



Medicine, Nursing and Health Sciences

Graduate Research Projects

Honours, BMedSci and PhD
Opportunities for Translational Research

Southern Clinical School



Southern Clinical School (SCS) is a health professional school based at the Monash Medical Centre, a Southern Health Hospital and Victoria's largest hospital network. In addition to training, the School is a vibrant hub of research via strong collaborations between Monash University and Southern Health. SCS is at the forefront of clinical translational research with demonstrated research strengths in cardiovascular disease, inflammatory diseases, nutrition, women's and children's health and neurosciences.

Unlike other research schools, our senior academic staff are mostly health professionals who work closely with colleagues in Southern Health, translating scientific discoveries into clinical practice in an innovative and collaborative environment to shape the health professionals of the future. The Monash Health Translation Precinct (MHTP) is based at MMC and consists of SCS, MIMR and Prince Henry's Institute and provides exceptional collaboration opportunities.

A message from the Head of School, Professor Eric Morand

The Southern Clinical School of the Faculty of Medicine, Nursing and Health Sciences comprises the Faculty's academic departments based at Southern Health. It is the Faculty's largest medical clinical school and also hosts its Nutrition and Dietetics department. There is close integration between Southern Health clinical services and the departments including Medicine, Surgery, Paediatrics, Obstetrics and Gynaecology and Nutrition and Dietetics. Moreover, the School has extensive laboratory based research programs that are integrated with clinical research activities across multiple disciplines, and also hosts three major University Centres of Excellence, the Centre for Inflammatory Diseases, Ritchie Centre for Baby Health Research (jointly with MIMR), and the Cardiovascular Research Centre. Many group leaders are recognised as international leaders in their areas of expertise.

As a result, there is a strong focus on both basic and translational research with real clinical issues driving research questions addressed in the laboratories. Similarly, laboratory derived discoveries can be rapidly tested in relevant clinical settings.

The School has a strong track record of welcoming and supporting Bioscience research students and BMedSci students in productive graduate (honours and doctoral) programs within the School. A growing number of gifted students have progressed from Honours or BMedSci students through successful PhDs, postdocs to become successful, independent researchers and biomedical professionals in the Southern Clinical School and beyond.



What's at SCS-MMC?

A HUB of activity

In conjunction with our collaborators MIMR and PHIMR, SCS provides world class equipment and other facilities similar to other Monash sites, but also offers student rooms, and a clinically grounded context. Monash Medical Centre has a gymnasium, on site ATM and bank and café and is a short walk to all the cafes and shops in Clayton mall precinct.

Our Location

The Southern Clinical School incorporates the four hospitals of Southern Health but is principally based at Monash Medical Centre (MMC), Clayton. This is approximately a 15 minute walk (south) from the main Monash University campus at Clayton. The Clayton railway station is only minutes walk and a number of bus services stop at MMC. The main administration centre is located in Block E, Level 5, MMC.

Facilities

Over 15 000 people work at Southern Health and there are a large number of facilities available. There is an extensive education program run both by Monash University and Southern Health on campus at MMC with daily meetings covering all areas of medicine and biomedicine.

Library MMC

The MMC Clayton library has a collection of 16,000 books, approximately 700 journals and access to around 1,500 electronic journal titles. The library cooperates with the other Southern Health libraries located at Dandenong, Moorabbin, Kingston, and Casey as well as the Monash University Library. Opening hours are 8 am – 5.30 pm Monday to Friday.



Honours Information

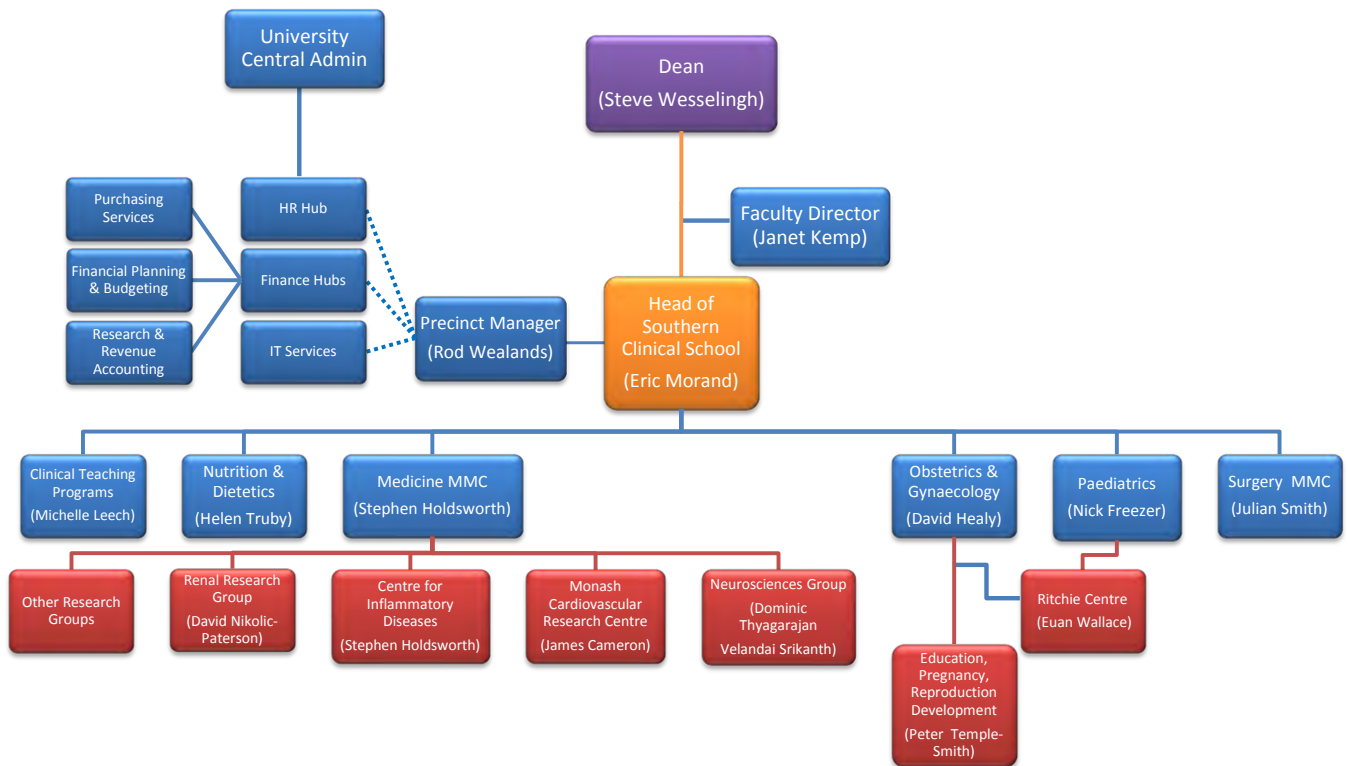
If you are thinking of a career in biomedical research Southern Clinical School is a great place to start. The School is within easy walking distance of Monash University's Clayton campus and only a few minutes drive from Caulfield campus.

Our research staff undertake internationally recognised basic and clinical/translation research. Many are recognised as international leaders in their areas of expertise. Our research covers a broad range of topics including inflammatory and cardiovascular diseases, and neurosciences to name a few. Southern Clinical School has an outstanding track record in successful supervision of honours students, many of whom have gone on to PhD studies and successful careers.

Scholarships

Southern Clinical School can offer scholarships to exceptional Honours, BMedSci and PhD students.

Southern Clinical School Organisational Chart



Work with the best...

Some of the supervisors at Monash Medical Centre, Southern Clinical School:



Head of School/Centre for Inflammatory Diseases (Arthritis)

Professor Eric Morand

Professor Eric Morand trained as a specialist rheumatologist in Melbourne and at the Royal National Hospital for Rheumatic Diseases, Bath, UK, gaining Fellowship of the Royal Australasian College of Physicians in 1992.

Overlapping with this, he began research training at the Bath Institute for Rheumatic Diseases in 1991 and continued working towards a PhD granted by Monash University in 1995. The Arthritis group was founded during this period and has since held continuous funding from bodies including the NH&MRC, NIH (USA), and Arthritis Australia. The group led by Professor Morand has trained many successful PhD and MD candidates. His main interests are molecular mechanisms of action of glucocorticoids, and biomarkers of SLE. He holds multiple patents and founded the spinoff company Cortical Pty Ltd. Professor Eric Morand was appointed Head of the Southern Clinical School in 2011.



Head of Department of Surgery MMC

Professor Julian Smith

Professor Smith has broad basic and clinical research experience in general and cardiothoracic surgery including organ transplantation and minimally invasive surgical techniques. Current research areas include cardiac surgery without the use of cardiopulmonary bypass, new devices in artificial heart technology, and the evaluation of outcomes in cardiothoracic surgery especially with respect to new technologies such as microsurgery, minimally invasive and robotic-assisted surgery.



Head of Medicine MMC/Director of Centre for Inflammatory Disease

Professor Stephen Holdsworth

Professor Stephen Holdsworth is the Director of the Centre for Inflammatory Diseases, Head of Monash University's Department of Medicine (Monash Medical Centre), Head of Clinical Immunology and Director of Research Strategy at Southern Health. He is a clinician-scientist who is a nephrologist, clinical immunologist and career academic. His long-standing research interests have focussed on the mechanisms in immune glomerular injury relevant to understanding and treating human vasculitis and glomerulonephritis (GN). His work has substantially contributed to revelations that cell-mediated immunity and pathological coagulation induce crescentic GN. The evidence substantiating this assertion derives from key in vivo studies in animals models bracketed with human observations confirming the relevance of experimental discoveries to human disease.



Centre for Inflammatory Disease – Glomerulonephritis

Professor Richard Kitching

Professor Richard Kitching is a clinician-scientist, his Clinical Specialty being nephrology. His research helped established that the T-helper cell subsets (Th1, Th2 and most recently Th17) are applicable to glomerulonephritis. He studies mechanisms of autoimmune renal disease and explore hypotheses related to the pathogenesis of immune and autoimmune renal injury. Professor Kitching is a member of the Editorial Board of the Journal of the American Society of Nephrology and is a Section Editor on the board of Nephrology. He was awarded the Australian and New Zealand Society of Nephrology T.J. Neale Award for Outstanding Contribution to Nephrological Science in 2007. Professor Kitching is the chair of the Scientific Programme and Education Committee of the Australia and New Zealand Society of Nephrology. He has teaching and leadership roles in the Monash University, Faculty of Medicine Nursing and Health Sciences in the MBBS degree and the Bachelor of Biomedical Sciences degree.



Centre for Inflammatory Disease – Leukocyte recruitment

Associate Professor Michael Hickey

Associate Professor Michael Hickey is an NHMRC Senior Research Fellow. His laboratory examines leukocyte recruitment in inflamed tissues, a process which underlies the pathogenesis of most inflammatory diseases. His research examines the control of leukocyte-endothelial cell interactions and leukocyte migration in the inflamed microvasculature, using intravital (in vivo) microscopy to examine the functional microvasculature in models of inflammation. Current diseases examined include contact sensitivity, glomerulonephritis, systemic lupus erythematosus, arthritis and cerebral inflammation. An additional focus is human endothelial cell biology.



Centre for Inflammatory Diseases – Coagulation and Inflammation

Associate Professor Peter Tipping

Associate Professor Peter Tipping is an NH&MRC Principal Research Fellow, who has been continuously funded by the NHMRC for the past 20 years and has supervised 18 honours students and 13 PhD students over this period. He is a clinician/scientist with expertise in animal models of human inflammatory diseases and has received international recognition for work using mouse models to dissect the pathogenic mechanisms in crescentic glomerulonephritis.



Centre for Inflammatory Disease – Autoimmunity

Professor Ban Hok Toh

Professor Ban-Hock Toh leads the Centre for Inflammatory Diseases Autoimmunity team. He held appointments at Universities in Singapore and Malaysia, before joining Monash University in 1972. Professor Toh was the Head of the Department of Immunology and Senior Staff Specialist in Immunology at the Alfred Hospital. He was Chief Examiner for the Royal College of Pathologists Australia in Immunology, Regional Editor (Australasia) for Autoimmunity, Commonwealth Medical Fellow, MRC Immunology Unit, London, Fogarty Visiting Scientist, National Institutes of Health, USA, Visiting Professor, University of Singapore and University of Innsbruck, Austria.



Centre for Inflammatory Disease – Gastroenterology

Professor William Sievert

Professor William Sievert is Director, Gastrointestinal and Liver Unit, Southern Health, which incorporates two large teaching hospitals, the Monash Medical Centre and Dandenong Hospital. He is also a tenured Professor in the Faculty of Medicine, Nursing and Health Sciences at Monash University. Professor Sievert has a long-term interest in liver disease and directs an active clinical research unit comprising physician-scientists, clinical research nurses and research students. The Clinical Research Unit has been continuously active over ten years and regularly contributes to international trials of new antiviral agents for hepatitis B and C in addition to developing and leading national investigator-initiated studies. He also directs a basic research laboratory investigating mechanisms of inflammatory liver injury and hepatic fibrogenesis, with a translational focus on identification and development of potential hepatic antifibrotic agents. Professor Sievert has been active in medical education including the development of new undergraduate and graduate medical curricula at Monash University.



Centre for Inflammatory Disease – Innate immunity and infection

Associate Professor Kumar Visvanathan

Associate Professor Kumar Visvanathan heads up the Innate Immunity Laboratory and is also an infectious diseases physician at Monash Medical Centre. His interest in sepsis stems from the time he spent as a Post-doctoral fellow at Rockefeller University in New York, investigating the role of super-antigens in septic and toxic shock.

Since his return to Australia, his research has expanded to incorporate the involvement of the innate immune system in sepsis, hepatitis and other inflammatory diseases. Dr Visvanathan's career highlights include receiving the Frank Fenner award for advanced research in infectious diseases from the Australasian Society of Infectious Diseases, an NHMRC Practitioner award, numerous publications and several patents.



Centre for Inflammatory Disease – Respiratory Diseases

Professor Phil Bardin

Professor Phil Bardin obtained a PhD from Southampton University (UK) working under Stephen Holgate, an eminent researcher in allergy and asthma. His field of study was viruses (particularly rhinovirus), their interaction with asthma and role in exacerbations. In 2000, he accepted a position as Director of Respiratory Research at Monash Medical Centre and commissioned a virus research laboratory. The laboratory is one of only a handful worldwide that is able to conduct studies of RV and its impact on allergic diseases. Recent research has also included studies of RSV in collaboration with David Jans at Monash University and innate immune responses with Bryan Williams at Monash Institute of Medical Research.



Paediatric Surgery

Professor Wei Cheng

Professor Cheng is a paediatric surgeon and a scientist. Clinically, he is interested in congenital abnormalities and laparoscopic surgery in children.

His lab, situated in the Monash Institute of Medical Research, focuses on the developmental biology and human genetic research of the hindgut development as well as gut regeneration. He actively fosters collaborations across disciplines and across the world.



Head of Department of Nutrition and Dietetics

Professor Helen Truby

Professor Truby is a nutrition scientist and clinical dietitian with extensive experience in conducting dietary studies including randomized controlled trials and intervention protocols in adults and children. Current research areas include energy expenditure and appetite control in children with chronic diseases and in obesity.



Emergency Medicine and Clinical Toxicology Research

Professor Andis Graudins

Professor Andis Graudins is the coordinator of emergency medicine research across the Southern Health Emergency Medicine program as well as a consultant emergency physician and clinical toxicologist at Southern Health and clinical toxicologist working for the NSW and Victorian Poisons Information Centres. Professor Graudins is a clinical and basic science toxicology researcher. Clinical research interests include paracetamol poisoning and pharmacokinetics of modified-release paracetamol formulations in humans. Basic science research utilises in-vivo animal models to assess treatment of cardiovascular drug poisoning with novel inotropic and antidote agents such as levosimendan, fructose-1, 6-diphosphate and 4-aminopyridine. Dedicated laboratory space for emergency medicine and toxicology basic science research is located in the Monash University Department of Pharmacology.



Nephrology Research

Associate Professor David Nikolic-Paterson

Associate Professor David Nikolic-Paterson runs a research program investigating the signaling pathways (JNK, p38 MAPK, Syk, c-fms) that regulate inflammation, fibrosis and apoptosis in the pathogenesis of kidney disease. He is based in the Department of Nephrology at Monash Medical Centre and his studies use conditional gene deletion and pharmacologic kinase inhibitors in mouse models of kidney disease, as well as cell culture studies.



Head of Epidemiology and Prevention Unit, Stroke and Ageing Research Centre

Professor Amanda Thrift

Professor Amanda Thrift is the Head of the Epidemiology and Prevention unit of the Stroke and Ageing Research Centre, Department of Medicine (Monash Medical Centre), Monash University. She is a career epidemiologist, having gained her PhD in epidemiology in 1995. Her long-standing research interests are in the field of epidemiology of stroke and vascular disease, particularly relating to developing countries. She has ongoing research studies on the prevention and management of stroke in the community, and the identification of risk factors for stroke and vascular diseases in those living in deprived settings (including Iran, India and Vietnam).



Vascular Brain Ageing

Associate Professor Velandai Srikanth

Associate Professor Velandai Srikanth is an NHMRC/NHF Career development Fellow. He is the Head of the Stroke and Ageing Research Centre based in Southern Clinical School, Monash Medical Centre. He is the overall head of the centre and also leads the Vascular Brain Ageing division with an emphasis on the vascular determinants of dementia, falls and gait disorders. He is a specialist geriatrician in the Department of Neurology at Southern Health (MMC) involved in the post-acute care of patients admitted to the acute stroke unit. He conducts a comprehensive stroke clinic aimed at rapid assessment and secondary prevention of transient ischaemic attack (TIA) and stroke, and a cognitive disorders clinic.



Acute Stroke and Imaging

Associate Professor Thanh Phan

Associate Professor Phan is Head of Stroke at Monash Medical Centre and has developed a first class stroke team, providing stroke services in the areas of Transient Ischemic Attack, acute thrombolysis, interventional radiology and stroke unit care. He is actively involved in the teaching of Advanced Physician Trainees in both Neurology and Stroke. He leads the Acute Stroke and Imaging division within the centre. He conducts cutting edge research involving brain imaging in stroke, and also in developing computational models of the cerebral circulation. He is at the forefront of research into service delivery systems for stroke and TIA.



Public Health and Translation

Associate Professor Dominique Cadilhac

Associate Professor Cadilhac is the inaugural Head of the Translational Public Health Research Unit at the Centre. She is an expert in public health research, particularly in the areas of health service delivery models, translational research, economic evaluation, program evaluation and chronic disease prevention in vascular disease, in particular stroke. She is one of the lead investigators to have established the Australian Stroke Clinical Registry. She has also contributed to more than 100 'quality of stroke care' individual hospital reports to facilitate direct translation of evidence into practice. She was awarded the 2010 top ranked National Heart Foundation Research Fellow for Victoria.



Monash Cardiovascular Research Centre

Professor James Cameron

Professor James Cameron is Director of the Monash Cardiovascular Research Centre and Associate Director (Research and Education) of MonashHEART. He holds senior medical staff appointments with MonashHEART and Epworth Hospital. Since 2006 he has been Professor of Electronic Engineering (Biomedical) at La Trobe University. Currently he is Vice-President of The International Society for Vascular Health (ISVH) and Chairman of the Australasian Regional Committee of the ISVH. Professor Cameron acts as principle investigator in a number of pharmaceutical industry studies. He has developed clinical laboratory systems used extensively for assessment of arterial properties in Australia and overseas. The arterial assessment techniques he has developed have provided important evidence demonstrating the concept of the systemic arterial stiffness as a valid therapeutic target.

Student Snapshot

Honours students – Where are they now?

Many honours graduates of SCS have gone on to exceptional careers.

Dr Michael Kuligowski

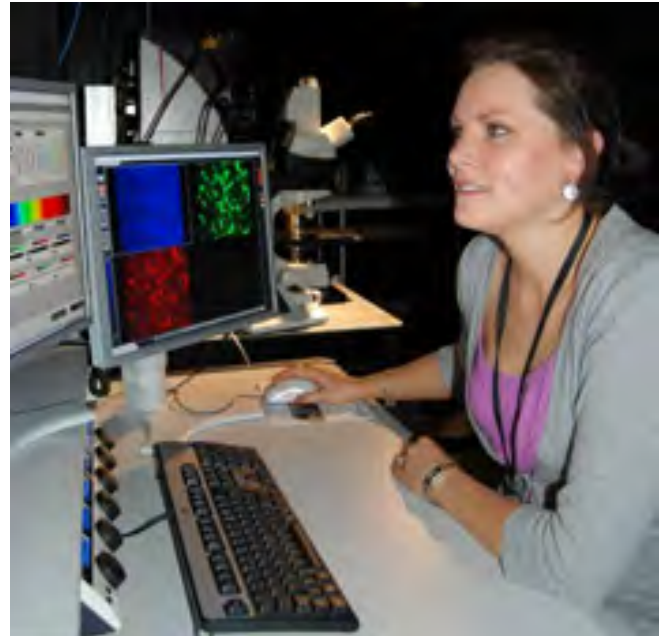
Postdoctoral Fellow, Immune Disease Institute, Harvard Medical School, Boston

Michael undertook his PhD at the Centre under the joint supervision of Associate Professor Michael Hickey and Associate Professor Richard Kitching. He performed some ground-breaking imaging studies which revealed a novel mechanism whereby neutrophils undergo adhesion in inflamed glomerular capillaries, leading to publications in the leading international journals *Blood* & *Journal of Immunology*. After completing his PhD, Michael took up a postdoctoral position at the Immune Disease Institute at Harvard Medical School, where he is being trained in advanced new imaging techniques including in vivo multiphoton confocal microscopy, by internationally-leading researchers.

Department of Medicine/Centre for Inflammatory Diseases

Dr. Jennifer Timoshanko Research Associate, Imperial College, London

Jenni Timoshanko undertook her Honours and PhD in the Centre for Inflammatory Diseases, under the supervision of Associate Professor Peter Tipping. During this time she investigated the cytokines responsible for glomerulonephritis, an inflammatory disease of the kidney. Jenni was extremely productive and was able to produce 10 papers describing her work. These have been published in prestigious international scientific journals such as *Journal of Immunology*, *American Journal of Pathology* and the *Journal of the American Society of Nephrology*. In recognition of her efforts, Jenni was awarded a C.J. Martin Fellowship from the National Health & Medical Research Council. This allowed her to take up a position as a postdoctoral fellow at the Imperial College in London, UK.



Project Areas

The Southern Clinical School offers projects in a wide variety of different areas of medicine and biomedical science. Projects are classified into eight different themes and these are listed below with the relevant page numbers

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1. Centre for Inflammatory Diseases

The Centre for Inflammatory Diseases concentrates on a wide variety of inflammatory diseases including kidney disease, vasculitis, arthritis, trafficking of cells and cardiovascular disease. There are 10 main themes:

Theme 1

Mechanisms of immune injury in autoimmune vasculitis and glomerulonephritis

Theme 2

Glucocorticoid-induced molecules in the control of inflammation and arthritis

Theme 3

Proinflammatory roles for coagulation proteins and their receptors

Theme 4

Control of leukocyte recruitment and microvascular permeability during inflammation

Theme 5

Mechanisms of liver fibrosis

Theme 6

Asthma, inflammation and viral infections

Theme 7

Atherosclerotic vascular disease: Role of the immune system

Theme 8

Respiratory infection

Theme 9

Innate immunity and infection

Theme 10

Inflammation in type 2 diabetes and its complications

Theme 1: Mechanisms of immune injury in autoimmune vasculitis and glomerulonephritis

Supervisor: Professor Stephen Holdsworth
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Supervisor: Professor Richard Kitching
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Description: Glomerulonephritis (GN) is the most common cause of end stage renal failure in Australia and world-wide. The overall aim of this theme is to further our understanding of key events in the generation of nephritogenic immune responses, autoimmunity as it pertains to the kidney and effector responses in the kidney, so that potential therapeutic targets can be identified. Research in our laboratories covers a range of key questions as to why the kidney can be a target of immune attack. It uses a variety of techniques that involve models of disease, transgenic and knock out mice, molecular biology, cell culture, analysis of immunological endpoints, and histological and functional readouts.

Our laboratories work to define mechanisms of immune renal injury, with a particular focus on the role of T cells. Glomerulonephritis (GN) is a common cause of end stage renal failure. The overall aim of this theme is to further our understanding of key events in the generation of nephritogenic immune responses, autoimmunity as it pertains to the kidney and effector responses in the kidney, so that potential therapeutic targets can be identified. Research in our laboratories covers a range of key questions as to why the kidney can be a target of immune attack. We are well funded and publish regularly in the best journals in the field.

We perform our research using a range of classical immunological techniques in murine models of renal disease. We use a variety of techniques that involve models of disease, transgenic and knock out mice, molecular biology, cell culture, analysis of immunological endpoints, and histological and functional readouts. A variety of projects are available - examples of specific currently available projects are given below.

The laboratory is made up of postdoctoral scientists, research assistants, and several PhD students and in most years one or two BMS honours students. As we don't have a regular BSc Honours stream, we can devote more time and effort to helping BMS honours students achieve high standards. A number of our honours students have gone on to undertake PhD studies with us, and two Postdoctoral Career Scientists are BMS graduates.

Theme 1 projects include:

1. The role of Neutrophils in Immunoregulation of Adaptive Immunity inducing Arthritis and Glomerulonephritis

Supervisor: Professor Stephen Holdsworth

Email: Stephen.holdsworth@monash.edu

Innate immune cells are activated during the development of arthritogenic and nephritogenic immune responses mediating arthritis and kidney failure in glomerulonephritis. We have recent evidence that neutrophils also modulate or limit the extent of adaptive injurious immunity. We have shown neutrophils migrate to lymph nodes with dendritic cells (DCs) as adaptive immunity develops. In this project we will use intravital microscopy of lymph nodes to define the physical interactions between DCs, neutrophils and T cells. We will explore the role of neutrophils by in vivo depletion and transfer of genetically manipulated neutrophils deficient in likely candidate molecules mediating immunomodulation of DC induced T cell activation.

2. How do Mast Cells turn off disease inducing Autoimmunity?

Supervisor: Professor Stephen Holdsworth

Email: Stephen.holdsworth@monash.edu

Supervisor: Dr Shaun Summers

Email: Shaun.Summers@monash.edu

We have recently revealed a novel new pathway of immunoregulation. In experimental vasculitis mast cells direct T regulatory cells to turn off autoimmunity. This project will explore the mechanisms of the effects using in vivo co-culture assays of Tregs mast cells and injurious antigen specific T effector cells. The molecular basis of the effect will be defined using mast cells deficient in key immunomodulatory molecules and lymph node. Intravital microscopy will reveal the physical cellular interactions between Tregs, mast cells, dendritic cells and T effectors that facilitate this new pathway of immunomodulation.

3. Restoring the Balance: Generation of Therapeutic T Regulatory cells to treat Autoimmune ANCA associated Vasculitis

Supervisor: Professor Stephen Holdsworth

Email: Stephen.Holdsworth@monash.edu

We have developed a reliable reproducible animal model of autoimmune anti-myeloperoxidase anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis to use in experiments aimed at using new biological therapies without the toxicities of currently used immunosuppressive drugs.

Dendritic cells drive the generation of immunity by presenting autoantigen to autoreactive T cells. However this is insufficient to initiate autoimmunity. Antigen binding to the T cell receptor must be accompanied by a second signal to ensure the induction of immunity. CD40 expressed by DCs provide this. In the absence of this, signal regulatory cells, not effector cells are generated. We have preliminary data that using isolated DC deficient in CD40 (CD40^{-/-} mice) pulsed with MPO we can inject naïve mice and generate antigen specific T regulatory cells. In this study we will generate therapeutic Tregs and use them to prevent and treat animals with autoimmune ANCA associated vasculitis.

4. Effector Th1 and Th17 responses in glomerulonephritis using a novel TcR transgenic cell transfer model

Supervisor: Professor Richard Kitching

Email: Richard.Kitching@monash.edu

Cell mediated immunity is important in severe rapidly progressive forms of glomerulonephritis. We have recently established a new model of glomerulonephritis where a model antigen, ovalbumin can be planted in the glomerulus and antigen-specific T cells polarized to a Th1 or Th17 transferred in to cause pure Th12 or Th17 cell mediated injury. Further studies currently planned and offered as honours projects include:

- Determining whether effector injury can be enhanced in the same manner in Th1 and Th17 mediated injury by TLR2, TL4 or TLR9 agonists?
- Do CD4⁺ and CD8⁺ cells play synergistic roles in cell mediated injury?
- Do Th1 and Th17 synergise in the development of glomerular injury?
- Can co-transfer of GFP⁺ Foxp3 Tregs ameliorate injury?

Techniques involved in this project include: culture of TcR Tg T cells with antigen, cytokines and antibodies; in vivo animal work; molecular biology; flow cytometry, histology, immunohistochemistry and immunofluorescence and ELISA.

5. Can inhibiting IL-12p40 prevent or treat experimental crescentic glomerulonephritis?

Supervisor: Professor Richard Kitching

Email: Richard.Kitching@monash.edu

IL-12p40 forms part of both IL-12 (important for Th1 responses) and IL-23 (important for Th17 responses). Targeting IL-12p40 is an approach to treating proliferative and crescentic forms of GN that could be successful in both Th1 and in Th17 mediated RPGN. Agents targeting IL-12p40 have been effective in experimental non-renal inflammatory disease and are in Phase II clinical trials. This project will determine the capacity of apilimod (a small molecule IL-12p40 inhibitor) or anti-IL-12 monoclonal antibodies to inhibit experimental crescentic glomerulonephritis. An initial study will commence treatment at the induction of disease and continue for 21 days; later studies will commence at day 7 or day 10 and continue until day 21 or day 35.

Techniques involved in this project include in vivo animal work; molecular biology; flow cytometry, histology, immunohistochemistry and immunofluorescence and ELISA.

6. Induction of nephritogenic autoimmune anti-myeloperoxidase responses using a Staphylococcus aureus derived peptide

Supervisor: Professor Richard Kitching
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Supervisor: Dr. Joshua Ooi
Email: Joshua.ooi@monash.edu

Experimental data suggests that the loss of tolerance to myeloperoxidase (MPO), which is found prominently in neutrophils, leads to glomerulonephritis; known as MPO-ANCA associated glomerulonephritis. It has also been reported that in some patients a Staphylococcus aureus infection precedes the loss of tolerance to myeloperoxidase. This project will test the hypothesis that molecular mimicry by a Staphylococcus aureus derived peptide can lead to the loss of tolerance to myeloperoxidase and lead to MPO-ANCA associated glomerulonephritis.

Techniques involved in this project include in vivo animal work; lymphocyte proliferation assays, histology, immunohistochemistry and immunofluorescence; and ELISA and ELISPOT.

7. The role of renal dendritic cells in a mouse model of kidney transplantation

Supervisor: Professor Richard Kitching
Email: Richard.kitching@monash.edu
Supervisor: Dr. Sarah Snelgrove
Email: Sarah.snelgrove@monash.edu

In Australia, approximately two-thirds of organ transplants are kidney transplants. When this procedure is performed, there is a period of time during which there is no blood supply to the kidney (termed ischaemia), followed by restoration of blood flow (reperfusion). Ischaemia/reperfusion injury (IRI) is a major cause of kidney dysfunction and has a crucial impact on graft survival. Renal IRI induces an influx of leukocytes including dendritic cells (DCs) to the kidney. DCs are antigen presenting cells which initiate tolerogenic and immunogenic immune responses. Renal DCs have not been extensively studied, and the importance of these cells in the kidney is only now being recognised. We are using a mouse model of IRI to mimic what happens during a kidney transplant operation. The aim of this project will be to investigate the role of renal DCs following IRI and to characterise the phenotype, recruitment and function of these cells in the kidney. Studies currently planned and offered as honours projects include

- the role of renal DCs in IRI under immunosuppression
- the effect of IRI on the antigen presenting capacity of renal DCS
- Which type of DC adheres best in the kidney

This project will utilise whole animal in vivo work, tissue culture, flow cytometry, cell transfer, working with TcR transgenic T cells and in vivo imaging by multi-photon microscopy.

Theme 2: Glucocorticoid-induced molecules in the control of inflammation and arthritis

Supervisor: Professor Eric Morand
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Theme 2 projects include:

Arthritis and Rheumatology Group

1. Actions of MIF in inflammation

Professor Eric Morand

Rheumatoid arthritis is a common idiopathic autoimmune disease affecting over 200,000 people in Australia. Cytokines are important therapeutic targets in arthritis. The Monash group has identified the cytokine macrophage migration inhibitory factor (MIF) as a key cytokine in arthritis, and is actively developing anti-MIF therapies for future use in patients with this disease.

The mechanism of action of MIF is not fully understood, but we have recently reported a probable mechanism for the interaction between MIF and glucocorticoids. Further dissection of the molecular pathways involved in MIF-glucocorticoid interactions will involve signal transduction studies, siRNA, reporter constructs, and similar technologies being applied to human and animal cells in vitro.

2. Rheumatoid synovial gene expression and signalling

Professor Eric Morand

We have obtained a data set from human rheumatoid arthritis joint (synovial) cells in which the expression of MIF has been silenced using siRNA. This will identify a set of genes regulated by MIF which require investigation for function. The project will translate novel microarray data into confirmed expression data using real-time PCR and functional assays in human cells.

3. MIF and Lupus

Professor Eric Morand and
Associate Professor Michael Hickey

Lupus (systemic lupus erythematosus or SLE) is a systemic autoimmune inflammatory disease of unknown aetiology. The role of MIF in lupus is now emerging as a result of work in this lab at Monash. The availability at Monash of MIF gene deficient lupus-prone mice is a world-first, and permits the examination of the contribution of MIF to this disease. Specifically, we will examine the mechanisms of reduced renal inflammation in MIF deficient lupus mice and examine the microcirculation of these mice in the skin, kidney and brain.

4. Annexin I and inflammatory signal transduction

Professor Eric Morand

Annexin I is a gene induced by glucocorticoids ('steroids') which is essential for the anti-inflammatory effect of these commonly used drugs. We have recently demonstrated major effects of annexin I on intracellular signal transduction events involved in inflammatory responses. The elucidation of these pathways is likely to lead to a definitive understanding of the role of annexin I in the control of cell activation. This project will utilise state of the art signal transduction research technologies which would be widely applicable in any future research positions and therefore represents an excellent training position.

5. GILZ and arthritis

Professor Eric Morand

Glucocorticoid-induced leucine zipper (GILZ) is a poorly understood glucocorticoid-induced regulatory protein involved in the control of other signal transduction pathways. We have recently determined the regulation of this protein by annexin I. Examination of the actions of GILZ in human rheumatoid tissues has not been undertaken. This project will apply the examination of GILZ to human arthritic tissues and cells, and will utilize signal transduction, siRNA, reporter constructs, and similar technologies.

Theme 3: Proinflammatory roles for coagulation proteins and their receptors

Supervisor: Associate Professor Peter Tipping

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Description:

Interactions between coagulation and inflammation.

Involvement of inflammation and coagulation is a feature of a number of important human diseases such as atherosclerosis, endotoxaemia, severe (crescentic) forms of glomerulonephritis and inflammatory arthritis. In the initiation phase of coagulation, tissue factor (TF) orchestrates the assembly of Factor VIIa and Factor X, forming a ternary complex in which Factor X is generated. The resulting complex is an efficient activator of protease activated receptors PAR-1 and PAR-2 as well as activation of thrombin and fibrin clot generation.

Coagulation receptors expressed on the surface of leukocytes and endothelial cells have potent effects on cellular functions, including their capacity to produce inflammatory mediators. These interactions between coagulation and inflammation suggest that therapies directed at inhibiting coagulation receptors in these diseases may have beneficial anti-inflammatory effects.

Projects in my group are directed at unravelling the basic cellular mechanisms by which key coagulation receptors -TF and PARs activate macrophages and other leukocytes. In addition, using experimental models of disease, we are exploring the importance of these interactions on development of inflammatory diseases in vivo, and the potential of new therapeutic agents to reduce injury. Examples of projects on coagulation and inflammation available in my group are included below.

Theme 3 projects include:

1. Tissue factor and PAR-2 signalling in macrophage activation

Associate Professor Peter Tipping

Tissue factor is a cell membrane protein which is essential for the initiation of coagulation. TF initiation of the coagulation cascade is intimately linked to inflammatory cell signalling. Our recent studies suggest that this protein may act as a signalling receptor which has the capacity to augment macrophage pro-inflammatory responses and that leukocyte expression of the cytoplasmic domain of TF contributes to antigen specific cellular adaptive immune responses via effects on leukocyte recruitment. The mechanisms of this signalling function have not been defined, but in other systems co-operation with the PAR-2 is required. We have also determined that the cytoplasmic domain of the TF molecule may play an important role in the inflammation response and we hypothesise that

PAR-2 signalling specifically phosphorylates TF. Therefore, we will study the mechanisms of TF receptor function and we will investigate the cell signalling pathways that are triggered by these two molecules using transfected monocytic cell lines and in peritoneal macrophages isolated from normal mice, mice lacking the cytoplasmic domain of TF (TF Δ CT Δ CT mice) and with mice that lack PAR receptors. This project will involve training in techniques such cell culture, molecular biology and protein biochemistry.

2. The role of protease activated receptors in atherosclerosis

Associate Professor Peter Tipping, Ms Anh Cao

Atherosclerosis is a chronic inflammatory disease of the large arteries and the major cause of heart attack and stroke in humans. Coagulation proteins play an important role in thrombotic events after rupture of atherosclerotic plaques but they may also be involved in earlier stages of plaque development, via their capacity to activate protease activated receptors (PAR's) on macrophages and smooth muscle cells in lesions. Apolipoprotein-E deficient mice (Apo-E $^{-/-}$) develop severe hypercholesterolemia and atherosclerotic lesions similar to those observed in man and allow the pathological mechanisms underlying the development of atherosclerosis to be dissected. By breeding these mice with protease activated receptor (PAR-1 and PAR-2) deficient mice, the specific contribution of these 2 receptors to the development of atherosclerosis can be determined. In this project, development of atherosclerosis will be mice studied in Apo-E deficient mice which also lack either PAR-1 or PAR-2. The effects on macrophage recruitment, smooth muscle proliferation and production of inflammatory mediated will be determined. This project will develop skills in animal models of atherosclerosis, basic surgical procedures, histological techniques, PCR genotyping, ELISA, real-time PCR and flow cytometry.

3. The role of PKR in atherosclerosis

Associate Professor Peter Tipping

The protein kinase R (PKR) is a cell signalling kinase involved in immune responses to infection. This protein has been shown to play a role in inflammation and recent studies suggest a role for PKR in atherosclerosis. In this project, the contribution of PKR in the development of atherosclerosis will be studied by breeding PKR deficient mice onto the Apo-E deficient background. The effect of PKR deficiency on the development of atherosclerosis will be determined as described in the project above.

Theme 4: Control of leukocyte recruitment and microvascular permeability during inflammation

Supervisor: Associate Professor Michael Hickey

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Theme 4 projects include:

1. Mechanisms of T cell recruitment and migration in Contact Sensitivity

Associate Professor Michael Hickey, Dr James Deane

Diseases such as psoriasis, allergic contact dermatitis and atopic dermatitis are inflammatory conditions caused by recruitment of T cells of the skin. T cells exist in many subsets, including CD4+ Th1, Th2, & Th17, CD8+, and T regulatory cells. Emerging evidence indicates distinctly different functional

roles for the various T cell subsets in inflammatory skin disease. In addition, the mechanisms whereby they gain entry into the skin may involve different adhesion molecules and chemokines for each subset.

The focus of our laboratory is the use of in vivo imaging to investigate the molecular mechanisms whereby leukocytes interact with the vascular endothelium, and migrate into sites of inflammation. This project will utilise state of the art imaging approaches (e.g. multi-photon confocal microscopy, and spinning disk confocal microscopy) to examine T cell-endothelial cell interactions in the vasculature of the skin, and also investigate the mechanisms of T cell migration within the inflamed interstitium. The mechanisms of adhesion and migration of CD4+, CD8+ and T regulatory cells will be examined.

2. Macrophage Migration Inhibitory Factor (MIF) and human endothelial cell function

Associate Professor Michael Hickey, Professor Eric Morand

The ability of endothelial cells to express adhesion molecules and chemokines underlies their role in the key feature of inflammatory responses, leukocyte recruitment. These molecules serve specific functions in enabling leukocytes traveling rapidly in the mainstream of blood flow to tether and roll and subsequently arrest on the endothelial surface, events which are required for leukocytes to enter inflammatory sites.

Recently we have used siRNA to inhibit expression of the proinflammatory mediator, macrophage migration inhibitory factor (MIF), in human endothelial cells in vitro. These experiments have demonstrated that MIF promotes endothelial adhesive function by amplifying expression of adhesion molecules and chemokines. This leads to an increased ability to induce rolling and adhesion of human leukocytes under flow conditions.

The aim of this project will be to examine this issue further, by determining whether MIF also regulates the subsequent step of leukocyte transmigration across the endothelial monolayer. These experiments will also investigate the intracellular signaling molecules whereby MIF promotes expression of adhesion molecules and chemokines. These experiments will utilise in vitro approaches to culture human endothelial cells, alter expression levels of inflammatory mediators and signaling molecules in these cells, and in vitro flow chamber assays to assess interactions between human endothelial cells and leukocytes under flow conditions.

3. Mechanisms of T cell recruitment in a novel model of T cell-mediated glomerular injury

Associate Professor Michael Hickey,
Professor Richard Kitching

Glomerulonephritis is an inflammatory disease of the kidney, the most important forms of which are mediated by the recruitment of inflammatory leukocytes to the glomerulus. Emerging evidence implicates CD4+ T cells as being key initiating leukocytes in this disease. However, the process whereby these T cells are recruited to the glomerulus and recognise their cognate antigen to promulgate the inflammatory process remains undefined.

We have developed a range of novel tools, including techniques for imaging the glomerular microvasculature in living mice, to enable the analysis of leukocyte function in the glomerulus. The aim of this project will be to investigate the mechanisms of antigen-specific T cell recruitment to the glomerulus. This project will utilise a range of techniques, including intravital microscopy of the kidney, in vitro T cell polarization, intracellular cytokine staining and immunohistochemistry for analysis of renal inflammation.

4. Tetraspanins as regulators of leukocyte migratory function

Associate Professor Michael Hickey,
Associate Professor Mark Wright

Tetraspanins are a family of novel transmembrane proteins whose functions have not been fully elucidated. Recent data have suggested that the tetraspanin CD37 is important in promoting leukocyte transmigration across the endothelium, and migration within the interstitium, suggesting that it might play key roles in inflammatory and immune responses. The aim of this project will be to investigate this issue in vivo by examining leukocyte-endothelial cell interactions and migration in the inflamed microvasculature of wild-type and CD37-deficient mice. This project, which is a collaboration between the laboratories of Associate Professor Michael Hickey (Centre for Inflammatory Diseases) and Associate Professor Mark Wright (Department of Immunology), will utilise a wide range of techniques, including in vivo imaging (multi-photon confocal microscopy, and spinning disk confocal microscopy) in living mice, as well as complementary in vitro approaches to determine the role of CD37 in leukocyte migration.

Theme 5: Mechanisms of liver fibrosis

Supervisor: Professor William Sievert
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Description:

Liver fibrosis and cirrhosis is the common end stage to all liver diseases in humans (such as infection with viral hepatitis, excessive alcohol intake or metabolic diseases). In response to injury, it has been shown that the hepatic stellate cell (HSC), the vitamin A storing cell of the liver, is responsible for the development of liver fibrosis and cirrhosis. When HSC's become activated they produce excess collagen and other scar components that are deposited in the liver. Overproduction of this matrix results in reduced liver function and liver failure. We study mechanisms of liver fibrosis and factors that determine its progression to cirrhosis. We use animal models of liver fibrosis and cirrhosis in our laboratory to enable us to determine which factors may be important in the development of this disease and identify new therapeutic targets. Several different but interrelated honours projects in Theme five are available. Projects will use a wide range of laboratory techniques including: Enzyme linked immunosorbent assays (ELISA), molecular biological techniques such as PCR and Real Time PCR, Western blot analysis, immunohistochemistry

Theme 5 projects include:

1. Activin A as a marker for liver fibrosis and cirrhosis in humans

Professor William Sievert

We have recently identified activin A, a reproductive protein, as being an important component in the development of liver fibrosis. This project will aim to identify the clinical utility of activin A as a surrogate marker for liver fibrosis in humans infected with viral hepatitis B and C. It will use a range of biochemical, molecular (such as real time PCR) and histological techniques to do so.

2. The coagulation pathway in liver fibrosis and cirrhosis

Professor William Sievert

It has recently been hypothesized that several blood coagulation factors, including plasminogen, plasmin and tissue factor, may be important in the development of liver fibrosis. This project aims to further analyse the importance of these coagulation pathway members in the development of liver fibrosis. It will use a broad range of histological, immunohistochemical and molecular biology techniques. This project will be performed in conjunction with Associate Professor Peter Tipping.

3. The effect of hepatitis C virus viral replication on hepatic stellate cell biology

Professor William Sievert

This project aims to further characterize the effects of HCV infection in hepatocytes results in HSC activation by using a cell culture system with a non-infectious form of the Hepatitis C virus. It will use a range of cell culture, molecular (such as real time PCR) and histological techniques to do so.

4. Mechanisms of alcohol related hepatocyte apoptosis in patients infected with viral hepatitis C

Professor William Sievert

Patients infected with viral hepatitis C who also consume excessive quantities of alcohol typically have a poorer diagnosis and prognosis. This is likely due to the increased amount of liver cell apoptosis (cell suicide) occurring within the liver. This project will investigate the mechanisms behind this increased liver cell apoptosis. It will use a range of cell culture, molecular (such as real time PCR) and histological techniques to do so.

Theme 6: Asthma, inflammation and viral infections

Supervisor: Dr Rheena Ghildyal,
Professor Phil Bardin
Professor David Jans

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Theme 6 projects include:

1. Inhibition of Nucleocytoplasmic Trafficking by Rhinovirus Proteases: Relevance to Asthma

Rhinoviruses (RVs) are the major cause of viral-induced exacerbation of asthma; viral-induced exacerbations are associated with 4 deaths every week in Victoria and 16 every week nationally. To date, the molecular mechanisms of RV pathogenesis are not understood, however, and current treatments are inadequate. Recent findings indicate that RV pathology in asthma may relate strongly to the inhibition of

host cell nucleocytoplasmic trafficking, resulting in perturbation of host cell functions such as transcription and translation; the basis of this inhibition in RV-infected cells may be the degradation of certain components of the nuclear pore complexes (NPCs) by RV proteases. Importantly, we recently showed that RV 3C protease is localised to the nucleus in transfected cells, and can directly disrupt active and passive transport across the nuclear envelope, presumably by degrading NPC components. We aim to examine the mechanisms underlying the inhibition of nucleocytoplasmic transport by RV 3C protease in primary cells from asthmatic airways compared to non-asthmatic airways. This should lead to an increased understanding of the role of 3C protease in RV pathology in asthma and may reveal targets for the design of therapeutics to combat RV infection/asthma exacerbations. Main techniques to be used are recombinant DNA technology, mammalian cell transfections, quantitative confocal laser scanning microscopy and in vitro nuclear transport assays, in addition to virology and immunochemical techniques.

Theme 7: Atherosclerotic vascular disease: Role of the immune system

Supervisor: Professor Ban-Hock Toh
Professor Alex Bobik

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Atherosclerosis is an occlusive disease of arteries that causes heart attacks and strokes. Together, they constitute the number 1 killer in our community. While a high fat diet plays an important role, there is increasing recognition that inflammatory and immunological mechanisms play key contributing roles.

Immunity: Our studies are directed towards a precise understanding of the role of the innate and adaptive immune system in the initiation and progression of atherosclerosis in the ApoE^{-/-} mouse model of this disease. In particular, our studies are focused on the role of macrophages, NKT cells, NK cells, CD4 T cells, regulatory T cells, B cells and the interplay between these lymphocyte subsets in this process. We have compelling evidence for a key role of the cytokine, MIF (Macrophage Inhibitory Factor) and for NKT cells in the initiation of atherosclerosis.

Significance: A precise understanding of the immunological processes leading to occlusive vascular disease can be expected to lead to novel treatment strategies to control atherosclerotic vascular disease that lead to heart attacks and strokes.

Working hypothesis: Lipids enter the vessel wall and are taken by antigen presenting cells (APCs such as macrophages, dendritic cells and B cells. These APCs present lipid antigen to NKT cells to initiate early lesions of atherosclerosis. Secretion of TH1 cytokines by NKT cells recruit NK cells and CD4 T cells that may themselves be activated by protein antigens such as HSP60, leading to lesion progression. Suppression by regulatory T cells is incomplete, contributing to lesion progression.

Students will be exposed to a unique intellectual environment that combines methods and expertise in Immunology and Inflammation at the Centre for Inflammatory Diseases, Department of Medicine, Southern Clinical School and in Vascular Biology at the Baker Heart Research Institute. Three PhD students are currently working on this project.

Performance of past honours students: Two of our current 3 PhD students were the top students in their honours year, attaining the top student Nairn medal.

Theme 8: Respiratory infection

Supervisor: Dr. Paul King

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Respiratory bacterial infection is extremely common and is probably the most common cause for patients needing to go and seek medical attention. The outcome in respiratory infection is primarily determined by the interaction between the bacterial pathogen and host immune response. The nature of the protective immune response is generally not well understood.

We have a longstanding research interest in assessing the immune response to common bacteria. Our work has concentrated on clinical samples from patients and cell lines. We have expertise in wide variety of techniques including flow cytometry, molecular biology, confocal microscopy and intracellular survival assays.

Theme 8 projects include:

1. The role of toll receptors in diagnosing respiratory infection

Supervisors: Dr Paul King
Associate Professor Kumar Visvanathan

Toll like receptors (TLRs) are expressed by phagocytic cells (neutrophils and macrophages) as an early response to infection and help direct the protective immune response. They are also potentially useful markers of specific infection. This project will assess phagocytic cells and fluid taken from the airways of patient using a test called a bronchoscopy. The cells will be labelled with specific antibodies for TLR 2, 3 and 4 and expression will be measured using flow cytometry. The fluid will be cultured for the presence of bacteria and viruses using standard culture methods. The results of the TLR expression and microbial culture will then be correlated. This project may be able to demonstrate that TLR expression is a new and powerful tool to diagnose respiratory infection.

2. Defining intracellular behaviour of nontypeable *Haemophilus influenzae*

Supervisor: Dr Paul King

Nontypeable *Haemophilus influenzae* (NTHi) is the dominant cause of respiratory bacterial infection including tonsillitis, sinusitis, ear infection and bronchitis. This bacterium has adapted to the human host and is found in the throat of most healthy adults. It only causes clinical disease in a minority of people it infects. One potentially important mechanism of causing disease is the ability to invade host cells and live intracellularly. This project will attempt to define the mechanisms of intracellular survival of NTHi using patient cells and cell lines. The techniques used will include confocal microscopy, flow cytometry and intracellular survival assays.

3. Defining body composition in COPD/bronchiectasis

Supervisors: Dr Paul King
Associate Professor Boyd Strauss

Chronic obstructive airways disease (COPD) is one of the most common diseases worldwide and the 4th leading cause of death. A key feature of COPD is nutritional deficiency/loss of protein mass even in subjects with normal weight. This project will investigate mechanisms that lead to nutritional deficiency in COPD.

Theme 9: Innate immunity and infection

Supervisor: Associate Professor Kumar Visvanathan

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Theme 9 projects include:

1. Possible role of chemokine antagonists for the treatment of malaria

Malaria kills millions worldwide, but therapeutic choices are becoming increasingly limited by resistance. Developing new classes of antimalarials from bench to bedside is a slow and costly process. Using existing drugs, created for other purposes, is likely to significantly accelerate that process since safety and pharmacokinetic and pharmacodynamic data are already extant. The fact that they haven't been previously used as antimalarials also lessens the risk of drug resistance. Vivax malaria is an important human pathogen causing up to 435 million human infections per annum. Most of these cases occur in the Asia Pacific region, and despite the reputation of vivax malaria as benign cause considerable morbidity and mortality. Chloroquine resistance is an increasing problem in *P. vivax* infections especially in New Guinea. *P. knowlesi* is an additional emerging infection in SE Asia which may also be vulnerable to DARC receptor blockade.

Vivax merozoites invade red blood cells using the ubiquitous chemokine receptor DARC (Duffy antigen receptor for chemokines). Maraviroc and other CCR5 antagonists have been developed to block HIV attachment to another specific chemokine receptor. These CCR5 antagonists are small molecules designed to mimic the attachment of chemokines to their specific receptor. However, DARC is a non-specific site of attachment by chemokines with a similar chemokine attachment site for some of the same chemokines that attach to CCR5. Currently no data exist regarding the attachment of chemokine receptor antagonists to DARC.

2. Vitamin D in chronic viral infections

A one year programme to examine the concept of vitamin D supplementation as an adjuvant for vaccination with hepatitis B vaccine undertaken in a laboratory with expertise in immunology of innate immunity and hepatitis B.

We propose to vaccinate 50 normal volunteers with hepatitis B (HBV) vaccine according to the manufacturer's recommendations. Vaccinees will also receive at the time of vaccination 1.0 mL of an oral Vitamin D emulsion in olive oil containing 50,000 IU Vitamin D or a matching oral placebo (olive oil). HBV vaccine was chosen because of its inclusion in the EPI and the strong serologic correlation with clinical protection from infection. The second dose of the vaccine will be administered at one month and the third at 6 months, these doses will not be accompanied by Vitamin D.

Blood and saliva samples will be obtained at the time of the first HBV vaccine dose, at one month post dose 1, and one month following the 6 month vaccination (dose 3). After obtaining written consent, whole blood will be collected. Serum will be separated and stored at -70C for further analysis including anti-HBs and liver enzyme (AST and ALT) and Vitamin D levels. Participants will be randomized into intervention and placebo groups without reference to the initial vitamin D level because we wish to investigate the potential adjuvant effect that would be translatable to a population setting where individual vitamin D levels would not be available.

3. Are the travel needs of immunocompromised patients being met?

There are large populations of patients with chronic medical conditions leading to immunosuppression. These patients travel more than is appreciated, both as tourists and as workers or visiting friends and relatives, but do not receive expert travel advice tailored to their conditions. A cross section survey of 100 patients from each of the HIV, renal transplant and rheumatology clinics at MMC will be undertaken. The questionnaire will cover the measurement of past and future travel, previous travel advice and vaccinations, at risk behaviours, screening for strongyloides, tuberculosis and viral hepatitis if at risk. A cross sectional survey of doctors' attitudes and knowledge of travel related risks and drug interactions will be included.

Theme 10: Inflammation in Type 2 diabetes and its complications

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Supervisor: Dr David Nikolic-Paterson
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Description:

The growing incidence of type 2 diabetes is a major medical concern. This metabolic syndrome is caused by the development of insulin resistance, which is normally a consequence of chronic obesity. During obesity, inflammation of adipose tissue (fat) and liver promote metabolic dysfunction and insulin resistance which results in type 2 diabetes. The onset of diabetes enhances the inflammatory response causing additional tissue damage to a number of organs including the heart, kidney, eye and nervous system. The overall aim of this theme is to create a greater understanding of the inflammatory process which takes place in tissues during the development of type 2 diabetes and its complications. Our research examines the role of a specific inflammatory cell (macrophages) in the development of obesity, insulin resistance and diabetic nephropathy. Our lab uses genetically modified mice and pharmacological inhibitors in models of obesity and type 2 diabetes to explore the molecular mechanisms by which macrophages promote injury. Our analyses include metabolic readouts, gene and protein expression in tissues, immunohistochemical assessment of pathology and cell culture assays of inflammation and metabolism.

Theme 10 projects include:

1. The role of JNK signalling in macrophage-mediated tissue injury in type 2 diabetes.

Our animal studies have identified that obese mice which are genetically deficient in either JNK1 or JNK2 are protected from the development of insulin resistance and type 2 diabetes.

This project will use previously collected tissues to examine how these deficiencies affect macrophage accumulation and their inflammatory responses in fat and the liver. Additional cell culture studies will utilise genetic deficiencies or pharmacological blockade to identify the importance of JNK signalling in specific interactions between macrophages and adipocytes or hepatocytes.

2. Women and Children's Health

The Ritchie Centre

Director: Professor Euan Wallace

The Ritchie Centre is one of four Research Centres within Monash Institute of Medical Research and is affiliated with the Monash University Southern Clinical School through the Department of Obstetrics and Gynaecology, and the Department of Paediatrics. The Ritchie Centre has a world leading reputation in women's health research; fetal development and neonatal research; sleep medicine; and stem cell biology. The Ritchie Centre is one of the few research units that have world-class laboratories and access to clinical patients (women and babies) in a major teaching hospital, allowing seamless translation of experimental work to clinical trials and healthcare.

There are four *Research Themes* in The Ritchie Centre:

- **Women's Health**
- **Fetal and Neonatal Health**
- **Infant and Child Health**
- **Cell Therapy and Regenerative Medicine**

Honours and PhD Projects are available in all of these themes and some projects involve more than one theme. Some examples of projects are listed below with more detailed information following

- endometrial regeneration and regulation
- stem cell therapies in lung disease, pelvic floor prolapse and spinal surgery
- fetal and neonatal development of the lungs, heart, brain and kidney
- transition of the cardio-respiratory system at birth
- disorders of the circulation and breathing during sleep in preterm infants
- understanding Sudden Infant Death Syndrome
- novel bed-side tests of brain function in extremely low birth weight babies,
- physiological and mathematical models of the control of breathing in the newborn causes of apnoea and its consequences on heart and brain function
- causes and treatment of obstructive sleep apnoea in infants and children
- new therapies for preterm lung disease
- pathophysiology of preeclampsia and the development of new therapies
- prevention of perinatal brain injury (cerebral palsy)

Women's Health

Targeting the source of oxidative stress in preeclampsia

Supervisors: Dr Rebecca Lim
Professor Euan Wallace

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Project Description:

Preeclampsia remains the leading cause of maternal and fetal morbidity and mortality worldwide. Clinical management relies on anti-hypertensive medications to stabilize the mother's blood pressure, however disease progression remains unaffected. Currently, the only way progression of preeclampsia can be halted is through the delivery of the placenta and fetus. The decision to deliver balances between the severity of maternal disease against the prematurity of the fetus. While preeclampsia is multifactorial, the underlying cause is maternal endothelial dysfunction that results from vasoactive factors and oxidative stress originating from the placenta.

We have shown that NADPH oxidase 2 (Nox2) is a key enzyme responsible for the production of free radicals in endothelial cells following exposure to preeclamptic serum in vitro, this was accompanied by a breakdown in endothelial integrity which closely mimics what we see in the human disease. We hypothesise that Nox2 is pivotal to disease progression in preeclampsia. In this current project, we will test this hypothesis by inducing preeclampsia in Nox2^{-/-} mice and their wild-type counterparts. With the use of these knockout mice, we can better understand the redundancy within the maternal system and develop therapeutics towards non-redundant oxidases. By blocking the oxidative stress cascade, we may be able to provide a world's first treatment for preeclampsia.

How does the endometrium (lining of the uterus) regenerate?

Project Leader: Dr Caroline Gargett

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Project Description:

Human endometrium is highly regenerative, growing 1 cm of mucosal tissue each menstrual cycle following menstruation. The thin atrophic endometrium of postmenopausal women also regenerates into a premenopausal endometrium which can support a pregnancy in women who take hormone replacement therapy. It is likely that epithelial progenitor cells and mesenchymal stem cells that we recently identified in human endometrium are responsible for this remarkable regenerative capacity. A microarray study comparing human endometrial epithelial cells from pre- and post-menopausal women identified 49 differentially expressed WNT signalling

genes, which have important roles in stem cell function and in developmental processes. The aim of this project is to examine the role of the Wnt signalling pathway in mediating estrogen-induced regeneration of postmenopausal endometrium and/or endometrial epithelial progenitor cell populations.

Techniques:

Isolation of endometrial epithelial cells from human endometrium, gene microarray, q RT-PCR, FACS, flow cytometry, immunohistochemistry, immunofluorescence.

Identification of human endometrial epithelial stem/progenitor cells

Project Leaders: Dr. Caroline Gargett
Dr Hiroataka Masuda

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Project Description:

We have identified that human endometrium has a small resident population of epithelial progenitor cells using adult stem cell assays. We have also shown in preliminary assays that a novel marker, H3D12 purifies the epithelial progenitor population. The aim of this study is to verify if the novel marker H3D12, which selects for clonogenic endometrial epithelial stem/progenitor cells, enriches for tissue reconstituting cells. This study would identify a marker for purifying endometrial epithelial progenitor cells for the first time and would allow studies to be undertaken to investigate their role in endometriosis, a common disease affecting 6–15 per cent of young women.

Techniques:

Isolation of endometrial epithelial cells from human endometrium, FACS, flow cytometry, kidney capsule transplantation of FACS sorted cells, immunohistochemistry, immunofluorescence

Do endometrial mesenchymal stem cells (MSC) have immunomodulatory properties like bone marrow-derived MSC that would allow their use in cell based therapies for non identical individuals?

Project Leaders: Dr Caroline Gargett
Dr Ursula Manuelpillai

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Project Description:

Mesenchymal stem cells (MSC) are rare populations of undifferentiated cells found in many tissues that are capable of self renewal and differentiating into multiple mesodermal lineages. We first discovered a novel MSC population in the endometrium, the highly regenerative lining of the uterus, (eMSC). MSC from other tissues such as bone marrow and fat have immunomodulatory properties which makes them ideal for transplantation in cell based therapies in non-identical individuals. In order to use eMSC in a non-identical individuals (allogeneic) it is necessary to characterise their immune properties determine their utility for allogeneic use in regenerative medicine applications Techniques:

Isolation of endometrial stromal cells from human endometrium, FACS or magnetic bead sorting of MSC, flow cytometry, multiplex cytokine arrays, lymphocyte proliferation assays.

Pregnancy, parturition and conception in the spiny mouse – A busy 24h!

Project Leaders: Dr. Hayley Dickinson
Associate Professor David Walker
Professor Alan Tilbrook (Physiology)

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Project Description:

The spiny mouse is a precocial rodent species with a relatively long gestation that exhibits a postpartum estrus within 24h of parturition. The mechanism of delivery (labor) is not known in the spiny mouse, but we have recently discovered that the ovary, via an active corpus luteum, is essential for the maintenance of pregnancy to term. This project will explore the mechanism of luteolysis in this species and determine the sequence of events leading to the delivery of 1 litter and ovulation and conception of the next litter, all within a 24h period.

Critical Windows of Organ Development Susceptible to Maternal Stress

Project Leaders: Dr Hayley Dickinson
Associate Professor David Walker

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Project Description:

In this study we propose to identify the times during pregnancy when organ systems such as the lung, heart, pancreas, liver, brain, adrenal and placenta are susceptible to the effects of excess maternal stress hormones. Knowledge of when particular fetal organ systems are most vulnerable to maternal stress, illness and malnutrition would give a rational basis for knowing more about how to handle and /treat such illnesses during pregnancy. In these studies we will use a most appropriate rodent species, the spiny mouse. The spiny mouse produces the same 'stress' hormone as the human (cortisol), and gives birth to offspring at a similar stage of maturation as the human at birth.

We will administer dexamethasone, cortisol or saline to pregnant spiny mice for 60h on days 15, 25, 30 or 35 of gestation (term is 39 days) and determine the fetal, newborn and adult consequences for the offspring. Fetal growth and blood flow will be monitored throughout pregnancy using our established ultrasound technique. Fetal, neonatal and adult tissue will be processed for histological, genomic, proteomic and hormone analysis. Offspring will be exposed to a battery of behavioural, physiological and body composition tests to thoroughly assess their developmental outcome.

Fetal and Neonatal Health

Impact of dopamine in the immature brain

Project Leaders: Dr Flora Wong
Professor David Walker
Professor Adrian Walker
Dr Suzie Miller

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Project Description:

Dopamine is commonly prescribed to preterm babies to raise their blood pressure, but its effect in the immature brain is uncertain. This project aims to define the effects of dopamine in the immature brain using a preterm lamb model, in order to evaluate the therapeutic potential of dopamine in improving brain oxygenation and reducing brain injury in preterm babies. Our proposal is based on our preliminary findings in preterm babies that dopamine might promote brain oxygenation to meet metabolic requirement of the brain, thus offering protection against hypoxic-ischaemic injury. We plan to use complementary human-lamb studies: in preterm human infants receiving dopamine therapy, we will monitor their cerebral oxygenation over three days using Near Infrared Spectroscopy (NIRS). In preterm fetal lambs receiving dopamine infusion, we plan to correlate changes in cerebral blood flow and metabolism with dopamine dosage and level of dopamine in cerebrospinal fluid.

Novel approaches to bedside monitoring of cerebral oxygenation in infants with HIE undergoing therapeutic hypothermia

Project Leaders: Dr Flora Wong
Professor Adrian Walker

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Project Description:

Hypoxic ischaemic encephalopathy (HIE) is a major problem worldwide with significant mortality and morbidity. Based on recent evidence that therapeutic hypothermia is beneficial to term newborns with HIE, neonatal units now offer cooling as recommended therapy. Yet, there are significant unresolved issues in the application of cooling, including uncertainty of appropriate cerebral monitoring during cooling and re-warming, potential side effects with impact on cerebral circulation and oxygenation, and long-term neurodevelopmental outcome. This project aims to improve and refine the cooling therapy, by using the Tissue Oxygenation Index measured by Near Infrared Spectroscopy (NIRS). We plan to continuously monitor the cerebral oxygenation of HIE infants by NIRS, and relate the measurements to neurodevelopmental outcome. The study will provide bedside information to aid clinical assessments with the potential to guide therapeutic interventions in these critically ill infants.

Use of activated protein C (aPC) to reduce brain injury from birth asphyxia

Project Leaders: Dr Flora Wong,
Associate Professor David Walker,
Dr Hayley Dickinson

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Project Description:

Birth asphyxia leads to significant brain injury and long term neurodevelopmental problems including cerebral palsy, cognitive and other neurological dysfunction. Activated Protein C (aPC) is a vitamin K-dependent plasma glycoprotein, and has cytoprotective, anti-inflammatory and anti-apoptotic properties. aPC has been shown to be neuroprotective in adult animal models of brain injury and stroke. We propose to explore aPC as a possible new therapy for brain injury following birth asphyxia. This project aims to evaluate the therapeutic potential of activated-Protein C (aPC) in reducing hypoxic-ischaemic brain injury and improving neurodevelopmental outcomes in a newborn spiny mouse model subjected to clinically relevant asphyxia at birth. We will use our well-validated model of birth asphyxia in the spiny mouse to determine if treatment of birth-asphyxiated pups with aPC prevents the neuropathology in brain slides, and improves postnatal behavioural deficits on cognitive-behavioural testing which we have already described in recent publications.

Does antioxidant treatment during late-pregnancy improve neonatal outcome in an ovine model of intrauterine growth restriction (IUGR)?

Project Leaders: Dr. Suzie Miller,
Professor Graham Jenkin,
Professor Euan Wallace,
Dr Tamara Yawno,
Associate Professor David Walker

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Project Description:

Intrauterine growth restriction (IUGR) affects up to 10 per cent of the population and is associated with an increased risk of perinatal mortality and increased risks of short and long-term morbidity. It has been shown in human IUGR that markers of oxidative stress are significantly upregulated in the placenta and fetus. Oxidative stress, and elevated levels of reactive oxygen species, may have detrimental effects on the developing fetus, and may be responsible for some of the poor outcomes that are observed in IUGR infants. We hypothesise that treatment with the antioxidant melatonin will reduce oxidative stress and improve fetal and neonatal wellbeing and that administration of insulin-like growth factor-1 (IGF-1) will protect the fetal brain in the face of infection and hypoxia. In this project we will induce IUGR in fetal sheep; the ewes' fetuses or neonates will be treated with melatonin or IGF-1 or placebo. We will monitor a range of outcome measures in the lambs to assess whether melatonin or IGF-1 improves outcome. This project will combine whole animal physiology, surgical techniques and postnatal animal monitoring with studies of cardiac structure and function and brain histology and immunohistochemistry. This project may impact on the treatment options available to obstetricians treating human IUGR or Cerebral Palsy.

The effects of steroid administration on the cardiovascular system of IUGR fetuses

Project Leaders: Dr Suzie Miller,
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Professor Euan Wallace

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Project Description:

Glucocorticoids are routinely administered to pregnant women at risk of preterm delivery in an effort to mature the fetal lungs for birth. There is no question that this treatment saves the lives of many newborns. However, glucocorticoids are powerful regulators of vascular function and, as such, glucocorticoid treatment may place the growth restricted (IUGR) fetus at risk, since they already demonstrate cardiovascular impairment. Using our ovine model of intrauterine growth restriction (IUGR) we have shown that blood flow responses to betamethasone (a synthetic glucocorticoid) are quite different in IUGR fetuses when compared to normally grown fetuses, which may have consequences that persist into adulthood. The effects of these changes in blood flow and subsequent impact on development of specific organs remains entirely unexplored and therefore in this project we will look closely at the brain, heart and lungs to examine possible differences between IUGR and normal fetuses administered betamethasone, as well as perinatal outcomes.

This project will combine whole animal physiology, surgical techniques and animal monitoring and experimentation with studies of cardiac and lung structure and function. We hope that this project will provide an important insight into the mechanisms occurring, and possible management strategies, in human IUGR pregnancies.

Reparative effects of follistatin in hyperoxia-induced lung injury as a model of bronchopulmonary dysplasia

Supervisors: Professor Euan Wallace
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Project Description:

Our research focuses on the wellbeing of mother and child with particular interest in pulmonary distress. Regenerative medicine is a relatively new field of medicine with aims to help natural healing processes work faster, or use special materials to replace damaged tissue. We are specifically interested in the reparative and anti-inflammatory potential of follistatin. Follistatin has been shown to be efficacious for the treatment of bleomycin-induced lung injury in adult mice, however whether it may be useful as a treatment for neonatal lung injury has yet to be investigated.

This project will investigate the therapeutic benefits of follistatin in reducing lung inflammation and fibrosis in a neonatal mouse model of bronchopulmonary dysplasia. Various techniques will be employed such as small animal surgery, stem cell culture, immunohistochemistry, FACS, real-time PCR and western blotting. This project will provide valuable pre-clinical data to support future human clinical trials of follistatin therapy.

Exploring a new frontier: The immune system of the premature infant and its relevance for the risk of developing chronic lung disease

Project Leaders: Dr Claudia Nold,
Dr Andrew Ramsden
Dr Marcel Nold

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Project Description:

Chronic lung disease (CLD) is the most common disease of the preterm infant, with a prevalence that has changed little over the past 30 years despite enormous research efforts. This program will explore the molecular causes and thereby identify potential biomarkers as well as possible therapeutic strategies for this major disease. Inflammation is increasingly recognised as the mainstay in the development of CLD; on the other hand, very little is known about the immune system of preterm babies. With observations on blood taken from preterm infants, we will for the first time systematically map the "biochemical fingerprint" of the causative inflammatory process during the postnatal period over which CLD develops. In a prospective, case-control observational human study of preterm infants born between 24 and 28 weeks gestation, we will determine the expression profile and the dynamic changes across a comprehensive spectrum of 36 pro- and anti-inflammatory cytokines as well as markers of cellular activation in 50 babies. Blood samples will be taken from the cord, in the first 24 hours of life, on days 7 and 14, and at 36 weeks corrected gestational age and analysed using a cytokine profiler to provide semi-quantitative information on the levels of the candidate cytokines and inflammatory mediators. In addition, the cells themselves will be probed by flow cytometry. Total RNA will also be isolated to analyse proteins not covered by the profiler.

Novel anti-inflammatory approaches for currently untreatable diseases of the preterm baby: protein C and IL-37 in animal models of chronic lung disease of prematurity and necrotising enterocolitis

Project Leaders: Dr Marcel Nold
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Project Description:

Severe chronic lung disease (CLD) of the preterm newborn causes considerable suffering for affected children and families and contributes substantially to health care costs. Necrotising enterocolitis (NEC) is a disease of the premature gut that is very poorly understood and that carries a high mortality. Importantly, no effective therapy is known for either of these devastating diseases. Neonatal immunity has been neglected by biomedical research; therefore, the immense importance of inflammation for the development of CLD and NEC is only beginning to be recognised. In this study, we will assess the therapeutic potential of two innovative anti-inflammatory mediators, protein C (PC) and interleukin (IL)-37, in well-established animal models of neonatal CLD and NEC.

Amnion-infection and hyperoxia are important contributors to human CLD, causing an arrest of alveolar development, increased inflammation, apoptosis of pneumocytes, and subsequently considerably compromised lung function. Therefore, our model for CLD comprises an intraamniotic injection of a pro-inflammatory compound (LPS); then, the newborn pups will either breathe room air or 85% O₂. At 2 and 28 days of life, we will assess whether increased levels of PC or IL-37 can protect the young mice from developing CLD-like pathology by analysing biochemical markers of inflammation, histological slides for alveolarisation and vascularisation, and improved respiratory and clinical performance compared to controls. To mimic NEC, newborn mice will not be allowed to breast-feed, but will be fed an equivalent to formula, for 3 days. In addition, they will briefly be exposed to cold and hypoxia. The resulting pathology in the gut resembles human NEC, and again we will assess the protective properties of PC and IL-37 on the cellular level by histology and on the molecular level by analysis of various biochemical markers.

Signaling of interleukin (IL-)37, a new member of the IL-1 family of cytokines

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Project Description:

IL-37 was discovered *in silico* in 2000, but received very little attention (not even 10 publications) in general and nothing at all was known about its function until 2010, when our group described the fundamental anti-inflammatory properties of this cytokine. IL-37 belongs to the IL-1 family of cytokines and imparts a strong inhibition of the production of pro-inflammatory cytokines. Interestingly, this protection from inflammatory responses is not limited to one or a few triggers, but covers a wide spectrum of inflammatory assaults - a rare property, which renders IL-37 a prime candidate for clinical use. Before such steps can be taken, further research on the mechanism of action of this unusual cytokine is necessary. In this project, we will describe the yet unknown cell surface receptor for IL-37 using immunoblotting techniques, sophisticated imaging technology (FRET), molecular approaches including cloning and reporter assays, and *in vivo* strategies involving transgenic and knockout mice. We will also investigate how IL-37 modulates the function of immune cells using transfections, ELISAs, and flow cytometry. Last but not least, we are interested in the intracellular signal transduction elicited by this fascinating cytokine.

Oxygen therapy for preterm infants – optimising delivery

Project Leaders: Dr K Tan
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Project Description:

Premature infants with respiratory distress syndrome (RDS) require oxygen treatment. However, there are risks with oxygen therapy and so the oxygen levels (oxygen saturation) of these babies have to be controlled strictly. Oxygen saturation levels are measured using pulse oximeters, and if the levels are

outside the target range; the bedside nurse or doctor will adjust the amount of oxygen given to the infants. Manual control of oxygen often fails to achieve adequate oxygen saturation targeting. Automation of the control process may improve oxygen saturation targeting and reduce variability of oxygenation in premature infants.

The aim of this project is to develop automated oxygen delivery, with the two main objectives as;

1. Development of (mathematical) models of oxygenation in preterm infants with RDS (with collaboration from Department of Electrical and Computer Systems Engineering, Monash University).
2. Development of controller device for oxygen delivery.

Transition to life after birth

Project Leaders: Professor Stuart Hooper,
Dr Kelly Crossley,
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Project Description:

The transition to air-breathing after birth is one of the greatest physiological challenges that we will ever face during our lives. Within moments of birth, the airways must be cleared of liquid, to allow the entry of air, which greatly increases blood flow through the lungs and closes shunts that allow blood to by-pass the lungs during fetal life. When the umbilical cord is cut the infant loses ~1/3 of its blood volume and venous return to the heart is reduced by ~50 per cent. It is truly amazing that most infants smoothly transition from fetal to newborn life at birth. However, many don't and these huge physiological changes provide life threatening challenges for these infants that can have life-long repercussions. To reduce the risks for newborn infants during this challenging period, we need to better understand these changes and the factors controlling them. The aim of this project is to study the changes that occur at birth and to identify factors that both facilitate and impede these changes.

Imaging the entry of air into the lungs at birth

Project Leaders: Professor Stuart Hooper,
Dr Melissa Siew
Dr Marcus Kitchen (Physics)

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Project Description:

Surviving the transition to air-breathing at birth is dependent upon the clearance of liquid from the airways to allow the entry of air into the gas exchange regions of the lung. This process occurs very smoothly in most infants, but preterm infants have much difficulty in clearing their lungs of liquid and allowing air to enter the regions where gas exchange can occur. We have developed a unique imaging technique, using a synchrotron, which allows us to observe the entry of air into the lungs at birth and simultaneous changes in blood flow to the lungs. Using this technique we can study and identify the factors that facilitate air entry into the lungs at birth, particularly in animals born preterm. We can also image the ~10-fold increase in blood flow to the lungs that occurs

when the lungs fill with air. The aim of this project is to use our imaging technique to identify factors that promote and impede the entry of air into the lungs at birth in animals born preterm and that promote the increase in pulmonary blood flow at birth. These experiments will provide important information for doctors caring for very preterm infants and will be conducted at a Japanese synchrotron.

Ventilation-induced lung injury in very preterm infants

Project Leaders: Dr Megan Wallace
Professor Stuart Hooper

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Project Description:

Preterm birth is the greatest cause of death and disease in newborn infants because their lungs are too immature to take over the role of gas exchange at birth. As a result, very preterm infants often need respiratory support at birth, but this can damage their lungs and lead to abnormal lung development known as bronchopulmonary dysplasia. Little is known of the mechanisms by which assisted ventilation causes lung injury or how this injury causes abnormal lung development. However, we have recently identified several factors (CTGF, CYR61 and EGR1) that rapidly mark the presence of lung injury and that may lead to the abnormal lung development seen in infants with bronchopulmonary dysplasia. Several projects are possible including; determining if the levels of CTGF, CYR61 and EGR1 in blood can predict the degree of lung injury that a newborn has experienced, identifying types of ventilation that are more gentle and more injurious, determining whether CTGF, CYR61 and EGR1 are actually leading to abnormal development and identifying treatments that may prevent injury and the resulting abnormal development. These projects may involve caesarean sections and neonatal ventilation with the analysis of blood and lung tissue for CTGF, CYR61 and EGR1 levels and the degree of lung injury using histological and molecular approaches, or they may involve in vitro methods of injuring lung cells and manipulating the levels of these factors to determine if they mediate abnormal lung development.

Fetal lung growth and development

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Professor Stuart Hooper

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Project Description:

At the time of birth the lungs must take on the role of gas-exchange, a role they have never performed before. To survive therefore, the lung must be appropriately grown and mature by the time of birth. Infants born preterm, before the lungs have had time to develop, or with lungs that have not developed properly (lung hypoplasia), are at high risk of death or disease. To improve the outcome for these infants we must understand the mechanisms that regulate normal lung development, so that we can find new ways to accelerate it. We do know that the lungs are filled with liquid during fetal life and that degree of lung expansion is critical for normal lung development. However, the mechanisms involved are largely unknown. This project will investigate genes/proteins that are likely candidates for mediating lung growth using in vitro approaches.

The effect of intrauterine inflammation on the development of atherosclerosis

Project Leaders: Dr Tim Moss,
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Project Description:

Exposure to inflammation before birth is common in human pregnancies and has profound effects on fetal development. Limited human data suggest that exposure to inflammation before birth is associated with atherosclerosis. This project is aimed at providing well-controlled experimental data to confirm this association, and will result in the establishment of an animal model that will allow us to investigate potential underlying mechanisms.

Experimental work for this project will be conducted at MIMR and The Royal Children's Hospital. We will use transgenic (apoe^{-/-}) mice that are predisposed to develop atherosclerosis. We induce intrauterine inflammation in pregnant apoe^{-/-} mice by injecting lipopolysaccharide into each amniotic sac during a brief surgical procedure (controls receive saline). We will then collect tissues from offspring at various stages to quantify (initially) the degree of intrauterine inflammation and the presence of vascular changes identified using light microscopy. Tissues will also be collected for molecular analysis (e.g. qPCR) of potential mediators of the development of atherosclerosis.

Mechanisms of inflammation-induced lung 'maturation'

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Professor Stuart Hooper

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Project Description:

Inflammation within the uterus during pregnancy increases the risk of preterm birth and alters fetal development. One of the consequences of intrauterine inflammation is increased production of surfactant by the immature lungs, which results in a reduced risk of respiratory distress syndrome (RDS) in preterm babies born after exposure to inflammation within the uterus. The mechanism whereby intrauterine inflammation leads to increased surfactant production by the preterm lungs is unknown. Identification of this mechanism may lead to new interventions to prevent RDS. The aim of this project is to identify potential mediators of the effect of intrauterine inflammation on preterm lung development.

Experiments for this project use either sheep or mouse models of intrauterine inflammation, based on intra-amniotic injection of lipopolysaccharide into the amniotic sac. Various components of these studies can form suitable Honours projects, using a variety of methodologies (e.g. molecular biological techniques, whole animal physiology, histology).

Protecting the brain from injury at preterm delivery

Project Leaders: Dr Graeme Polglase
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Project Description:

Brain injury is common in preterm infants and is a major cause of long-term adverse neurodevelopment, including mental disability and cerebral palsy. Human data and animal studies have shown that brain injury pertaining to preterm birth occurs through two major mechanisms: 1) an inflammatory cascade in the brain and 2) alterations to cerebral blood flow.

Our current research is focused on understanding events that occur in utero, during the time of birth, and upon subsequent respiratory support after birth, can lead to brain injury in preterm neonates. Several projects are available in this area, including: investigating the effect of the antenatal environment, including inflammation and corticosteroids, on brain injury, and how the initiation of ventilatory support may increase brain injury. Our focus is to establish techniques to reduce/prevent brain injury related to perinatal events. The experiments include whole-animal physiology, molecular biology and immunohistochemistry.

Amniotic fluid infection and fetal brain injury

Project Leaders: Dr Tim Moss
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Project Description:

Ureaplasmas are the micro-organisms most often isolated from the amniotic fluid of women who deliver their babies preterm. It appears that the presence of ureaplasmas in amniotic fluid is also associated with damage to the developing fetal lungs and brain.

This project will utilise samples of fetal brain tissue collected from preterm fetal sheep that were exposed throughout much of gestation to amniotic fluid ureaplasma colonisation. Work for this project will involve preparation and analysis of histological sections of various brain regions for measurements of general brain morphology and immunohistochemical identification of effects on specific cell types within the brain.

Infant and Child Health

Postnatal Consequences of Intrauterine Growth Restriction on Cardiovascular Control During Sleep in Infants

Project Leader: Associate Professor Rosemary Horne
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Project Description:

Intrauterine growth restriction (IUGR) has been associated with increased risk of cardiovascular disease, high blood pressure, obesity and insulin resistant diabetes later in life. The causes of this increased susceptibility remain unclear. Cardiovascular control undergoes dramatic maturation changes within the first six months of life. In the newborn period infants spend approximately 70 per cent of their time asleep and it is during

sleep that infants are at increased risk of cardiovascular instabilities. To date there has been no description of the consequences of IUGR on the maturation of cardiovascular control during sleep in human infants. We have previously described normal maturation of both blood pressure (BP) and heart rate (HR) control in both healthy full-term infants and infants born preterm. In these novel studies we will expand our previous studies to examine the effects IUGR on the maturation of BP and HR control during sleep within the first 6 mo of life. This study will provide information on the postnatal consequences of IUGR and aid in understanding any contributing factors that may contribute to increase blood pressure and cardiovascular complications later in life.

Development of Cerebrovascular Control During Sleep in Infants: Effects of prone sleeping and implications for SIDS

Project Leaders: Associate Professor Rosemary Horne,
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Project Description:

It has been suggested that Sudden Infant Death Syndrome (SIDS) may be due to an inadequate compensatory response to a hypotensive challenge resulting from either a cardiovascular or respiratory event during sleep. Sleeping in the prone position is still a major risk factor for SIDS, and as yet the reason for this is unknown. We, and others, have previously identified that infant autonomic cardiovascular control and arousability from sleep are impaired in the prone position and this is most marked at 2-3 months of age when SIDS risk is highest. Furthermore, preterm infants are at increased risk for SIDS and we have previously identified impaired autonomic cardiovascular control and arousability in preterm infants compared with age matched term infants. The impaired arousability in SIDS may be related to poor regulation of brain blood flow and oxygen level during sleep. In these novel studies we will expand our previous studies to examine the effects of sleeping position and prematurity on blood pressure (BP) and heart rate (HR) control and cerebral oxygenation using Near Infra Red Spectroscopy (NIRS).

Postnatal Maturation of Infant Sleep Physiology

Project Leader: Associate Professor Rosemary Horne
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Project Description:

It has been suggested that despite appearing well and physiologically normal prior to their deaths, victims of Sudden Infant Death Syndrome (SIDS) may have had a pre-existing abnormality which impaired their ability to arouse from sleep. In support of this hypothesis, we have previously shown that arousal processes are modified by major SIDS risk factors, prone sleeping and maternal smoking. An incomplete progression of sub-cortical to full cortical arousal may provide a marker to identify "at risk" infants with an increased likelihood of succumbing to SIDS. This may have the potential to minimise the incidence of SIDS by increasing awareness of both parents and medical staff, in association with close monitoring and early intervention; however this would be impossible without normative values for comparison.

This study will examine recordings of undisturbed nocturnal sleep in healthy infants throughout the first 12 months of life. We will compare changes in baseline cardiorespiratory variables and spontaneous arousal processes both between infants and within individual infants across development. In addition, using spectral analysis techniques, we will investigate maturational changes in EEG activity, and on heart rate variability (as a measure of autonomic control).

Effectiveness of treatment for the resolution of Sleep Disordered Breathing, cardiovascular, behavioural and neurocognitive symptoms in pre-school children

Project Leader: Associate Professor Rosemary Horne,
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Dr Sarah Biggs

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Project Description:

Our previous studies have identified that sleep disordered breathing (SDB) is associated with increased blood pressure and heart rate and also with impaired neurocognition and behaviour. In current clinical practice, only those children with more severe SDB are treated, primarily with adenotonsillectomy (A/T). A/T has been shown to improve sleep quality and neurobehavioural outcomes, however to date there have been no studies on the effects of treatment on the cardiovascular system. Perhaps more importantly, there have been no studies to assess what happens in untreated children with milder symptoms as currently it is believed that children 'will grow out of' their SDB. In this study we will follow up the children previously studied to determine the effects of SDB treatment and non treatment on both the cardiovascular system and neurobehavioural outcomes.

A clinical tool for the detection of children at high risk of obstructive sleep apnoea

Project Leaders: Dr Gillian Nixon
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Project Description:

Obstructive sleep apnoea (OSA) affects 1–3 per cent of children and is a major health issue in childhood, with significant impacts on cognition, behaviour and cardiovascular health. The cardinal symptom of OSA is snoring. Approximately 35% of children snore- over one million children in Australia- but only about 10% of snoring children (1-3% of the population) will have OSA. Formally defining the presence of OSA in a snoring child requires polysomnography, a technically challenging and expensive (about \$1000 each) test only available in paediatric tertiary referral hospitals. Such facilities could never meet the demand if all snoring children were referred. We are developing a clinical scoring tool that will help predict children at highest risk of OSA without the need for polysomnography. The tool involves clinical evaluation of the patient including features such as age, body mass index (BMI), symptoms of OSA (snoring, restless sleep) and clinical findings, plus simple sleep tests that can occur in a patient's home.

Executive function and frontal lobe activity in children with sleep disordered breathing

Project Leader: Associate Professor Rosemary Horne
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Project Description:

Recent research by our group has revealed that even mild SDB is associated with deficits in executive function, in particular working memory and planning ability. Debate exists as to whether the mechanism for executive function deficit is due to neurological changes in frontal lobe function or is a symptom of daytime sleepiness caused by disrupted sleep associated with SDB. Research has also reported that these deficits do not resolve 6-months after treatment for SDB, suggesting that any insult to the developing brain caused by hypoxia and/or arousal during sleep may be permanent. Questions remain however, as to whether there is a critical period during childhood in which this insult leads to irreversible damage, or whether SDB left untreated for an extended period of time results in gradual deterioration of the brain's ability to recover. This study will compare executive function in children with SDB across a wide age range and across differing severities against published norms and for the first time will provide objective evidence as to the association between SDB related events and executive function in children.

Novel therapy for inflammation and microvessel loss in Diabetic Cardiomyopathy

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Project Description:

According to the International Diabetes federation it is estimated that annually some 76,000 children aged less than 15 years develop Type-1 diabetes worldwide. Hence there is an urgent need to define the mechanisms of cardiac complication during diabetes and also develop effective, safe and low-cost therapies. Coronary heart disease is the leading cause of death in the diabetic population and the mechanisms involved are not fully understood. Recently it has been demonstrated that loss of coronary microvessels (microvessel rarefaction) contributes to diabetic cardiomyopathy. However, the dynamic regulation of coronary microvessel prevalence has not been investigated in this setting.

Our study is designed to better understand how loss of microvessels in heart muscle (a phenomenon known as rarefaction) occurs in diabetes, and how this loss may contribute to heart dysfunction and coronary heart disease. Inflammatory pathways play an important role in many cardiovascular diseases and may cause loss of coronary microvessels. Diabetic patients have elevated levels of inflammatory factors (cytokines) in the circulation and the heart. Hence understanding the mechanistic role of increased inflammation in the progression of diabetic cardiomyopathy is critical for the development of novel therapeutic strategies in the future. We will use a relevant animal model to study this phenomenon. Additionally, this project will test the therapeutic value of a chemical (resveratrol); commonly found in grapes, peanuts and red-wine in this setting. The long-term goal of this project is to rationally design new ways to prevent this problem or even reverse the process.

Cell Therapy and Regenerative Medicine

Cell Therapy Regenerative Medicine

Project Leader: Professor Graham Jenkin

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Project Description:

The innate capacity of the fetus to repair and regenerate tissues is being used to develop unique new models of organ and tissue regeneration using stem cells. Our research group has developed models of fetal compromise (intrauterine growth restriction), hypoxia induced brain injury and infection in pregnancy and respiratory compromise associated with premature delivery. This research will enable potential new therapies using novel stem cells, including adult stem cells, placental mesenchymal stem cells and amnion epithelial cells and their derivatives to be tested in appropriate animal models. Of particular interest are human amnion derived epithelial stem cells which have many of the characteristics of embryonic stem cells, but which can be obtained without the ethical issues associated with embryonic derived stem cells. In collaboration with Professor Euan Wallace and Dr. Suzie Miller, we are studying the properties of these cells, both in vitro and in vivo, their derivation, their characteristics including plasticity and their potential therapeutic use in repair of respiratory epithelium, cardiac tissue and neural tissues, as well as in spinal disk repair. The latter involves development of biomatrices using stem cells and tissue scaffolds in preclinical research projects on bone and cartilage repair. We are currently undertaking clinical trials, using adult mesenchymal progenitor cells, on spinal disk repair.

Development of a novel stem cell therapy for Cystic Fibrosis

Project Leaders: Professor Graham Jenkin
Professor Euan Wallace

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Project Description:

There is a dire need for a cell type therapy to replace dysfunctional lung epithelial cells in patients with cystic fibrosis who lack functional ion channels in their respiratory epithelium due to gene mutation. This research project aims to demonstrate that we can produce functional lung epithelial cells from placental stem cells. We will utilize a novel method of delivering these cells into the lungs of a mouse model of cystic fibrosis with the aim of incorporating the functional lung epithelial cells into the respiratory conducting airway and the lung. We propose to track placental stem cell-derived lung epithelial cells in the lung using the Imaging and Medical Beamline of the Australian Synchrotron. This technique will allow us to assess incorporation of labeled cells into lung airways and to determine their ultimate fate non-invasively. We will assess the effect of placental stem cell-derived lung epithelial cell delivery on the lung function of mice with cystic fibrosis. The proposed experiments will allow us to address significant challenges in the development of cell therapies for cystic fibrosis by applying novel and cutting edge technologies to achieve important translational outcomes.

Human amnion cells: a new therapy for preterm lung disease

Project Leaders: Professor Euan Wallace
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Professor Graham Jenkin

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Project Description:

The overall aim of our research is to study the utility of human amnion epithelial cells (hAECs) in repairing preterm lung injury. To do this, we will use two sheep models of in utero lung injury in the sheep, namely in utero ventilation and in utero infection (LPS). We will induce lung injury with these models separately and use our well characterised hAECs to explore whether the cells can ameliorate the lung injury in the fetal sheep. If successful, we will be well placed to readily apply this technology to very preterm human babies. Our previous research has shown that hAECs are capable of reducing inflammation and preventing fibrosis, in an adult model of lung fibrosis, and differentiating into alveolar type I and type II cells within the injured lung. We are now studying the effects of hAECs on preterm lung damage and have early pilot data showing that, in the preterm fetal lung, hAECs will reduce inflammation, reverse scarring and repair the lung exactly as they do with adult lung scarring. These projects will include whole animal physiology, surgical/techniques as well as histological, genomic and proteomic technologies including a novel technique that will allow us to identify a number of early response genes within the fetal and maternal blood that indicate that the fetal lung is being damaged, and that, with hAEC administration, this damage is prevented.

Human amnion epithelial cells as therapy for lung inflammation in preterm newborns

Dr Tim Moss, Professors Graham Jenkin and Euan Wallace

Project Description:

Bronchopulmonary dysplasia (BPD) is a life-threatening chronic lung disease that affects many infants born very preterm. Lung inflammation likely underlies the pathogenesis of BPD. Epithelial cells isolated from the amniotic membrane have stem cell-like properties and other characteristics that make them attractive as a potential cell therapy. The aim of this project is to identify the effect of human amnion epithelial cells on inflammatory responses of newborn preterm lambs. The experiments include whole-animal physiology, immunology, microscopy and molecular biology techniques.

Stem Cells and Tissue Scaffolds

Project Leaders: Professor. Graham Jenkin
Dr Tony Goldschlager

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Project Description:

In these studies, we are investigating the suitability of novel new biomimetic matrices to form tissue structures. Our aim is to produce biomimetic spinal discs for repair of discs damaged by trauma or degenerative processes. The use of stem cells to produce cartilage for the repair knee joints is also a major focus of this research. The advent of

tissue engineering in the last few decades, together with developments in the therapeutic use of stem cells, has given researchers the potential ability to suitably engineer cellular constructs for replacement of damaged tissues. We will study the characteristics of biomatrices both in vitro and in vivo in collaboration with commercial companies. We will determine the appropriateness of our cellular scaffolds for the production of engineered tissues. We will determine the most appropriate polymer compositions and stem cell combinations that can be developed into the most viable scaffold for therapeutic use

Spectroscopic Imaging of Stem Cells and Tissues

Project Leaders: Professor Graham Jenkin
Professor Euan Wallace

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Project Description:

The project uses state of the art Infra Red and Raman spectroscopic imaging technologies and light from the Australian Synchrotron to achieve physiological, histological and biochemical measurements in human stem cells and tissues, including lung, spinal disks and osteochondral defects. An exciting new project has recently commenced where the use of the new Medical Beamline at the Australian Synchrotron is being used to track the movement and fate of amnion epithelial stem cells in live animals and tissues after they have been administered to animals in preclinical trials for the treatment of adult, fetal and neonatal lung and brain damage.

Tracking human amnion epithelial cells in vivo in regenerative medicine

Project Leaders: Dr Rebecca Lim
Professor Euan Wallace
Professor Graham Jenkin

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Project Description:

We are exploring the use of human amnion epithelial cells (hAECs) as a cellular regenerative therapy for a variety of diseases including bronchopulmonary dysplasia and chronic lung disease of the preterm infant. In our previous studies, using an adult mouse model of pulmonary fibrosis, we have been able to identify these hAECs at post-mortem using human specific antibodies, in the lung, up to 4 weeks after injection. We have also shown that these cells differentiate into alveolar type I and type II cells within the injured lung. This project will utilise novel labelling techniques, including gold nanoparticles that will allow us to track the migration profile of these hAECs in real-time. These studies will provide important information regarding cell fate, migration patterns and engraftment and differentiation efficiency. There are a number of techniques that will be utilised to monitor the migration, location and differentiation of hAECs in vivo such as colloidal gold nanoparticles which can be incorporated into the cells, injected into an animal model and the cells tracked in real-time using the Synchrotron and MRI. The same technology allows post-mortem validation.

Molecular characterisation of reproductive stem cells for tissue engineering

Project Leaders: Dr Caroline Gargett

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Project Description:

Mesenchymal stem cells (MSC) are rare populations of undifferentiated cells found in many tissues that are capable of self renewal and differentiating into multiple mesodermal lineages. We first discovered a novel MSC population in the endometrium, the highly regenerative lining of the uterus, (eMSC) and can isolate them using two specific markers. We have also isolated a population of MSC from the human placenta decidua basalis (dbMSC) using eMSC markers. Potential use of reproductive stem cells for tissue engineering and cell-based therapies is attractive as it may be possible to use a patient's own stem cells to repair reproductive organs. However, the molecular characterisation of eMSC/dbMSC has not been done and is necessary prior to their application in regenerative medicine. This study will identify candidate genes that may control eMSC/dbMSC function.

Techniques:

Gene array, Real-time PCR, Western immunoblotting

3. Neurosciences Research Group

The Stroke and Ageing Research Centre (STARC) is based in the Southern Clinical School, Monash Medical Centre. It consists of internationally recognised experts in clinical, epidemiological and public health aspects of stroke, dementia, and other brain ageing phenotypes.

Projects available for potential honours students

1. The role of T-cells in acute stroke

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Associate Professor Thanh Phan
Email: thanh.phan@monash.edu

This is a project examining the role of T-lymphocytes in the evolution of acute ischemic stroke. It is unknown whether certain T-cells (Treg) have a protective role in stroke. This is an area that has generated significant interest in animal experimental models, and we aim to translate the findings from such animal models in human studies. The project involves laboratory measurement of several immune cell types in stroke patients.

2. Measuring ischemic stroke penumbra with high-resolution CT imaging

Associate Professor Thanh Phan
Email: thanh.phan@monash.edu

Associate Professor Velandai Srikanth
Email: velandai.srikanth@monash.edu

Dr Henry Ma
Email: hkma72@hotmail.com

The ischaemic penumbra is that part of the brain affected by stroke that may be salvaged by acute treatments. Measuring the penumbra is challenging and this project aims to use a state-of-the-art CT scanner to achieve this goal. It involves working in the brain imaging laboratory.

3. Imaging approach to phenotyping lacunar stroke

Associate Professor Velandai Srikanth
Email: velandai.srikanth@monash.edu

Associate Professor Thanh Phan
Email: thanh.phan@monash.edu

Lacunar stroke has been proposed to be due to small vessel disease. The aim of this study is to evaluate if this stroke mechanism holds true for all 'lacunar' strokes. This project involves working with stroke physicians and radiologists to phenotype patients.

4. Imaging amyloid angiopathy

Dr John Ly
Email: jly@netspace.net.au

Associate Professor Thanh Phan
Email: thanh.phan@monash.edu

As a result of recent advances in ligand development, it is now possible to image amyloid binding in the brain in vivo using PET imaging. We have recently phenotype a TIA like presentation of amyloid angiopathy (the clinical implication is that these patients are treated differently from the typical TIA patients). We are planning to evaluate amyloid binding in a number of other stroke syndromes. This project involves working in the imaging laboratory in Neurosciences and state-of-the-art PET scanner.

5. What can be learnt from a clinical trial feasibility study?

Professor Amanda Thrift
Email: amanda.thrift@monash.edu

Associate Professor Dominique Cadilhac
Email: dominique.cadilhac@monash.edu

This is a project to test the feasibility of undertaking a clinical trial of risk factor management within General Practice. Patients were recruited to this study following admission to hospital for a stroke. The patients were then randomised to an intervention or control group. The intervention comprises developing a management plan for patients so that high quality management is maintained once they return home. There is also an education component so teach patients about their risk factors and how to manage them. The aim of this project is to determine how representative the patients recruited are when compared to the patients that attend hospital. We also aim to see which patients tend to drop out and which patients tend to remain in the longer term. The overall aim is to make recommendations about the patients that should be targeted for such a clinical trial.

6. Introduction to health services research in stroke

Associate Professor Dominique Cadilhac
Email: dominique.cadilhac@monash.edu

Dr Monique Kilkenny
Email: monique.kilkenny@monash.edu

In the public health division, there is potential for projects for suitable students based on access to large datasets for undertaking research projects on stroke, as well as studies on blood pressure in the community. This will provide an insight into the usefulness of such work in translating evidence to practice, as well as enable skills in managing large datasets.

4. The Monash Cardiovascular Research Centre/Vascular Research Group

The Monash Cardiovascular Research Centre researches a wide variety of cardiac disease and is located at Monash Medical Centre.

Contacts

Professor James Cameron

Email: james.cameron@monash.edu

Dr Sarah Hope

Email: sarah.hope@monash.edu

MCRC has potential BBiomedSc honours projects in a number of cardiological topics:

(Retrospective) Assessment of radiation dose in diagnostic angiography and percutaneous coronary intervention in a tertiary referral centre.

Assessment of degree of stenosis in coronary artery disease as assessed by 3D quantitative angiography

The Vascular Research Group is located at Dandenong Hospital and has a wide interest in all forms of vascular disease particularly hypertension

Supervisor: Professor Barry McGrath

Telephone: 9554 8022

Email: barry.mcgrath@monash.edu

5. Nutrition and Dietetics

Bachelor of Nutrition and Dietetics Honours – BND(Hons)

The BND(Hons) course is for outstanding graduates who have completed a dietetic or nutritional science course. It is designed to develop research skills and competencies, specific techniques and a deeper understanding of an aspect of human nutrition. The program consists of an individual major research project and a compulsory coursework component which includes completing a systematic literature review. BND(Hons) provides a necessary first step to pursuing a research career in nutrition-related science.

Project areas:

- Clinical dietetics
- Community nutrition
- Population nutrition.

Projects offered include:

Exploring satiety responses

Food intake leads to the release of varied gut hormones that can suppress appetite. These hormones provide messages to the brain that in turn transmit signals effecting body metabolism and further food intake. A stronger understanding is needed of the impact of foods differing in macronutrient content, on appetite and satiety and whether effects differ in different population groups. Findings from studies of this type have particular relevance to the growing problem of obesity. Several projects linked by the use of similar methodologies for studying satiety will be offered-

1. In clinical paediatric patients- to explore responses to dietary supplements (dietetic student required)

Professor Helen Truby

Email: helen.truby@monash.edu

2. In healthy children of normal body weight

Dr Kate Huggins

Email: catherine.huggins@monash.edu

Dr Elizabeth Manickam

Email: elizabeth.manickham@monash.edu

3. In overweight adults with sleep apnoea – to examine the effects of food on appetite and on sleep patterns

Dr Maxine Bonham

Email: maxine.bonham@monash.edu

How and why is diet affected in women treated for breast cancer?

Supervisor: Anna Boltong
(Peter MacCallum Cancer Centre)
Email: anna.boltong@petermac.org

Supervisor: Claire Palermo
Email: claire.palermo@monash.edu

The aim of this project is to determine how dietary intake is affected following a diagnosis of breast cancer and to examine the effects of subsequent chemotherapy treatment and the underlying factors that contribute to dietary change. Weight gain is common in this population, the causes of which are thought to be multifactorial. The contribution from dietary change is largely unknown. The project is a sub-study of a larger project investigating the influences on taste and food pleasure in people receiving chemotherapy and implications for diet, social dining and nutritional status. The project will make use of quantitative dietary data to determine the nature of dietary change across the cancer treatment trajectory. Qualitative data will be collected from study participants via in depth interviews to determine reasons for dietary change. It is hoped this research will go some way toward identifying the most appropriate type and timing of dietary support for breast cancer survivors. A dietetic student is required.

The effect of fat type and fatty acid chain length on lipid uptake and appetite in healthy men and women

Supervisors: Dr Maxine Bonham
Email: maxine.bonham@monash.edu

Supervisors: Dr Karen Walker
Email: karen.walker@monash.edu

High intakes of saturated fat are commonly associated with an increased risk of heart disease. However, there is evidence to indicate that it is not only the type of fat you eat that influences disease risk but also the relative length of the fatty acid chains that make up the fat molecule (or triacylglycerol). Fats are usually described as short chain (less than 6 carbons), medium chain (6–12 carbon atoms), long chain (14–22 carbon atoms) and very long chain (greater than 22 carbon atoms). Medium chain triacylglycerols tend to be broken down to fatty acids after digestion and are rapidly absorbed and transported to the liver via the portal vein for rapid oxidation. As a result little of this fat becomes stored in body fat. Medium chain triacylglycerols may therefore affect body composition through increased satiety and increased energy expenditure. Coconut oil is an important food oil throughout south Asia. Although it has been widely regarded with caution here due to its high content (> 85%) of saturated fat, over 60% of this saturated fat content is made up of medium chain fatty acids (MCFA). In contrast, butter which is also high in saturated fat has only about 10% of its saturated fat content as MCFA. The aim of this project is to examine the effect of a breakfast meal containing a high content of coconut oil on postprandial lipid absorption and appetite suppression in healthy men and women compared to a breakfast meal high in long chain fatty acids.

The role of FODMAP carbohydrates in the genesis of gastrointestinal symptoms associated with irritable bowel syndrome: An evaluation of the current therapeutic strategy of adding glucose to high fructose foods to minimize fructose mal-absorption

Supervisors: Dr Jane Muir
Dr Jaci Barrett
Dr Sue Shepherd
Professor Peter Gibson

Email: jane.muir@monash.edu
Department of Medicine, Monash University,
Box Hill Hospital campus

One in seven Australians suffer from irritable bowel syndrome (IBS), a condition that is characterized by abdominal bloating, pain, and irregular bowel habit. Our research team has identified dietary triggers that might be responsible for the induction of symptoms in the majority of patients with IBS. These triggers involve a group of small carbohydrates that are commonly found in a wide variety of foods and can be poorly absorbed in the small intestine and include; fructose (in apples, pears and fruit juice, high fructose corn syrups), lactose (milk), fructans (onions, garlic, wheat), galacto-oligosaccharides (legumes) and sugar alcohols [sorbitol (pears & apple) and mannitol (mushroom, celery, cauliflower)]. We have named this group of compounds FODMAPs – Fermentable Oligo-, Di- and Mono-saccharides And Polyols. One of the major FODMAPs to cause problems for patients with IBS relates to foods with high levels of free fructose. There is some evidence in healthy adults that taking supplements of glucose with foods containing free fructose will enhance the absorption of fructose. This strategy, however, has not been formally tested in patients with IBS. The aim of this project is to investigate if glucose can also assist in fructose absorption in patients with IBS who are known to malabsorb fructose.

Investigating children's body image perception and satisfaction in an ethnically diverse population.

Supervisors: Professor Helen Truby
Laura Tirlea

Email: helen.truby@monash.edu

The Children's Body Image Scale (CBIS) was developed in 1999 and was updated in 2008, to link it with newer BMI percentiles for children aged 7–12 years. It remains the only pictorial scale that is derived from children's measured body mass index (BMI), thus enabling body size perception to be mapped against a child's actual BMI. It is unique in its construction and has been widely used to measure children's body image in many studies in Australia, the UK and the USA. The CBIS was developed for a Caucasian population and although there are different scales for males and females, there is demand for the scale to be used in more ethnically diverse groups. The aim of this project is to further develop the CBIS to measure body image perception and satisfaction in an ethnically diverse population of children. To do this, the scale will be revised to make it more acceptable for non-Caucasian children and then will test its acceptability in a community sample of children drawn from different ethnic groups.

Consumer's perceptions of Australian Dietary Guidelines and their influence on food choice

Supervisor: Dr Claire Palermo
Email: claire.palermo@monash.edu

Supervisor: Professor Helen Truby
Email: helen.truby@monash.edu

The Australian Dietary Guidelines provide recommendations about the types and amounts of foods, food groups and dietary patterns. They aim to promote health and well being and prevent diet related disease. There is little evidence on how consumers view these guidelines. The increasing prevalence of nutrition related disease may indicate that they do not influence food and eating behaviour. After a systematic review of the evidence the guidelines have been recently revised (June 2011). This study will explore consumer's perspectives and views of the revised dietary guidelines, specifically about how they help or hinder their food selection. Consumer attitudes and beliefs around the guidelines and whether any key messages are missing will also be explored. A qualitative ethnomethodological (study of social practice) approach using focus groups and in-depth interviews will be used. The findings may be used to inform dietitians and government on more appropriate use of the guidelines to improve the diets of individuals and populations.

Other projects include

- **Identification of sarcopaenic obesity in the older population**
Supervisor: Associate Professor Boyd Strauss
- **Body composition changes following pregnancy**
Supervisors: Associate Professor Boyd Strauss and Dr E McCarthy
- **Vitamin C status in hospital patients**
Supervisor: Dr G Wilcox
- **Potassium source in the diets of the haemodialysis and near end-stage renal failure populations**
Supervisors: Karen Salamon and Judy Tweedie
- **Implementation of evidence based practice to improve nutrition outcomes in people receiving haemodialysis in one of Southern Health's satellite centres**
Supervisors: Janine Engstrom and Mary Anne Silvers
- **Assessment of appetite regulation and energy expenditure in women with and without Polycystic Ovary Syndrome**
Supervisors: Professor Helena Teede and Dr Lisa Moran
- **Assessment of diet and physical activity in Australian women with and without Polycystic Ovary Syndrome: The Australian Longitudinal Women's Health Study**
Supervisors: Professor Helena Teede and Dr Lisa Moran

More information from
Associate Professor Boyd Strauss
Telephone: +61 3 9594 1390
Email: boyd.strauss@monash.edu

Other projects are detailed on the Nutrition and Dietetics website: www.med.monash.edu.au/nutrition-dietetics/bnd-honours.html

6. Surgery

The Department of Surgery (Monash Medical Centre) offers research projects centred around both the laboratory and clinical domains, which ultimately aim to improve our understanding and the practice of surgery. Students with special surgical interests are invited to discuss these with Professor Julian Smith.

1. Surgical anatomy projects

Supervisor: Professor Julian Smith

Location: Department of Surgery,
Monash Medical Centre

Telephone: 9594 5500

Email: julian.smith@monash.edu

Description

Projects are available within all the surgical disciplines to explore the anatomical basis of surgical conditions and of the practice of surgery. Examples include:

- Studies of regional anatomy relevant to surgery
- Studies of regional anatomical variations relevant to surgery
- Methods of teaching and of learning of surgical anatomy

Projects may be conducted in association with the Department of Anatomy and Cell Biology. There may be a dissection, investigational and/or clinical basis to each of these projects.

2. Respiratory medicine and thoracic surgery projects

Supervisor: Professor Phil Bardin

Location: Department of Surgery,
Monash Medical Centre

Telephone: 9594 2710

Email: philip.bardin@monash.edu

Description:

The basic science laboratories of our group are located in the Monash Institute of Medical Research (MIMR) and on the Clayton campus of our collaborator Prof David Jans. The laboratories are staffed by predominantly post-doctoral scientists with an interest in respiratory disease and virology with an emphasis on asthma and COPD. The studies below will provide an entry to laboratory science in a friendly collegial environment with an emphasis on translating basic science to the bedside. Some ongoing projects are listed below:

- Chemokine responses to rhinovirus and RSV infection.
- Allergic sensitisation of airway cells and responses to rhinoviruses and RSV.
- The effect of epithelial cell infection with rhinoviruses on airway fibroblast cells.
- Traffic of rhinovirus and RSV proteins into the cell nucleus and regulation of nuclear transport.
- Cellular transdifferentiation and rhinovirus infection.
- Growth and propagation of lung tissue from surgical resection specimens.

- Growth and propagation of nasal tissue from surgical resection specimens.
- Characterisation of cell growth ex vivo in tissues obtained from surgical specimens.
- Cell death by necrosis and apoptosis in tissue explants generated from surgical specimens.

3. Ophthalmology projects

Supervisor: Dr Marcel Favilla

Location: Department of Surgery,
Monash Medical Centre

Telephone 5990 6185

Email: mfavilla@bigpond.net.au

Description:

The Ophthalmology Unit is the second largest provider of cataract surgery in Victoria, with the majority of patients managed as day-case surgery at the Cranbourne Day Surgery. The aim of the unit is to provide improved access to surgical care with reduced waiting times, providing care in a resource-efficient model.

The department is interested in a number of health issues related particularly to excellence in care and service delivery, and new models of interdisciplinary care with particular emphasis on the patient outcomes of improved vision, regained independence and enhanced quality of life.

4. Dandenong and District Hospital – general surgery and colorectal surgery projects

Supervisor: Associate Professor Bruce Waxman

Location: Dandenong and District Hospital
Academic Surgical Unit

Telephone 9554 8657

Email: bruce.waxman@monash.edu

Description:

a. Primary prevention of perineal problems: Elective caesarean section for the Primigravida: An informed choice

A combined quantitative and qualitative research project, the former documenting perineal problems of urinary, sexual and defaecatory problems in primigravidas having vaginal delivery vs caesarean section and the latter a combined focus group and questionnaire to survey women's attitudes to being provided information about the potential risk of vaginal delivery and being given a choice of either vaginal delivery or caesarean section.

b. Care of the critically ill surgical patient: Improving junior medical officers communication skills and ability to recognise signs of critical deterioration

A qualitative study analysing the effectiveness of the RACS based CCrISP course and a quantitative analysis of the effectiveness of the course by determining abilities of junior medical officers to assess signs of clinical deterioration. A project combined with the Simulation Centre at the Monash Medical Centre, Moorabbin and RACS.

c. Disaster management and the surgeon

Developing a database and register for surgeons an education and training program and promoting a greater awareness of the Medical Controller's role in DISPLAN, following the aftermath of the Bali Bombings and the Tsunami Disaster Medical Responses, shortcomings have been recognised in the efficiency and response of Australian Medical Teams. The objectives of this project would be to assess the existing disaster management arrangements, develop a database of medical officers, particularly surgeons willing to be deployed and increasing the awareness of medical practitioners of the role of Medical Controller and DISPLAN. A project combined with DISPLAN Victoria.

d. Communication skills and surgeons: Hand over and communications between junior medical staff and consultants

A qualitative study determining the different models of medical hand over between junior medical officers in surgical units and communications with consultants. The project would also evaluate the role of nurse practitioners providing after hours medical cover for junior medical officers.

e. Medical Officers' careers in the Australian Defence Force: Past performance and recruitment potential

A qualitative and quantitative study evaluating the careers and achievements of medical practitioners in the Australian Defence Force and the recruitment potential and particularly the problems of return of service obligation (ROSO). A combined project with the Australian Defence Force.

f. Medical Officers' careers in the Royal Flying Doctor Service: Past performance and recruitment potential

A qualitative and quantitative study evaluating the careers and achievements of five medical practitioners in the Royal Flying Doctor Service and the recruitment potential and particularly the problems of return of service obligation (ROSO). A combined project with the Royal Flying Doctor Service.

g. Pruritus Ani and the effect of incomplete wiping of the anus after defaecation

A quantitative study analysing the wiping habits of a series of volunteers to evaluate the effectiveness of toilet paper wiping, an alcohol based wipe and a bidet on cleansing the perineal skin. It will be combined with a clinical series of patients suffering from pruritus ani and those with incontinence and the effectiveness of wiping the anus after defaecation.

h. Wound infection and colorectal surgery

A quantitative analysis to access the effectiveness of various techniques in reducing wound infection, particularly the use of high inspired oxygen during the operation on wound infection rates. A randomised controlled trial comparing the use of high inspired oxygen in a series of patients having elective colorectal surgery in Southern Health.

i. Gender and outcome of surgery for large bowel cancer

A quantitative analysis of the influence of gender on the prognosis of patients having elective surgery for large bowel cancer and exploring potential hypotheses for the tendency for females to have a better prognosis and how this may influence trials of different treatment regimens in large bowel cancer combined with the Anticancer Council of Victoria and Monash Institute Reproduction & Development.

j. Small bowel obstruction and the role of Gastrograffin meal and follow-through

A quantitative analysis on long term follow up of patients having had small bowel obstruction and gastrograffin meal and follow through as to whether they may develop further small bowel obstructions requiring hospital admissions in the future.

k. Laparotomy, division of adhesions and the use of a physical barrier in preventing subsequent adhesions and managing chronic abdominal pain

A quantitative analysis of patients undergoing surgery before the division of adhesions is only either with small bowel obstruction or chronic abdominal pain and the effectiveness of physical barriers viz. spray gel® and Sefrafilm® in reducing the frequency of admissions to hospital with small bowel obstruction or chronic abdominal pain.

l. Division of abdominal adhesions and the irrigating scalpel: Evaluation of the effectiveness and morbidity associated with the use of the irrigating scalpel

A quantitative study auditing the results of operations using the irrigating scalpel and an evaluation of the physiological basis of its effectiveness. This satellite project will be on the effect of irrigation solutions on rusting of surgical blades.

m. Irrigating anastomosis technique: Evaluation of its effectiveness and morbidity

A qualitative study to assess the use of the irrigating anastomosis technique in increasing the efficiency of suture anastomosis and its effectiveness on anastomotic healing and wound infection. A quantitative audit to evaluate the effectiveness of this technique.

n. Defacatory problems after vaginal delivery

Socially disabling problems arise from pelvic floor injury after vaginal delivery. The advent of physiological measurements of anorectal function has allowed the 52 improved assessment of these difficulties and subsequent planned approach to surgical management. This clinically based project aims to further refine the tools of assessment and monitoring of anorectal dysfunction and its subsequent planned management, and establishment of an education program for women in the child bearing age group.

5. Breast surgery projects

Supervisor: Dr Jane Fox
Location: Monash Medical Centre,
Moorabbin Campus
Telephone: 9594 6122
Email: jane.fox@monash.au

Description:

Breast cancer: Early morbidity after axillary surgery

Supervisor: Dr Jane Fox

This project will prospectively study the effect of axillary dissection with emphasis on the morbidity related to the intercostobrachial nerves and to early lymphoedema, and the importance of patient education.

6. Upper gastrointestinal surgery projects

Supervisor: Mr Stephen Blamey and
Telephone: 9887 8530
Email: sblamey@netspace.net.au

Supervisor: Dr Dan Croagh
Telephone: 0428 121 121
Email: dan.croagh@gmail.com

Location: Monash Medical Centre, Clayton

Description:

- Relief of symptoms following cholecystectomy.
- Quality and value of lymphadenectomy in gastric cancer resection.
- Management of nausea after upper G.I. surgery.
- Management strategies for postoperative infection in G.I. surgery.

7. Cardiothoracic surgery projects

Supervisor: Professor Julian Smith,
Telephone: 9594 5500
Email: julian.smith@monash.edu

Supervisor: Mr Aubrey Almeida
Telephone: 9594 3017
Email: AubreyAlmeida@hotmail.com

Supervisor: Associate Professor Andrew Cochrane
Telephone: 9594 4515
Email: andrew.cochrane@southernhealth.org.au

Supervisor: Mr Adrian Pick
Telephone: 9594 4515
Email: apick1@optusnet.com.au

Description:

1. Robotic cardiac surgery – clinical application, early follow-up of results; robotic, micromanipulation and nanotechnology research in association with the Department of Mechanical Engineering.
2. Cognitive function after cardiac and thoracic surgery – measurement of subtle changes in cognitive function, with a computer based test.
3. ASCTS Victorian Cardiac Surgery Database project – development of a risk adjustment model for outcomes of cardiac surgery and the assessment of other cardiac surgical outcomes.
4. Markers of renal dysfunction after cardiac surgery
5. A comparison of the outcomes of the surgical treatment of atrial fibrillation utilising radiofrequency, cryotherapy or high intensity focused ultrasound
6. Trials of 3f, Medtronic Mosaic and Edwards bioprostheses in the aortic position
7. Minimally invasive lung resections compared with open thoracotomy – evaluation of post-operative pain and quality of life

8. Dental and oral maxillofacial surgery projects

Supervisor: Associate Professor Geoff Quail
Location: Monash Medical Centre, Clayton
Telephone: 9594 5493
Email: geoffrey.quail@monash.edu

Description:

Dental and Maxillofacial Surgery Unit provides a 24-hour service to Southern Health including inpatient and outpatient services and receiving specialist referrals from the primary dental care clinics. It is staffed by specialist consultants, a full-time hospital dental officer and a maxillofacial surgery registrar.

a. Surgical and dental implications of Thalassaemia A Major

Southern Health has the largest cohort of thalassaemia patients in Australia. This study will examine

The prevalence of blood bone and viral infections in patients requiring repeated blood transfusions since infancy.

Jaw bone density in these patients compared with matched controls. Effect of the condition on dental eruption and craniofacial skeletal morphology.

b. Sleep Apnoea therapy

A mandibular advancement splint is an effective non-invasive technique for treating this troublesome condition. This study will assess subjective changes in day time somnolence and alertness and document changes in oxygen saturation through the use of the appliance.

c. Cleft palate condition

Southern Health has one of the largest multidiscipline and busiest cleft lip and palate clinics in Australia. This study will evaluate the nature of congenital defects referred for assessment and management and the stability of palatal expansion prior to alveolar bone grafting, the integrity of the alveolar graft, the effectiveness of pharyngoplasty and patient and parent appreciation of the condition and compliance with treatment.

d. The incidence of cleft lip and palate related to soil contaminants in a Third World Country

9. Ear, nose and throat surgery projects

Supervisors: Mr Douglas Buchanan,
Mr Sarin Wongprasartsuk

Location: Monash Medical Centre,
Moorabbin campus

Telephone: 9707 2777

Email: *sarin.wongprasartsuk@monash.edu*

Description:

Activin and related peptides in burns: Examination of burns tissues and correlation of activin and related peptide levels in the serum of such patients.

Activin and related peptides in head and neck SCC and other malignancies.

Bacterial biofilms – This is in the treatment of chronic ENT infections/over operated sinuses / exposed bone in the nose and ear.

Eustachian tube morphology in the activin gene knockout mice. Examination of Eustachian tube/cleft palate morphology. Samples are already collected and are awaiting processing and analysis.

Efficacy of Coblation Tonsillectomy in children with obstructive sleep apnoea syndrome.

10. Neurosurgery projects

Supervisor: Associate Professor Andrew Danks

Location: Monash Medical Centre, Clayton

Telephone: 9594 2886

Email: *Andrew.Danks@southernhealth.org.au*

Description:

Trial of a novel chemotherapeutic agent in recurrent glioblastoma glioblastoma. This is an international phase 3 study run by a British drug company. The agent is Diphtheria toxin conjugated to the transferrin receptor. This receptor is expressed high level on high grade glioma cells. The agent is infused at a very slow rate into the tumour bed via catheters are already planted surgically.

A prospective randomised study of scalp clips versus artery forceps to maintain haemostasis during craniotomy.

11. Vascular/transplantation surgery projects

Supervisors: Mr Alan Saunder
Email: *alan.saunder@monash.edu*

Supervisors: Mr Ming Kon Yii
Email: *ming.yii@monash.edu*

Location: Monash Medical Centre, Clayton

Telephone: 9594 5503

Description:

Combined kidney and pancreas transplantation for Type I Diabetics with end-stage renal failure

Following kidney and pancreas transplantation, patients have improved renal function and no longer require insulin to control diabetes. The transplanted pancreas may drain into the bladder or small bowel. This study would examine

the differences (clinically, biochemically and immunologically) between these different methods of pancreas transplant exocrine management

Carotid surgery for stroke prevention

Internal carotid artery thromboendarterectomy to prevent strokes in patients with critical stenoses is a high volume procedure in vascular surgery. Complications of stroke, death and cranial nerve damage are markers of the quality of surgery. This study is to audit the outcome of 00 consecutive carotid operations and devise strategies to improve efficiency of this procedure.

Carotid angioplasty and stent

A new technique to treat carotid stenosis requires an endovascular intervention by balloon angioplasty and stenting. An audit of the indications, outcome and complications of the last 25 cases will be conducted.

The effectiveness of different endo-vascular intervention

Major technological advances have obviated the need for peripheral bypass surgery for many patients. We have a long experience in the introduction of new technology to vascular surgery. The aim of this project is to analyse the outcome of percutaneous vascular procedures for occlusive vascular disease at a patient and limb level, particularly with respect to efficacy, durability and cost-effectiveness.

The impact of endosurgery on aortic aneurysm repair

The advent of endovascular technology allows aortic aneurysms to be controlled by percutaneous techniques. This study will analyse pathophysiological and patient perceived differences between endovascular and traditional open surgical techniques of aneurysm repair.

Endoluminal stent graft repair of aortic aneurysms

This project is essentially a review of abdominal aortic aneurysm repair by stent grafting since its inception in late 1994. The main thrust of the project will involve review of all the patients that the vascular unit has been involved in throughout this period of time including patients in the private sector by the same group of surgeons. Apart from general review of the experience over the last 0 years, this project will also analyse various factors such as the use of balloon expandable stents to reduce endo leak proximally, the role of coiling in the reduction of endo leak and downward displacement of the stent graft over time, the effect of internal iliac coiling and risk factors associated with buttock ischaemia and lastly the effects of wide i.e. ectatic iliac arteries with enlarged bottom extension graft.

Varicose vein project

This project involves analysis of all the Doppler ultrasound findings in varicose vein and correlation with the clinical presentation and outcome of surgery.

CT angiogram comparison with digital subtraction angiography in failing arterio-venous fistula for haemodialysis access.

This project is in collaboration with the Renal Unit and the Radiology Unit. This prospective study will include 50 patients recruited fairly quickly. There is very little data from current literature to support the use of CT angiogram in arterio-venous fistula monitoring of failing AV fistula. This study will give us an indication of usefulness of CT in comparison to standard digital subtraction angiography.

CT angiogram comparison with digital subtraction angiography in failing arterio-venous fistula for haemodialysis access

This project is in collaboration with the Renal Unit and the Radiology Unit. This prospective study will include 50 patients recruited fairly quickly. There is very little data from current literature to support the use of CT angiogram in arterio-venous fistula monitoring of failing AV fistula. This study will give us an indication of usefulness of CT in comparison to standard digital subtraction angiography.

12. Intensive Care Unit projects

Supervisor: Associate Professor Geoffrey Parkin
Location: Monash Medical Centre, Clayton
Telephone: 9594 3276
Email: Geoffrey.parkin@southernhealth.org.au

Description:

- The open and closed loop control of water balance.
- The open and closed loop control of the volume state.
- Open and closed loop control of vasodilator and inotropic therapy.
- Measurement of the cardiac output from the airway in intubated patients.
- Ambulant control of the glucose in diabetes mellitus.

13. Orthopaedic surgery projects

Supervisor: Mr Simon Bell
Telephone: 9592 8028
Email: SNBell@bigpond.net.au

Supervisor: Mr Minoo Patel
Telephone: 9429 8084
Email: minoo.patel@monash.edu

Location: Monash Medical Centre, Clayton

Description

- a. **Membrane guided bone regeneration**
Prospective randomised animal study.
- b. **Bone length multiplier**
A long term prospective human observational study.
- c. **Lateral epicondylitis (tennis elbow)**
A human cadaveric, retrospective and prospective human biomechanical study.
- d. **Pronator quadratus compartment syndrome**
A human cadaveric and retrospective study.
- e. **Club foot**
A human retrospective study.
- f. **Perthes disease**
A human retrospective and prospective (multicentre) study.
- g. **Spina bifida**
Establishment of a data base and ongoing analysis.
- h. **Tibial fracture IMN versus TSF**
multicentre prospective human study.
- i. **Growth factors associated with adhesive capsulitis.**
- j. **The effect of the addition of Cortisone to the distension fluid during Hydro- dilatation for adhesive capsulitis.**
- k. **Correlation and validation of shoulder scoring between medical practitioners, physiotherapists and patient self assessment.**

l. **Correlation between the outpatient assessment of patients clinically for power and strength and versus the use of strength measurement devices – shoulder or elbow or knee.**

m. **Rotator cuff**

- Correlation of the response to local anaesthetic for impingement tendinitis and strength testing.
- Correlation of pathology on X-Ray and local anaesthetic response.
- Long term benefits of cortisone.

n. Evaluation of the benefits and costs of pre-operative education for patients undergoing surgery. Comparison of the private and public sector.

o. Efficacy of the pre-emptive injection of Ropivacaine to the operative site given prior to surgery versus prior to or immediately post closure.

p. Efficacy of the use of Parecoxib peri-operatively versus no Parecoxib for post operative pain relief.

q. Evaluation of post operative recuperative support systems for urban versus rural patients.

r. Evaluation of the long term outcome of compensation patients following surgery according to employment classification and other factors.

14. Plastic surgery projects

a. **Neurovascular island flap perfusion study**

Supervisor: Mr John Crook
Location: Southern Health hospital network
Telephone: 9899 6144/0412 001 380
Email: john@johncrook.com

Description:

The concept of vascular flaps has burgeoned since McGreggor first published his axial pattern flap concept last century. Since the advent of microvascular and musculocutaneous flap surgery in the early 1970's work in this field escalated. Behan and Wilson, Taylor et al, O'Brien et al, Crook and Taylor, and Cormack and Lamberty have all defined and re-defined the concept of vascular territories. Now Behan has pioneered neurovascular island flaps in the clinical setting, which has in many cases reduced the need for more complex microvascular surgery. His work has been clinically focused, and the emphasis has always been on solving specific reconstructive conundrums.

This study aims to explain the vascular phenomenon that allow neurovascular islands of tissue to be defined and transferred to create predictable, durable and sensate reconstructions in many areas of the body with a minimum of equipment and within a short operation window.

This is a project that has potential to convert into a higher degree, and will be valuable to anyone interested in pursuing a career in plastic and reconstructive surgery.

14. Plastic surgery projects

b. **Comparative study for small bone fixation**

Supervisor: Mr John Crook
Location: Southern Health hospital network
Telephone: 9899 6144/ 0412 001 380
Email: john@johncrook.com

Description:

A comparative study of all the small bone fixation sets looking at torque strength, load strength, compressive strength, ease of use and overall kit design. The researcher will require assistance from the engineering department and will also need volunteer medical students in order to complete the study, in particular when assessing the ease of use of the particular sets.

This is a well encapsulated project that is easily to design and carry out, and will be valuable to anyone interested in pursuing a career in hand surgery, plastic surgery or orthopaedic surgery.

15. Paediatric surgery projects

Supervisors: Professor Wei Cheng
Email: wei.cheng@monash.edu

Supervisors: Mr Chris Kimber
Email: Chris.Kimber@southernhealth.org.au

Location: Monash Medical Centre, Clayton

Telephone: 9594 4100

Description:

- Fetal cord ligation.
- Laparoscopic splenectomy in children.
- Long term follow-up of neonatal inguinal herniotomy.
- Fetal lung lesions, long term follow-up.
- Antenatal hydronephrosis, does early diagnosis influence outcome.
- Obesity surgery in children.
- Paediatric Surgery Research:
 - Focus on congenital abnormalities, especially the molecular genetics of the hindgut development:
 1. Role of p63 gene in bladder exstrophy
 2. Gli2 mutation in ano-rectal malformation
 3. VATER syndrome

Leaky bladders in babies: lessons from mice

Project Leader: Professor Wei Cheng

Telephone: 9594 5500

Email: wei.cheng@monash.edu

Project Description:

Bladder exstrophy is a congenital disease whereby baby is born with its bladder exposed to the exterior. The affected babies leak urine constantly. Untreated, the exposed bladder develops cancer. This condition requires multiple operations, consultations and life-long follow-up, which is a challenging physically, psychologically and financially to both the patients, the parents and the society at large.

From the inheritance pattern, we speculate that there is a high possibility of genetic abnormality. We are sequencing the DNA of the patients, searching for a specific gene mutation, based on our previous mouse knock-out model. We hope our translational work will help patients in genetic counselling and pave the way for future therapies.

Saving children's lives with opium

Project Leader: Professor Wei Cheng

Telephone: 9594 5500

Email: wei.cheng@monash.edu

Project Description:

Necrotizing enterocolitis is a severe condition affecting premature babies all across the world. Due a temporary lack of oxygen at birth, the baby's gut to suffer from ischaemia/reperfusion injury. The current treatment consists mainly of antibiotics and surgery, after the gut damage has occurred. To prevent such injuries, we have been inspired by polar bears which are capable of surviving ischaemia/reperfusion like condition in winter by hibernation. The agent responsible for lowering the metabolic rate is an endogenous opium. We are testing to use opioids to prevent necrotizing enterocolitis in susceptible babies, with cellular and murine models.

16. Urology projects

Supervisors: Associate Professor Mark Frydenberg

Location: Monash Medical Centre, Moorabbin and Cabrini Hospital

Telephone: 95091109

Email: frydenberg@optusnet.com.au

Description:

Multiple topics available related to prostate cancer including high risk prostate cancer through the analysis of a large patient database

7. Emergency Medicine and Clinical Toxicology

Southern Health and Monash University Emergency Medicine and Clinical Toxicology Research Group Projects for B Med Sci and Honours Students

Contact: Professor Andis Graudins
Location: Emergency Department,
Monash Medical Centre, Clayton
Telephone: 9594 6666
Email: andis.graudins@monash.edu

Background:

The Southern Health Emergency Medicine Research Group is coordinated by Professor Andis Graudins and comprise of medical, nursing and allied health researchers affiliated with the Southern Clinical School of Monash University and the three hospital campuses of the Southern Health Emergency Medicine Program (Monash Medical Centre, Dandenong Hospital and Casey Hospital). Research interests of the group are wide-ranging both in the areas of clinical research in emergency medicine, and toxicology as well as applied basic-science research in various aspects of clinical toxicology.

Specific projects for 2012 Academic year are based at a number of sites. Clinical projects are offered at all of the Southern Health Emergency Departments. Laboratory research is also possible in toxicology research in a dedicated laboratory in the Department of Pharmacology at Monash University, Clayton campus.

Toxicology Projects:

1. Development of an animal model of oral drug toxicity to assess the effectiveness of intravenous lipid emulsion (ILE) therapy in the reversal of cardiovascular toxicity of lipophilic drugs implicated in severe human poisoning.

ILE therapy has been touted as a novel antidote in severe CVS toxicity resulting from lipophilic drug poisoning. Several animal studies have suggested a positive effect when toxins are administered intravenously. Human case report data is not as compelling in the degree of effectiveness of this therapy. Using an established animal model, this project aims to investigate whether the effectiveness of ILE is less significant in a controlled environment of oral poisoning than that seen with intravenous toxin administration utilising a range of drugs implicated in human poisoning.

Site: Toxicology Laboratory in Department of
Pharmacology, Monash Clayton Campus.
Supervisor: Professor Andis Graudins

2. A retrospective review of digoxin poisoning and Digoxin Fab antibody use at Southern Health hospitals

Supratherapeutic digoxin concentrations are not an uncommon finding in elderly patients presenting to the ED with a multitude of medical problems. Many patients exhibit signs of digoxin toxicity. This chart review aims to correlate the incidence of symptomatic patients with elevated digoxin concentrations and define the appropriateness of use of digoxin specific Fab antibodies in patients with increased serum digoxin concentrations and suspected digoxin toxicity.

Site: Emergency Department,
Monash Medical Centre, Clayton, ED
Supervisor: Professor Andis Graudins

Emergency Medicine Projects:

1. Qualitative study on what factors influence patients' decisions to present to the Emergency Department (ED) with Stroke.

The treatment time to maximize survival or morbidity from acute stroke is known as the door to thrombolysis time, which measures the time it takes for the occluded artery to be opened up by the administration of tissue plasminogen activator, a thrombolytic agent. This time frame is less than 4.5 hours. From previous research it has been shown that only a small proportion of patients present to the ED within this time frame. In this study we will interview people when they arrive in the Emergency Department and determine what key decisions the patient and/or their family made prior to arrival and what influenced the decisions they made. This data will support a wider range of research we are undertaking with the National Foundation to evaluate and inform behavior of patients having a stroke.

Contact: Andis Graudins
Supervisors: Professor George Braitberg and
Associate Professor Ian Mosely
Site: Emergency Department,
Monash Medical Centre Clayton ED.

2. The development and implementation of a 'real time' adverse event monitoring system in the emergency department.

The Emergency Department, with its large undifferentiated patient load, high staff numbers with varying levels of experience, long hours and frequent interruptions is likely to have the highest rate of adverse events within a hospital. Despite this concern, research in ED adverse events is lacking, which means that evidence based planning of corrective interventions is almost impossible. The development of an adverse event monitoring system will be followed by appropriate data analysis and preparation of a report which will explore the nature of some possible interventions to reduce identified types of adverse events.

Contact: Andis Graudins.
Supervisor: Dr Robert Meek/ Professor Andis Graudins
Site: Dandenong Hospital ED

3. Evidence-based analgesia in the emergency department:

A. An assessment of intranasal ketamine as primary analgesia for adults with moderate to severe pain in the ED – a prospective observational study

Ketamine is a potential alternative analgesic agent to opioids in moderate to severe pain. To date, there is little controlled evidence assessing the efficacy of ketamine in emergency department acute pain scenarios. This project utilises sub-anaesthetic doses of intranasal ketamine in an assessment of reduction of pain scores and patient satisfaction in adult patients with moderate to severe pain.

Contact: Andis Graudins
Supervisors: Professor Andis Graudins
Dr Diana Egerton-Warburton
Associate Professor Ed Oakley
Site: Adult Emergency Department,
MMC, Clayton.

B. Intranasal ketamine in paediatric musculoskeletal injury pain – dose-finding study

Ketamine is a potential alternative analgesic agent to opioids in moderate to severe pain. To date, there is little controlled evidence assessing the efficacy of ketamine in emergency department acute pain scenarios. In paediatric patients, the optimal dose of intranasal ketamine resulting in analgesia without marked sedation is not well characterised. This study utilises an observational sequential dose-finding methodology in assessing the most effective dose of IN ketamine not resulting in sedation in moderate to severe musculoskeletal pain in the ED.

Contact: Andis Graudins
Supervisors: Professor Andis Graudins
Associate Professor Ed Oakley
Dr Diana Egerton Warburton
Site: Paediatric Emergency Medicine Department,
MMC, Clayton.

C. An assessment of three oral analgesic regimens in the treatment of moderate pain from musculoskeletal injuries in adult patients in the emergency department

Current analgesic guidelines suggest that patients with moderate pain should have an opioid analgesic included in their medication regimen. Oxycodone is suggested over codeine given that it does not need to be metabolised to gain analgesic effectiveness and also because a significant proportion of patients given codeine are poor metabolisers of this drug. However, some studies suggest that many patients respond well to simple analgesia with paracetamol and ibuprofen alone. This study examines the effectiveness of three drug regimens in the treatment of moderate pain in a double-blind randomised controlled fashion.

Contact: Andis Graudins
Supervisors: Dr Alastair Meyer
Professor Andis Graudins
Sites: This is a cross campus study at all three Southern Health emergency departments. Study is based at MMC, Clayton and Casey Hospitals.

Contacts Details

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