Transplant Recipients: Multiple Small Nodules in High-Resolution Lung Computed Tomography Scans Provide a Radiological Clue to Diagnosis. *Clin Infect Dis*

Gartside MG, Chen H, Ibrahim OA, Byron SA, Curtis AV, Wellens CL, Bengston A, Yudd LM, Eliseenkova AV, Ma J, Curtin JA, Hyder P, Harper UL, Riedesel E, Mann GJ, Trent JM, Bastian BC, Meltzer PS, Mohammedi M, Pollock PM () Loss-of-function fibroblast growth factor receptor-2 mutations in melanoma. *Mol Cancer Res* 7: 41-54

Gaundar SS, Bradstock KF, Bendall LJ () p38(MAPK) inhibitors attenuate cytokine production by bone marrow stromal cells and reduce stroma-mediated proliferation of acute lymphoblastic leukemia cells. *Cell Cycle* 8: 2975-2983

Graham JD, Hanson AR, Croft AJ, Fox AH, Clarke CL () Nuclear matrix binding is critical for progesterone receptor movement into nuclear foci. *FASEB J* 23: 546-556

- Graham JD, Mote PA, Salagame U, Balleine RL, Huschtscha LI, Clarke CL () Hormone-Responsive Model of Primary Human Breast Epithelium. *J Mammary Gland Biol Neoplasia* 14: 367-379
- Graham JD, Mote PA, Salagame U, van Dijk JH, Balleine RL, Huschtscha LI, Reddel RR, Clarke CL () DNA replication licensing and progenitor numbers are increased by progesterone in normal human breast. *Endocrinology* 150: 3318-3326
- Haferkamp S, Scurr LL, Becker TM, Frausto M, Kefford RF, Rizos H () Oncogene-induced senescence does not require the p16(INK4a) or p14ARF melanoma tumor suppressors. *J Invest Dermatol* 129: 1983-1991
- Haferkamp S, Tran SL, Becker TM, Scurr L, Kefford RF, Rizos H () The relative contributions of the p53 and pRb pathways in oncogene-induced melanocyte senescence. *Aging Cell* 1: 1-14
- Howard K, Barratt A, Mann GJ, Patel MI () A model of prostate-specific antigen screening outcomes for low- to high-risk men: information to support informed choices. *Arch Intern Med* 169: 1603-1610
- Johnatty SE, Beesley J, Chen X, Spurdle AB, deFazio A, Webb PM, Cancer ACSO, Goode EL, Rider DN, Vierkant RA, Anderson S, Wu AH, Pike M, Van Den Berg D, Moysich K, Ness R, Doherty J, Rossing MA, Pearce CL, Chenevix-Trench G () Polymorphisms in the FGF2 Gene and Risk of Serous Ovarian Cancer: Results From the Ovarian Cancer Association Consortium. *Twin Res Hum Genet* 12: 269-275
- Johnson M, Sharma M, Henderson BR () Review: IQGAP1 regulation and roles in cancer. *Cellular Signalling* 21: 1471-1478
- Johnson M, Sharma M, Jamieson C, Henderson JM, Mok MT, Bendall L, Henderson BR () Regulation of beta-catenin trafficking to the membrane in living cells. *Cellular Signalling* 21: 339-348
- Juarez JG, Thien M, Dela Pena A, Baraz R, Bradstock KF, Bendall LJ () CXCR4 mediates the homing of B cell progenitor acute lymphoblastic leukaemia cells to the bone marrow via activation of p38MAPK. *Br J Haematol* 145: 491-499
- Kasparian NA, Meiser B, Butow PN, Simpson JM, Mann GJ () Genetic testing for melanoma risk: a prospective cohort study of uptake and outcomes among Australian families. *Genetics in Medicine* 11: 265-278
- Kefford RF, Thomas NP, Corrie PG, Palmer C, Abdi E, Kotasek D, Beith J, Ranson M, Mortimer P, Watson AJ, Margison GP, Middleton MR () A phase I study of extended dosing with lomeguatrib with temozolomide in patients with advanced melanoma. *British Journal of Cancer* 100: 1245-1249
- Leachman SA, Carucci J, Kohlmann W, Banks KC, Asgari MM, Bergman W, Bianchi-Scarra G, Brentnall T, Bressac-de Paillerets B, Bruno W, Curiel-Lewandrowski C, de Snoo FA, Debnjak T, Demierre MF, Elder D, Goldstein AM, Grant-Kels J, Halpern AC, Ingvar C, Kefford RF, Lang J, MacKie RM, Mann GJ, Mueller K, Newton-Bishop J, Olsson H, Petersen GM, Puig S, Rigel D, Swetter SM, Tucker MA, Yakobson E, Zitelli JA, Tsao H () Selection criteria for genetic assessment of patients with familial melanoma. *J Am Acad Dermatol* 61: 677 e1-14
- Maniccia AW, Lewis C, Begum N, Xu J, Cui J, Chipitsyna G, Aysola K, Reddy V, Bhat G, Fujimura Y, Henderson B, Reddy ES, Rao VN () Mitochondrial localization, ELK-1 transcriptional regulation and growth inhibitory functions of BRCA1, BRCA1a, and BRCA1b proteins. *J Cell Physiol* 219: 634-641
- McKenzie H, Becker TM, Scurr LL, Kefford RF, Rizos H () Wild type and melanoma-associated mutant p16 proteins do not oligomerize in vivo. *Pigment Cell Melanoma Res* 22: 131-133
- Micklethwaite KP, Garvin FM, Kariotis MR, Yee LL, Hansen AM, Antonenas V, Sartor MM, Turtle CJ, Gottlieb DJ () Clinical-scale elutriation as a means of enriching antigen-presenting cells and manipulating alloreactivity. *Cytotherapy* 11: 218-28
- Mok MT, Henderson BR () A comparison of BRCA1 nuclear localization with 14 DNA damage response proteins and domains: identification of specific differences between BRCA1 and 53BP1 at DNA damage-induced foci. *Cell Signal* 22: 47-56
- Morey AL, Murali R, McCarthy SW, Mann GJ, Scolyer RA () Diagnosis of cutaneous melanocytic tumours by four-colour fluorescence in situ hybridisation. *Pathology* 41: 383-387
- Price MA, Zachariae R, Butow PN, Defazio A, Chauhan D, Espie CA, Friedlander M, Webb PM, The Australian Ovarian Cancer Study G, The Australian Ovarian Cancer Study - Quality of Life Study I () Prevalence and predictors of insomnia in women with invasive ovarian cancer: Anxiety a major factor. *Eur J Cancer* 45: 3262-3270
- Scaini MC, Rossi E, de Siqueira Torres PL, Zullato D, Callegaro M, Casella C, Quaggio M, Agata S, Malacrida S, Chiarion-Sileni V, Vecchiato A, Alaibac M, Montagna M, Mann GJ, Menin C, D'Andrea E () Functional impairment of p16(INK4A) due to CDKN2A p.Gly23Asp missense mutation. *Mutat Res* 671: 26-32
- Shah SP, Kobel M, Senz J, Morin RD, Clarke BA, Wiegand KC, Leung G, Zayed A, Mehl E, Kalloger SE, Sun M, Giuliany R, Yorlida E, Jones S, Varhol R, Swenerton KD, Miller D, Clement PB, Crane C, Madore J, Provencher D, Leung P, deFazio A, Khattra J, Turashvili G, Zhao Y, Zeng T, Glover JN, Vanderhyden B, Zhao C, Parkinson CA, Jimenez-Linan M, Bowtell DD, Mes-Masson AM, Brenton JD, Aparicio SA, Boyd N, Hirst M, Gilks CB, Marra M, Huntsman DG () Mutation of FOXL2 in granulosa-cell tumors of the ovary. *N Engl J Med* 360: 2719-2729
- Shanley S, Fung C, Milliken J, Leary J, Barnetson R, Schnitzler M, Kirk J () Breast cancer immunohistochemistry can be useful in triage of some HNPCC families. *Fam Cancer* 8: 251-255
- Spencer A, Prince HM, Roberts AW, Prosser IW, Bradstock KF, Coyle L, Gill DS, Horvath N, Reynolds J, Kennedy N () Consolidation therapy with low-dose thalidomide and prednisolone prolongs the survival of multiple myeloma patients undergoing a single autologous stem-cell transplantation procedure. *J Clin Oncol* 27: 1788-1793
- Tarhini AA, Millward M, Mainwaring P, Kefford R, Logan T, Pavlick A, Kathman SJ, Laubscher KH, Dar MM, Kirkwood JM () A phase 2, randomized study of SB-485232, rhIL-18, in patients with previously untreated metastatic melanoma. *Cancer* 115: 859-868
- Thompson JF, Scolyer RA, Kefford RF () Cutaneous melanoma in the era of molecular profiling. *Lancet* 374: 362-365
- Wallington-Beddoe CT, Gottlieb DJ, Garvin F, Antonenas V, Sartor MM () Failure to achieve a threshold dose of CD34+CD110+ progenitor cells in the graft predicts delayed platelet engraftment after autologous stem cell transplantation for multiple myeloma. *Biol Blood Marrow Transplant* 15: 1386-1393
- Watson AJ, Middleton MR, McGown G, Thorncroft M, Ranson M, Hersey P, McArthur G, Davis ID, Thomson D, Beith J, Haydon A, Kefford R, Lorigan P, Mortimer P, Sabharwal A, Hayward O, Margison GP () O(6)-methylguanine-DNA methyltransferase depletion and DNA damage in patients with melanoma treated with temozolomide alone or with lomeguatrib. *Br J Cancer* 100: 1250-1256
- Zheng G, Lyons JG, Tan TK, Wang Y, Hsu TT, Min D, Succar L, Rangan GK, Hu M, Henderson BR, Alexander SI, Harris DC () Disruption of E-cadherin by matrix metalloproteinase directly mediates epithelial-mesenchymal transition downstream of transforming growth factor-beta1 in renal tubular epithelial cells. *Am J Pathol* 175: 580-591

**INFECTIOUS AND IMMUNITY**

Centre for Infectious Diseases and Microbiology

**Director**

Professor Tania Sorrell

**Laboratory Manager**

Mr Gary Martinic

**Bacterial Pathogenesis Research Group Leader**

A/Prof Jon Iredell

**Senior Research Officer**

Dr Sally Partridge

**Scientific Officer**

Mrs Belinda Roychoudhry

**PhD Students**

Mr Andrew Ginn  
Mr Bjorn Espedido  
Ms Jubelle Valenzuela  
Mr Zhiyong Zong

**Fungal Pathogenesis Research Group Leader**

Dr Julianne Djordjevic

**Senior Research Officer**

Dr Alfred Widmer

**Scientific Officer**

Dr Catherine Wu

**Research Assistants**

Ms Sue Dowd  
Ms Namfon (Beth) Pantarat  
Ms Christabel Wilson  
Mr Xiaoming Zuo

**PhD Students**

Dr Methee Chayakulkeeree  
Ms Orla Morrissey  
Dr Geoffrey Playford  
Ms Anna Lau

**Honours Students**

Mr Johannes Bijosono Oei  
Ms Madoka Miyaki

**Molecular Mycology Research Group Leader**

A/Prof. Wieland Meyer

**Research Assistant**

Ms Krystyna Maszewska

**PhD Students**

Dr Azian Harun  
Miss Sirada Kaocharoen  
Mr Popchai Ngamskulrungraj  
Miss Luciana Trilles  
Dr Matthew O'Sullivan

**Mycology****Senior Scientific Officer**

Dr Catriona Halliday

**Research Officer**

Ms Jessie Lay

**Project Officer**

Ms Lou Orszulak

**Technical Officer**

Ms Ping Zhu

Centre for Transplant and Renal Research

**Director - Transplantation**

A/Prof Philip O'Connell

**Director - Nephrology**

Prof David Harris

**Director - Renal Medicine**

Prof Jeremy Chapman

**Senior Investigator****Renal Medicine**

Dr Brian Nankivell

**Laboratory Manager**

Mr Gary Martinic

**Business Manager**

Ms Lara Stretton

**Research Administrator**

Ms Debra Tucker

**Administration Support**

Ms Olivia Tedone

**Islet Transplantation****Senior research fellow**

Dr Wayne Hawthorne

**Visiting Research Scholar**

Dr Yiya Tang

**Scientific Officers**

Mrs Tina Patel  
Ms Lindy Williams  
Mrs Elvira Jimenez-Vera

**Research Officer**

Dr Peta Phillips

**Technical Officers**

Ms Kelly Moyle  
Ms Kay Waite

**Xeno Transplantation Group****Senior Scientist**

Dr Shounan Yi

**Research Officer**

Dr Helena Smith-Hurst

**Research Assistants**

Miss Jing Jing Wu  
Mrs Shihani Stoner  
Miss Vera Christou

**PhD Students**

Mr Matthew Vitalone  
Mr Moses Wavamuno

**Visiting scholars**

Dr Ming Ji  
Mrs Lei Sun  
A/Prof Sinan Yol

**Nephrology**

Director  
Prof David Harris

**Scientists**

Dr Yiping Wang  
Dr Guoping Zheng

**Visiting Scholars**

Mr Qi Cao  
Mrs Sun Yan

**Research Officer**

Dr Ya Wang

**Research Assistants**

Mr Jon Ince  
Mr Tim Tzu-Ting Zhu

**PhD Students**

Dr Vincent Lee  
Mr Alvin Tan  
Dr Ying (Cindy) Wang  
Mr Dong Zheng

**Kidney Regeneration Research Group Leader**

Dr Gopi Rangan

**Research Assistants**

Mrs Jane Burgess  
Mrs Kristina Schwensen

**PhD Students**

Miss Lena Succar

**Honours Students**

Miss Rabia Chaudry  
Ms Kristal O'Brien  
Ms Daria Stepanova

**Kidney research Research Group leader**

Dr Richard Poon

Centre for Virus Research

**Director**

Prof Tony Cunningham

**Deputy Director**

Dr Barry Slobedman

**Laboratory Manager**

Ms Monica Logan

**Administration Officer**

Ms Liz Millar

**Senior Investigator****Virology**

Prof Dominic Dwyer

**Research Officer**

Ms Janette Taylor

**Cytomegalovirus Research****Research Group Leader**

Dr Barry Slobedman

**PhD Students**

Mr Selmir Avdic  
Mr John Cao  
Ms Joanne Tan

**Honours Student**

Ms Samantha McAllery

**Herpes Immunopathogenesis****Research Group Leader**

Prof Tony Cunningham

**Research Fellow**

Dr Monica Miranda-Saksena

**PhD Students**

Ms Anupriya Aggarwal  
Mr Desheng Liu

**Honours Student**

Mr Ankit Srivastava

**Senior Research Officer**

Dr Min Kim

**PhD Student**

Ms Kirstie Fagg

**Honours Student**

Ms Naomi Osborne

**Molecular Viral Transport****and Assembly Group****Research Group Leader**

Dr Russell Diefenbach

**Post-doctoral Fellow**

Dr Barbara Kelly

**PhD Students**

Mr Arin Apcarian  
Ms Amber Campbell  
Ms Debbie Ko  
Mr Jin Wha Lee  
Ms Branka Mijatov  
Ms April Morton

**HIV Molecular Pathogenesis  
Research Group Leader**  
Professor Tony Cunningham

**Senior Research Officer**  
Dr Andrew Harman  
Dr Heather Donaghy

**Research Officer**  
Dr Najla Nasr

**PhD Students**  
Mr Joey Lai  
Ms Valerie Marsden  
Ms Sarah Mercier

**HIV Biology  
Research Group Leader**  
Dr Stuart Turville

**Honours Student**  
Ms Ivy Shi

**Research Assistant**  
Ms Anu Aggarwal

**HIV Retroviral Genetics  
Research Group Leader**  
Dr Nitin Saxena

**Research Fellow**  
Dr Bin Wang

**Research Assistant**  
Ms Maly Soedjono

**PhD Students**  
Mr Shwen Ho  
Ms Katherine Lau  
Ms Jingqin Wu  
Ms Julie Zhou

**Masters Students**  
Ms Vivianne Conceicao  
Mr Kabo Matlho

**Honours Student**  
Ms Tara Sasse

**Visiting Student**  
Ms Haijing Shi

**Varicella Zoster Research  
Research Group Leader**  
Dr Allison Abendroth

**Research Officer**  
Dr Megan Steain

**PhD Students**  
Mr Joshua Bowles  
Mr Rodney Henriquez  
Ms Jennifer Huch  
Ms Liz Sloan  
Mr Jeremy Sutherland

Institute of Dental Research

**Director**  
Prof Neil Hunter

**Deputy Director**  
Prof Nick Jacques

**Laboratory Manager**  
Dr Derek Harty

**Administration Officer**  
Ms Tracey Bowerman

**Researchers**  
Dr Mangala Nadkarni  
Dr Catherine Rathsam  
Dr Ping Ye  
Dr Peter Yun  
Mrs Ruth Harvey  
Mrs Mary Simonian  
Miss Gina Browne

**PhD students**  
Mr Jinlong Gao  
Mr Maruth Banavar  
Mr Ramin Mostofi  
Dr Nazilla Babapoor  
Ms Hongyu Xie  
Ms Nattida Charadram  
Dr Wei Zou Frank

**Masters students**  
Ms Nima Kianoush  
Mr Hossein Haghghat

**Honours Student**  
Ms Jenna Christensen

Institute for Immunology  
and Allergy

**Director**  
Prof Graeme Stewart

**Clinical Research Leader  
Immunology**  
A/Prof David Fulcher

**Immunology Senior Investigator**  
Dr Julian Bosco

**Research Co-ordinator**  
Ms Therese Burke  
Ms Kerry Lenton

**Laboratory Manager**  
Mr Stephen Schibeci

**Administration Assistant**  
Ms Coco Kang

**B cell Immunobiology  
Research Group Leader**  
A/Prof David Fulcher

**Research Assistant**  
Ms Nicole Fewings

**Genetics of Multiple Sclerosis  
Research Group Leader**  
Dr David Booth

**Post-doctoral Scientist**  
Dr Fiona McKay

**Research Assistants**  
Mrs Najwa Marmash

**PhD Students**  
Mr Ed Hoe  
Mr Kaushal Gandhi

**Hepatitis C Host Genomics  
Post-doctoral Scientist**  
Dr Vijay Suppiah

**Molecular Genetics  
of Asthma and Allergy  
Research Group Leader**  
Dr Graham Jones

**PhD Student**  
Ms Nusrat Rahman

## CANCER

Westmead Institute for  
Cancer Research

**Director**  
Prof Rick Kefford

**Deputy Director**  
Prof Christine Clarke

**PA to Rick Kefford**  
Ms Tina Cunningham

**Laboratory Manager**  
Dr Grigori Kaplan

**Flow Cytometry  
Senior Scientific Officer**  
Mr Mary Sartor

**Research Grants Officer**  
Ms Natalie Holsinger

**Technical Assistant**  
Ms Linda Bradford

**Administrative Assistant**  
Mrs Carol Godson

**Breast Cancer  
Research Group Leader**  
Prof Christine Clarke

**Research Officers**  
Dr Desiree Cloosterman  
Dr Dinny Graham  
Dr Heidi Hilton  
Dr Patricia Mote  
Dr Elizabeth Kuczek

**Research Assistants**  
Ms Amanda Croft  
Ms Adrienne Hanson  
Ms Silke Kantimm  
Ms Laurie Lacko  
Ms Nicole Santucci  
Ms Katherine Scarpin  
Ms Natalie Eriksson

**Technical Assistant**  
Ms Jadranka Tomas

**Breast Cancer Tissue Bank  
Project Manager**  
Mrs Jane Carpenter

**Scientific Officer**  
Ms Li Ma

**Database Administrator**  
Mr Matloob Khushi

**Tumour Bank Officer**  
Ms Lisa Broughton

**Tumour Bank Data Officer**  
Ms Heather Woodward

**Melanoma Cell Cycle**  
Research Group Leader  
Dr Helen Rizos

**Research Officers**  
Dr Therese Becker  
Dr Lyndee Scurr  
Dr Kavitha Gowrishankar

**Research Assistants**  
Ms Monika Frausto  
Ms Carina Fung  
Ms Malama Irvine  
Ms Branka Mijatov  
Ms Suzanah Philipsz  
Ms Stephanie Snoyman  
Mr Jerry Zhou

**PhD Students**  
Dr Sebastian Haferkamp  
Ms Heather McKenzie  
Mr Jason Todd  
Mr Sieu Tran

**Cellular Therapies  
Research Group Leader**  
Prof Ken Bradstock  
A/Prof David Gottlieb

**Senior Scientific Officers**  
Ms Vicki Antonenas

**Research Officers**  
Dr Leighton Clancy  
Dr Biju George

**Research Assistants**

Mr Andrea Anfosso  
Ms Upinder Sandher

**PhD Students**

Dr Emily Blyth  
Ms Jenny Lau  
Dr Philip Saunders

**Familial Cancer**

**Research Director**  
A/Prof Judy Kirk

**Laboratory Director**

Dr Jenny Leary

**Scientific Officer**

Ms Barb Guild

**Data Manager**

Mrs Nishath Syed

**Gene Expression**

**Research Group**  
Dr Beric Henderson

**Research Officers**

Dr Mariana Brocardo  
Dr Cahora Medina-Palazon  
Dr Myth Tsz Shun Mok  
Dr Manisha Sharma

**PhD Students**

Ms Kirsty Brodie  
Ms Cara Jamieson  
Mr Michael Johnson

**Honours Student**

Ms Kate Mills

**Gynaecological Oncology**

**Research Group Leader**  
Dr Anna deFazio  
A/Prof Paul Harnett

**Research Officers**

Dr Catherine Emmanuel  
Dr Ying Lei

**Research Assistants**

Ms Yoke-Eng Chiew  
Ms Cathering Kennedy

**Project Manager**

Ms Jillian Hung

**PhD Students**

Ms Liying Gu  
Ms Kylie Pryor

**Leukaemia Cell Biology**

Research Leader  
Dr Linda Bendall

**Research Associate**

Dr John Hewson

**Research Officers**

Dr Carole Ford  
Dr Nadia Harun  
Dr Robert Welschinger  
Dr Marilyn Thien

**Research Assistants**

Mrs Rana Baraz  
Mr Adam Cistern  
Ms Gurdip Hansra  
Mr Florian Liedtke  
Mr Jacky Wong

**Phd Student**

Ms Shivashi Gaundar

**Masters Student**

Ms Jose Maring

**Melanoma Genomics and  
Genetic Epidemiology  
Research Group Leader**

A/Prof Graham Mann

**Research Officers**

Dr Gulietta Pupo  
Dr Varsha Tembe  
Dr Paula Torres

**Project & Business Manager**

Ms Helen Schmid

**Research Interviewers**

Ms Kate Mahendran  
Dr Stephanie Seddon  
Ms Caroline Watts

**Biospecimen Manager**

Ms Charlie Agha-Hamilton

**Administrative Assistant**

Ms Gayathri St. George

**Research Assistants**

Ms Sarah Gaskin  
Ms Elizabeth Holland  
Mrs Svetlana Pianova

**PhD Students**

Ms Sarah-Jane Schramm  
Ms Robyn Dalziel

**Translational Oncology  
Research Group Leaders**

Prof Christine Clarke  
Dr Rosemary Balleine

**Research Officer**

Dr Nirmala Pathmanathan

**Research Assistant**

Ms Pamela Provan

**LIVER AND METABOLIC****Storr Liver Unit****Director**

Prof Jacob George

**Deputy Director**

Prof Christopher Liddle

**Laboratory Manager**

Ms Linda Frost

**Administration officer**

Ms Tiffany Moyle

**Postdoctoral Scientists**

Dr Liang Qiao  
Dr Kumar Subramaniam  
Dr Jianhua Wang  
Mr Khemanganee Liyanage  
Mr Vijay Suppiah

**Research Assistants**

Ms Renuka Rao  
Ms Carol Devine  
Mrs Sally Coulter  
Ms Caroline Wilson  
Ms Jayshree Sesha  
Mrs Vikki Ho  
Ms Joanne Bymora  
Ms Marina Kaceveska  
Mr Yingdi Liu  
Mr George Wilson

**Translational research**

Mrs Sengkee Teo  
Ms Keshni Sharma  
Ms Jasmin Canete  
Mrs Nicole Murphy  
Mrs Glenda Fraser  
Mr Iqbal Mohi Mohammed Abdul  
Ms Megan Spindler  
Ms Jamie Leigh Patterson  
Ms Lee Russell  
Mrs Susan Holdaway  
Mr Majid Hashemi

**PhD Researchers**

Dr Sarah Walker  
Dr Kerry-Lee Milner  
Dr Vanessa Patullo  
Mr Chris Scott  
Dr David van der Poorten  
Dr Briohny Smith  
Ms Masha Shahidi  
Mr Scott Read  
Ms Amanda Johnston  
Mr Alexis St George  
Ms Medhi Ramezani-Moghadam

**Honours Students**

Mr Lewis Tsang  
Mr Kenny Ip  
Ms Yin-Ling (Jasmin) Ngan

**NEUROSCIENCE AND VISION****Centre for Vision Research****Director**

Prof Paul Mitchell

**Deputy Director**

A/Prof Jie Jin Wang

**Administration Manager**

Kirsten Jakobsen

**Postdoctoral Researchers**

Dr Gerald Liew  
Dr Bamini Gopinath  
Dr Haitao (Sarah) Li  
Dr Suriya Foran

**Senior Statistician**

Ms Elena Rochtchina

**Statisticians**

Mr George Burlutsky  
Ms Annette Kifley  
Mr Erdahl Teber

**Senior Photographic Grader/  
Data Manager**

Ms Ava Grace Tan

**Senior Photographic Grader**

Ms Mireille Moffitt

**Photographic Graders**

Ms Victoria Cosatto  
Mr Alan Wainwright  
Ms Nichole Joachim  
Mr David Cook

**Study Coordinators**

Ms Jennifer Green  
Ms Rochelle Jeffery  
Ms Tania de Loryn  
Ms Lily Wong

**Research Assistants**

Ms Thomas Hong  
Ms Elena Palamara  
Ms Cheryl McKendrick  
Ms Stephanie Cassar  
Ms Kimberly Spooner

**PhD students**

Dr Calvin Fong  
Dr Reena Fotedar  
Dr Gowri Kanthan  
Dr Michael Karpa  
Dr Ami Pai  
Dr Chameen Samarawickrama  
Dr Yasser Tariq

## Brain Dynamics Centre

### Director

Prof Lea Williams

### Senior Researchers

Dr Anthony Harris  
Dr Chris Rennie  
A/Prof Evian Gordon  
Dr Mayuresh Korgaonkar  
A/Prof Michael Kohn  
Prof Peter Robinson  
Emeritus Professor Russell Meares  
Prof Richard Bryant  
A/Prof Simon Clarke

### Administration

Ms Jan Ambrose  
Ms Debbie Gallagher  
Ms Marie Nagy  
Mr Paul Wood-Bradley

### Research Study Coordinators

Ms Claire Day  
Dr Thida Thein

### Post-doctoral Fellows

Dr Donald Rowe (honorary)  
Dr Justine Gatt  
Dr Jong-Won Kim  
Dr Kerri Brown  
Dr Kim Felmingham  
Dr Peter Drysdale  
Dr Peter Loxley  
Dr Pulin Gong  
Dr Sacha Van Albada

### PhD Students

Mr Adrian Allen  
Ms Ainslie Hatch  
Mr Alan Chiang  
Mr Andrew Phillips  
Mr Cliff Kerr  
Ms Donna Palmer  
Mr Hal Henke  
Mr HuiYing Wu  
Mr James Henderson  
Mr James Roberts  
Ms Jean Starling  
Ms Kasia Kozlowska  
Mr Kevin Aquino  
Mr Matt Barton  
Mr Michael Kohn

### Honour Students

Mr Kunaal Prasad  
Ms Rebecca Koncz

### Research Assistants

Ms Angela Robl  
Ms Anna Watters  
Ms Aleksandra Klimova  
Ms Alicia Wilcox  
Ms Eva Battaglini  
Ms Lisa Hancock

## CARDIO-RESPIRATORY

Ludwig Engel Centre for  
Respiratory Research

### Director

A/Prof John Wheatley

### Deputy Director

Dr Terence Amis

### Chief Investigators

Dr Kristina Kairaitis  
A/Prof Peter Middleton  
Dr Tracey Robinson

### Lab Manager

Ms Sharon Lee

### Research Officer

Ms Odette Erskine

### Research Assistants

Mr Hugh House  
Ms Melanie Madronio  
Ms Manisha Verma  
Ms Rita Ginn

### Research Study Co-ordinators

Ms Joann Stevens  
Ms Louise Tyler  
Ms Angela Wong

### PhD Students

Mr Jason Amatoury  
Dr Jin-Gun Cho  
Miss Jyotishna Narayan  
Dr Jimmy Chien

### MBBS Honours student

Mr Praveen Gounder

## Centre for Heart Research

### Director

Prof Pramesh Kovoor

### Research Leaders

Dr Eddy Kizana  
Prof David Ross  
Dr Aravinda Thiagalingam  
Dr Stuart Thomas

### Post Doctoral Researchers

Dr Jacob Ross  
Dr Renuka Rao

### Research Assistants

Mr Kaiman Huang  
Mr Gary Wu

### Technical Officers

Mr Tony Barry  
Mr Juntang Lu

### PhD Students

Mr Jim Poulipoulos  
Dr Calvin Hsieh  
Dr Ajita Kanthan  
Dr William Chik  
Dr Joseph Chiha  
Mr Phil Students  
Dr Oliver Gibbs  
Dr Gnalini Gnanesweran

## WMI EXECUTIVE

### Director

Professor Tony Cunningham

### Chief Operating Officer

Mr Mark Dado

### Executive Officer

Mrs Margot McEwan

## OPERATIONS AND SUPPORT

### Operations and I.T Manager

Dr David Facey

### Facilities and Grants

#### Administration Manager

Mr Mark Smith

### Finance Manager

Mr Mark Wissam

### Finance Officer

Mrs Renata Alavanja

### Communications

Ms Victoria Hollick  
Mrs Lynn Wiezell

### IT Projects Manager

Mr Ian Magee

### Computer Support Officers

Ms Chris Cannon  
Mr Blair Lawton  
Mr Bruno Marion

### Administration Officers

Mrs Brenda Wilson  
Ms Rhonda Hale  
Ms Denise Brown

### Laboratory Managers

Mr Luke Dawson  
Dr Grigori Kaplan  
Mr Steven Schebeci  
Ms Linda Frost  
Mr Gary Martinic  
Mrs Monica Logan  
Mrs Sharon Lee

### Safety and Training Manager

Mr Brian Horsfield

### Reception

Mrs Dezley Brunell

### Stores Officer

Mr Cecil Nast

### Biomedical Engineer

Dr Rob Wilkins

### Research Facilities

#### Co-ordinators

Mrs Christine Browne  
Mrs Vanessa Rothwell

### Wash Room Technician

Ms Fiona Longley

## CORE TECHNOLOGY FACILITIES

### Confocal Microscopy

#### Imaging Scientist

Dr Hong Yu

### DNA Microarray

#### Microarray Technician

Ms Najwa Marmash

### Flow Cytometry

#### Manager

Dr Maggie Wang

### Electron Microscope

#### EM Unit Manager

Mr Ross Boadle

### Histology Services

#### Histology Technician

Ms Virginia James

### Protein Production Facility

#### Proteomics Officer

Dr Eve Diefenbach

### DNA Sequencing

#### Technicians

Mr Cairo Forrest  
Mr Geoff Totaan

# WESTMEAD MILLENNIUM INSTITUTE AT A GLANCE

## RESEARCH DIVISIONS

### Infection and Immunity

Centre for Infectious Diseases and Microbiology  
Centre for Transplant and Renal Research  
Centre for Virus Research  
Institute of Dental Research  
Institute for Immunology and Allergy

### Cancer

Westmead Institute for Cancer Research

### Liver and Metabolic

Storr Liver Unit

### Neuroscience and Vision

Brain Dynamics Centre  
Centre for Vision Research

### Cardio-respiratory

Ludwig Engel Centre for Respiratory Research  
Centre for Heart Research

## CORE TECHNOLOGY FACILITIES

Confocal Microscopy  
DNA Microarray  
Flow Cytometry  
Electron Microscopy  
Protein Production  
DNA Sequencing  
Histology

## COLLABORATIVE RESEARCH CENTRES

NHMRC Centre of Clinical Research Excellence to Improve Outcomes in Immunosuppressed Haematology Patients

NHMRC Centre of Clinical Research Excellence in Anxiety and Neuroscience

Australian Centre for HIV and Hepatitis Virology Research

Australian Centre for Pancreatic Islet Transplantation

NSW Breast Cancer Tissue Bank

International Melanoma Consortium

Kathleen Cuninghame Foundation Consortium for Research into Familial Breast Cancer

Genes Associated with Multiple Sclerosis in Europeans (GAME)

Swedish and Australian Collaboration for Research into Atopic Dermatitis

National Pancreas Transplantation Centre

## THE WESTMEAD MEDICAL RESEARCH FOUNDATION

Medical research relies on the support of individuals, business, community and service groups. The Westmead Medical Research Foundation is the main fundraising body supporting Westmead Millennium Institute.

The Westmead Medical Research Foundation is grateful for any support, as every donation is valuable.

Donations over \$2.00 are tax deductible. Donations can be made by sending a cheque, money order or credit card details to the following address (please indicate if you have a specific interest in a particular research area).

The Westmead Medical Research Foundation, PO Box 74,  
Westmead NSW 2145, or contact us on our toll free number: 1800  
639 037.

We wish to thank the staff and families who assisted in the production of the WMI Annual Report 2009/10.

Production Manager: Victoria Hollick.  
Graphic design and production: CMC.

### Founding donors include:

Australian Cancer Research Foundation, The Westmead Medical Research Foundation, Robert W Storr Estate, University of Sydney, and Staff Specialists of Westmead Hospital.



Westmead Millennium Institute  
for Medical Research

PO Box 412

Westmead NSW 2145

Telephone +61 2 9845 9000

Fax +61 2 9845 9100

[www.wmi.usyd.edu.au](http://www.wmi.usyd.edu.au)

