STAFF
A/Prof Hilary Warren, NHMRC Senior Research Fellow (2006) and ANU Senior Fellow (2006, 2007), John Curtin School of Medical Research; Visiting Fellow, ANU Medical School; Visiting Research Fellow, The Canberra Hospital
Dr Ron Jackson, (part time 2007)
Mr Joseph Ng, (January 2007 to August 2007)
Dr Neli Azmanova, (August 2007 to December 2007)
Ms Yvonne Gonzalez, (from July 2008)

STUDENTS
Mr Dean Yee PhD student at the John Curtin School of Medical Research, ANU.
A/Prof Hilary Warren as Supervisor (2007) and Co-supervisor (2008) with Dr Mark Hulett (Latrobe University)
Mr Kenny Janes, Honours student 2007 supervised by A/Prof Hilary Warren

COLLABORATIVE ASSOCIATES
Professor Chris Parish, Division of Immunology and Genetics, John Curtin School of Medical Research, ANU
Dr Lauren Wilson, Infectious Diseases Unit, The Canberra Hospital (to August, 2007) and Visiting Fellow, John Curtin School of Medical Research, ANU (to August 2008)
Dr Dipti Talaulikar, Department of Haematology, ACT Pathology, and ANU Medical School

RESEARCH PROJECTS
The research projects in the Cancer Research Unit are focused on the biology of human Natural Killer cells. NK cells are part of the innate immune system and are essential in the early stages of viral infection prior to establishment of antigen specific immune responses. NK cells also kill cancer cells by detecting changes in the level of class I MHC antigens and expression of stress induced molecules. NK cells mediate antibody dependent cell cytotoxicity and are one of the mechanisms by which therapeutic monoclonal antibodies are effective in treating various cancers. Understanding processes that lead to NK cell expansion and migration are relevant to the use of NK cells in therapy of cancer.

Receptors and ligands regulating human natural killer cell (NK) proliferation. HS Warren
Mechanisms underlying human NK cell migration. D Yee, PhD project
Selective NK cell engraftment in NOD/SCID mice. K Janes, Honours project
The interaction between NK cells and cells infected with human coronavirus 229E. HS Warren and L Wilson
Lymphocyte populations in diffuse large B-cell (and other aggressive) non-Hodgkin’s lymphoma. D Talaulikar, HS Warren, C Hawkins, B Shadbolt, M McNiven

FUNDING
2007
National Health and Medical Research Council, Senior Research Fellowship, A/Prof HS Warren, $116,750
National Health and Medical Research Council, Equipment grant, Dr D Linares, Prof C Nolan, Dr N Teoh, Prof G Farrell, A/Prof H. Warren, MicroBeta Microplate scintillation/ luminescence counter, $54,613
The Canberra Hospital Private Practice Fund, A/Prof HS Warren and Dr L Wilson, The interaction between Natural Killer cells and cells infected with human coronavirus 229E. $84,995
2008

The Canberra Hospital Private Practice Fund, Dr D Talaulikar, A/Prof HS Warren, Dr C Hawkins, Dr B. Shadbolt, Ms M McNiven, Lymphocyte populations in diffuse large B-cell (and other aggressive) non-Hodgkin’s lymphoma $28,882

PUBLICATIONS


PRESENTATIONS/ABSTRACTS


Analysis of Heparanase Expression in Human Natural Killer (NK) Cells. Yee DY, Hulett MD and Warren HS. Australasian Society for Immunology 38th Annual Scientific Meeting, Canberra, December, 2008

AWARDS

Yee DY. ASMR Young Investigators Forum, Canberra. June 2007. ASMR Student Member Presentation Prize

Other activities:

A/Prof H Warren

Editorial Board Member: Immunology and Cell Biology

Yvonne Gonzales, Michelle McNiven, Dr Hilary Warren, Dr Dipti Talaulikar, Dean Yee
STAFF
Dr Ahmad Farshid, Interventional Cardiologist
Dr Ian Jeffery, Staff Specialist
Dr Ren Tan, Staff Specialist
Dr Darryl McGill, Staff Specialist
Dr David Coles, Staff Specialist
Dr Simon O’Connor, Visiting Cardiologist
Dr Charles Itty, Cardiology Research Fellow
Dr Ben Jacobson, Cardiology Registrar
Dr Muayad Alasady, Cardiology Registrar
Dr Daniel Sathianathan, Cardiology Registrar
RNs, Cardiology Research
Pearle Taverner, Study Co-ordinator
Paul Marley, PCI Database Co-ordinator
Russell Appeldorff, Study Co-ordinator

RESEARCH PROJECTS
2007–2009
Clinical and Angiographic Predictors of Coronary Artery Disease Progression.
Dr Ahmad Farshid and Dr Daniel Sathianathan. Predictive Value of Echocardiographic Parameters on Cardiovascular Outcomes in Patients with stage 4–5 chronic renal disease (Dr Ahmad Farshid, Dr M Alasady, Dr B Jacobson, and Dr G Talaulikar, Renal Physician 2007–2009)

Reperfusion Arrhythmias in ST Elevation Myocardial Infarction. Dr Ren Tan and Dr Charles Itty
Clinical Trials 2005 to 2009
OAT TRIAL. A clinical trial sponsored by the National Heart, Lung, and Blood Institute of the National Institutes of Health to test the hypothesis that opening occluded coronary arteries 3-28 days after myocardial infarction with EF<50% or proximal coronary occlusion will reduce the occurrence of death, class IV congestive heart failure requiring hospitalisation and recurrent MI by 25% during a 3 year follow-up. This center has enrolled 3 patients. The study commenced in August 2001 and is still ongoing in the follow-up stage. The results have been published; N Engl J Med. 2006 Dec 7;355(23):2395–407

ACUITY STUDY. A randomised comparison of Bivalirudin versus Clexane in patients undergoing early invasive management for acute coronary syndromes without ST-segment elevation sponsored by the Medicines Company. This study commenced in February 2004 and completed in Jan 2007. This centre has recruited 20 patients. Published results; Lancet. 2007 Mar 17;369(9565):907–19

APEX STUDY. A multicenter, randomised, double-blind, parallel-group, placebo-controlled study of Pexelizumab in patients with Acute Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. Procter and Gamble Pharmaceuticals sponsor this study. This study commenced in September 2004 and completed in May 2007. There were 14 patients recruited in this study. Published results: JAMA. 2007 Jan 3;297(1):43–51

HAT STUDY. Home Automatic External Defibrillator (AED) Trial. The aim of the study is that a simply employed strategy of providing an AED for home use will improve survival beyond that achieved from the typical lay response to sudden cardiac arrest. Study population will involve select post-myocardial infarction patients at risk for sudden cardiac arrest (anterior myocardial infarction). This study is sponsored by Seattle Institute for Cardiac Research. This centre has recruited 39 patients. The study commenced in December 2002 and was completed in November 2007. Published results: N Engl J Med. 2008 Apr 24;358(17):1793–804

TRANSCEND STUDY. A large, simple, randomised, double-blind, multicentre, international trial comparing the effects of Telmisartan with placebo on outcomes in patients at high risk for cardiovascular events and intolerant of ACE1. 5 patients recruited. These two studies commenced in October 2001 and completed in June 2008. Published results: Lancet. 2008 Sep 27;372(9644):1174–83

ACACIA Registry. To identify the current management of Acute Coronary Syndromes Australia-wide at admission to hospital, during the in-patient stay and at discharge and 6 and 12 months post discharge. We enrolled 64 patients from Nov 2005 till May 2006. The study was published in 2007 in the Internal Medicine Journal, Volume 37, p741–748

I-PRESERVE STUDY. Irbesartan in Heart Failure with Preserved Systolic Function. The I-Preserve study is an evaluation of the effect of the angiotensin II receptor blocker, irbesartan versus placebo in reducing mortality and cardiovascular morbidity in subjects with heart failure with preserved systolic function. The study commenced in July 2002 and this centre has recruited 2 patients and the study was completed in December 2008. Sanofi-Aventis sponsors Published results: N Engl J Med. 2008 Dec 4;359(23):2456–67

ORIGIN STUDY. A Multicenter, International, Randomized, 2x2 Factorial Design Study to Evaluate the Effects of Insulin Giargine Versus Standard Care, and of Omega-3 Fatty Acids Versus Placebo, in Reducing Cardiovascular Morbidity and Mortality in High Risk People With Impaired Fasting Glucose, Impaired Glucose Tolerance of Early Type 2 Diabetes Mellitus. Aventis Pharma sponsored this study. The study commenced in January 2004 and is still ongoing. There are 4 patients in the follow-up phase.

Champion Study. A Clinical Trail Comparing Cangrelor to Clopidigrel in Subjects who Require Percutaneous Coronary Intervention. It commenced in July 2006 and is ongoing. It has currently 14 patients enrolled. Follow-up phase will commence in March 2009.

ROCKET STUDY. A Study to demonstrate that Rivaroxiban is non-inferior to warfarin in the prevention of the composite endpoint of stroke and non-CNS systemic embolism in subjects with non-valvular atrial fibrillation. It commenced in June 2007 and is still ongoing. It has currently has 3 patients enrolled.

TRACER STUDY. A Study designed to address the effects of SCH 530348 when administered in addition to the standard of care for a minimum of 1 year in subjects with documented atherosclerotic disease and symptoms of acute coronary syndrome. It has just commenced in July, 2008, currently 6 patients.

FREEDOM STUDY. A Study to evaluate whether percutaneous coronary intervention (PCI) with drug-eluting stenting PCI/DES is more or less effective than the existing standard of care, coronary artery bypass surgery (CABG). It commenced in August 2006, and it is still ongoing. There are 9 patients enrolled.

DAL-OUTCOMES. A Study to evaluate the effects of Dalcitrapiol on cardiovascular risk in stable CHD patients with a recent ACS. Recruiting phase 12 patients enrolled.

ICE Study. International collaboration on Endocarditis Prospective Cohort Study of Infective endocarditis, awaiting final ethics approval.

ANTS Registry. Registry collecting data stent thrombosis: Australian Network for Thrombosis in Stents-ongoing.

STABILITY TRIAL. A clinical Outcomes Study of Darapladib versus Placebo in patients with Chronic CHD to compare the incidence of Major Adverse Cardiovascular Events. Awaiting study medication arrival.

Atmosphere. A study to evaluate the efficacy and safety of both aliskiren monotherapy and aliskiren/enalapril combination therapy compared to enalapril monotherapy, on morbidity and mortality in patients with chronic heart failure. Awaiting ethics approval.

Research projects conducted in Cardiology Department 2007 to 2009

6 Month Post Ptca Follow-Up. Commenced In January 2001 and is ongoing. P Marley RN, P Taverner RN, Dr A Farshid

Xience Stent Project: Safety and Efficacy of Xience V Drug eluting Stent, P Marley RN, Dr Ahmad Farshid

Prevention of Contrast Induced Nephropathy Using rotational coronary Angiography, Dr M Alasady, Dr A Farshid, Craig Lawlor RN. Infective Endocarditis, Dr M Alasady, Dr D Sathianathan, Dr A Farshid, Dr Ian Jeffery, Dr McGill, Dr S O'Connor, Dr D Coles, Dr R Tan

PRESENTATIONS/ABSTRACTS

World Congress of Cardiology 2–6 September 2006 Barcelona:
ST Resolution in Elderly Patients undergoing Primary PCI for STEMI (oral presentation), RP Tan, A Yeung, A Farshid, D Coles, D McGill, S O'Connor, I Jeffery

Comparison of ST Resolution in Primary PCI for Anterior vs Inferior STEMI, RP Tan, A Yeung, A Farshid, D Coles, D McGill, S O'Connor, I Jeffery

Scientific abstracts presented at Cardiac Society of Australia and New Zealand 2007:
Prevention of Contrast Induced Nephropathy Using rotational coronary Angiography. Dr M Alasady, Dr A Farshid, Craig Lawlor RN
Infective Endocarditis in the Elderly. Dr M Alasady, Dr D Sathianathan, Dr A Farshid, Dr Ian Jeffery, Dr McGill, Dr S O'Connor, Dr D Coles, Dr R Tan

Clinical Re-Stenosis. Our experience at The Canberra Hospital, Dr C Allada, Dr Coles, Dr A Farshid, Dr I Jeffery, Dr D McGill, Dr S O'Connor, Dr R Tan

FUNDING

Clinical Trials: Pharmaceutical Sponsors; NHLBI(National Health Lung & Blood Institute
Cardiology Department Special Purpose Account. Private Practice Fund, The Canberra Hospital

PUBLICATIONS

A Novel ultra-thin bare metal stent (BMS): results from a worldwide registry. Dr A Farshid and the Principal investigators from the Matsuri Trial

STAFF

Dr Walter Abhayaratna, Director Clinical Trials Unit, Staff Specialist in Cardiology, Senior Lecturer in Medicine, Australian National University

Ms Katherine Johnson, Manager Clinical Trials Unit

Ms Christine Brown, Senior Cardiac Research Sonographer

Ms Anthea Oon, Clinical Trials Coordinator

Mr David Larkin, Clinical Trials Coordinator

Ms Karen Gravenmaker, Clinical Trials Coordinator

Ms Kate Hayes, Research Coordinator

Mr Luke Cartwright, Trainee Cardiac Sonographer

Ms Jo Horn, Clinical Trials Coordinator

Ms Marilyn Hines, Clinical Trials Coordinator

Ms Maree White, (Nursing) Clinical Trials Coordinator

Ms Wendy Frylink, Administrative Service Officer

Ms Tarryn Albrecht, Administrative Service Officer

Ms Catherine Knight-Agarwal, Dietician

Ms Mari Eronen, Dietician

Mr Kym Smith, Cardiac Sonographer
COLLABORATIVE ASSOCIATES

Associate Professor Christopher Nolan, Senior Endocrinologist, ANU Medical School

Associate Professor Dennis Wilson, Endocrinologist, Clinical Director of Endocrinology/Consultant, Principal Investigator

Associate Professor Christian J Lueck, Head, Department of Neurology, Canberra Hospital, ANU Medical School

Associate Professor Marc Budge, Director, Department Aged Care and Rehabilitation Services, Canberra Hospital, ANU Medical School

Dr Wichat Srikusalunukul, Department of Aged Care and Rehabilitation Services, ACT Health

Associate Professor Mark Hurwitz, Director Thoracic Medicine, Canberra Hospital, ANU Medical School

Professor Francis J Bowden, MBBS Director Canberra Sexual Health Centre, Staff Specialist in Infectious Diseases, Professor of Medicine, Australian National University

Dr Marian Currie, Research Program Manager AUIM Research Manager, Academic Unit of Internal Medicine, Canberra Hospital

Dr Doug Taupin, Gastroenterology Unit, Canberra Hospital, Visiting Fellow ANU Medical School

Prof Richard Telford, ANU College of Medicine, Biology & Environment

Dr Steven Yew, Renal Medicine Department, Canberra Hospital

Dr Girish Talaulikar, Renal Medicine Department, Canberra Hospital

A/Prof Paul Pavli, Gastroenterology Unit, Canberra Hospital

Dr Jay Govind, Occupational and Pain Medicine

Dr Satoru Sakuragi, Okayama University, Japan, Postdoctoral Fellowship

RESEARCH PROJECTS

A5351022
Investigators: A/Prof Chris Nolan
1 year, randomised, double blind, placebo controlled, Phase 3 study to evaluate the efficacy and safety of CP-945,598 in the treatment of overweight, oral agent-treated subjects with Type 2 diabetes mellitus.

Abadacept UC
Investigators: A/Prof Paul Pavli
Phase II Multi-centre Randomized Placebo Controlled Study to evaluate the Clinical Efficacy and Safety of Induction Maintenance Therapy with Abatacept in Subjects with Active Ulcerative Colitis who have had an Inadequate Response and/or Intolerance to Medical Therapy.

Abadacept CD
Investigators: A/Prof Paul Pavli
Phase III Multi-centre Randomized Placebo Controlled Study to evaluate the Clinical Efficacy and Safety of Induction Maintenance Therapy with Abatacept in Subjects with Active Crohn’s Disease who have had an Inadequate Clinical Response and/or Intolerance to Medical Therapy.

Acute Pancreatitis
Investigators: Dr Doug Taupin
Randomised, controlled trial of serum lipase versus clinical assessment in the establishment of oral refeeding in Acute Pancreatitis.

Advance
Investigators: A/Prof Chris Nolan
Factorial, randomised trial of blood pressure lowering with a fixed low-dose perindopril-indapamide combination and intensive glucose control with a modified-release gliclazide-based regimen for the prevention of vascular disease among high risk individuals with Type 2 diabetes.

Asphelia
Investigators: A/Prof Paul Pavli
Single Dose-Escalation Randomized, Double-Blind Placebo-Controlled, Trial of ASP1002 (Trichuris suis Ova[TSO]) Therapy in Patients with Mild to Moderately Active Crohn’s Disease.
ASPREE/BIOBANK
Investigators: Dr Walter Abhayaratna, A/Prof Marc Budge
A double-blind, randomized, placebo-controlled primary prevention trial designed to assess whether daily active treatment of 100mg enteric-coated aspirin will prolong life, free of dementia or significant persistent physical disability, in healthy participants aged 70 years and above.

ENVIS-ion
Investigators: A/Prof Marc Budge
Aspirin for the prevention of cognitive decline in the Elderly: a Neuro-Vascular Imaging Substudy from ASPREE.

BC20779
Investigators: A/Prof Chris Nolan & A/Prof Dennis Wilson
Multicenter, double-blind, randomized, placebo-controlled, dose ranging phase 2 study to investigate efficacy, safety, tolerability and pharmacokinetics of the DPP-IV inhibitor RO4876904 in patients with type 2 diabetes.

Begin
Investigators: A/Prof Christian Lueck
Betaferon treatment and Exercise Gathering in early Multiple Sclerosis.

Canberra Heart Study
Investigators: Dr Walter Abhayaratna
Primary aim: Initiated in 2002, this cohort study will re-assess over 1300 subjects.

CHIPS
Oral ivermectin versus topical treatment for pediculosis capitis (head lice) in primary school students: a pilot study.
Investigators: Professor Francis J Bowden, Associate Professor Graham Reynolds, Dr Marian J Currie and Professor Nicholas Glasgow.
Primary aim: To measure the feasibility of administering oral ivermectin in the treatment of head lice in a cohort of primary school students in the Australian Capital Territory (ACT).

CogniMS
Investigators: A/Prof Christian Lueck
Multi-centre, multinational observational study.
Primary aim: Observes cognition in relapsing-remitting MS patients to predict course of MS and testing Betaferon as a treatment.
CSL Flu
Investigators: Dr Walter Abhayaratna
A Phase IV, Randomized, Observer-Blind, Placebo-Controlled, Multi-Centre Study to Evaluate the Efficacy, Safety and Tolerability of CSL Limited’s Influenza Virus Vaccine in Adults aged >18 to < 65 years.

Direct
Investigators: A/Prof Dennis Wilson
3 Protocols in 1 trial:
1. (SH-AHM-0045/EC556) Effects of candesartan cilexetil (candesartan) on diabetic retinopathy in Type 1 diabetic patients without retinopathy.
2. (SH-AHM-0046/EC557) Effects of candesartan cilexetil (candesartan) on diabetic retinopathy in Type 1 diabetic patients with retinopathy.
3. (SH-AHM-0047/EC558) Effects of candesartan cilexetil (candesartan) on diabetic retinopathy in Type 2 diabetic patients with retinopathy.

HSV
Investigators: A/Prof Frank Bowden
Double-blind, randomised, controlled study to evaluate the immunogenicity and safety of herpes simplex candidate vaccine (gD2-AS04) in healthy HSV seronegative and seropositive female participants aged 10–17 years.

LOOK
Lifestyle of Our Kids Study
Investigators: Dr Walter Abhayaratna, Dr Richard Telford

Navigator
Investigators: A/Prof Chris Nolan
Multinational, randomised, double-blind, placebo-controlled, forced-titration, 2x2 factorial design study of the efficacy and safety of long-term administration of long-term administration of nateglinide and valsartan in the prevention of diabetes and cardiovascular outcomes in subjects with impaired glucose tolerance (IGT).

Options
Investigators: A/Prof Chris Nolan & A/Pros Dennis Wilson
Phase IIb, randomised, double-blind, placebo-controlled study to assess the efficacy, safety and tolerability of 24 weeks treatment with different doses of AOD9604 tablets on weight loss in obese adults.
PATH Through Life: Mid-Life Cardiovascular Substudy
Investigators: Dr Walter Abhayaratna
Characterizing the Interrelationships between Central and Brachial Blood Pressure, Arterial Stiffness, Left Ventricular Function and Cognition.

Perform
Investigators: A/Prof Christian Lueck
Prevention of cerebrovascular and cardiovascular events of ischaemic origin with terutroban in patients with a history of ischaemic stroke or transient ischaemic attack. An international, randomised, double-blind, two parallel group study comparing terutroban 30mg once daily versus aspirin 100mg once daily administered orally for a 3 year mean duration (event driven trial).

Reassure
Investigators: A/Prof Chris Nolan & A/Prof Dennis Wilson
A randomised, double blind, placebo controlled, parallel-group, fixed dose, rimonabant (20mg), multicentre study on HbA1c in overweight or obese patients with type 2 diabetes not adequately controlled on two oral antidiabetic agents.

Investigator: Dr Jay Govind
A randomised, controlled trial, to evaluate the effectiveness of transforminal and other injections with five groups to test three therapeutic agents (steroids, local anaesthetic, normal saline) in the treatment of Sciatica.

Voluntary Kidney Donor Study
Investigators: Dr Stephen Yew, Dr Girish Talaulikar & Dr Walter Abhayaratna
A study to evaluate the cardiovascular risk in voluntary kidney donors with post-donation glomerular filtration rate (eGFR) < 60ml/min compared to age and sex matched controls (with eGFR of > 60ml/min) and to persons with stage 3 chronic kidney disease (eGFR 30-60 ml/min).

Tiotropium
Investigators: Dr Mark Hurwitz
Randomised, double-blind, placebo-controlled, parallel-group, efficacy and safety comparison of one-year treatment of two doses (5mcg and 10mcg) of tiotropium inhalation solution delivered by the Respimat Device in patients with Chronic Obstructive Pulmonary Disease (COPD).

UCB 085
Investigators: Dr Paul Pavli
A phase IIIb, multinational, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of certolzumab pegol, a pegylated Fab’ fragment of a humanized anti-TNF-alpha monoclonal antibody, administered subcutaneously at week 0, 2 and 4 in subjects with moderately to severely active Crohn’s disease.

UCB 088 (following study from UCB 085)
Investigators: Dr Paul Pavli
A phase IIIb, multinational, open-label, follow-on trial to C87085 designed to assess the long-term safety of certolzumab pegol, a pegylated Fab’ fragment of a humanized anti-TNF-alpha monoclonal antibody, administered at 0, 2 and 4, and then every 4 weeks thereafter, in subjects with moderately to severely active Crohn’s disease who have participated in study C87085.
Heparanase proteins in type 1 diabetes (A/Prof JD Wilson, Dr C Simeonovic, Ms Catherine Priest, ANU MBBS student)

Type 1 diabetes is an autoimmune disease in which autoreactive T lymphocytes and other insulitis leukocytes infiltrate the islets of Langerhans and destroy the insulin-producing beta cells. For extravasation and invasion into tissues immune cells deploy a range of degradative enzymes such as heparanase and matrix metalloproteinases to migrate through the subendothelial basement membrane. Previous studies in mice have shown that islets are especially enriched in heparan sulphate, the substrate for heparanase, and that heparanase plays a critical role in the autoimmune destruction of islet beta cells and the development of type 1 diabetes.

A flow cytometry assay was developed for the quantitative assessment of intracellular heparanase protein in human peripheral blood lymphocytes. Using this assay no significant differences were found between levels in normal controls, type 1 patients at onset or after several years of disease. Qualitative and quantitative differences in active heparanase in these cells will now be examined using western blotting analysis.

Vitamin D Deficiency In Pregnancy – a pilot study (Dr S Perampalam, A/Prof C Nolan, A/Prof P Hickman)

The aims of this study were to determine the prevalence of vitamin D deficiency in pregnant women attending antenatal clinics at The Canberra Hospital and to evaluate the effectiveness of vitamin D supplementation in pregnancy using the current guidelines. The last aim was to determine the effect of maternal vitamin D status on infants’ birth weight, length and head circumference. The Canberra Hospital Endocrinology team and an ANU medical student are engaged in this project. The project is underway and we have successfully recruited about 50 participants.

Clinical Trials (A/Prof JD Wilson, Ms Juliet Langridge, Ms Elaine Slater)

Increasing interest in the past few years in different means for treating patients with type 2 diabetes has led to trials with agents such as Liraglutide which increases the insulin response to meals. There have also been trials of agents such as Sitagliptin to enhance the action of naturally occurring hormones which have this action.

Liraglutide Effect and Action in Diabetes (LEAD-2)

Effect on glycaemic control after once daily administration of Liraglutide in combination with metformin versus metformin and glimepiride combination therapy in subjects with type 2 diabetes.

Patients were entered into a six month double-blind double-dummy randomised active control parallel-group multicentre multinational trial with an 18 months trial extension period. This was one of a group of trials with this agent.
These have been successfully completed and the agent is being considered for listing for the treatment of type 2 diabetic patients in the USA and Europe.

Co-administration of Sitagliptin and metformin in patients with type 2 diabetes.

Patients with inadequate glycaemic control were recruited to a one year multicentre, randomised, double-blind factorial study with a one year extension. This was one of a suite of studies with this agent which have been completed and Sitagliptin is now approved for prescription to patients with type 2 diabetes in Australia. We are currently taking part in a follow up related study using Sitagliptin in a combined tablet with pioglitazone. This is a phase 1, double-blind, randomised, placebo controlled clinical trial to study the safety, efficacy and mechanism of action of Sitagliptin and pioglitazone in patients with type 2 diabetes mellitus who have inadequate glycaemic control on diet and exercise.

L2T3 and Basal Plus

There is continuing interest in the optimal way to use the available insulin preparations. Patients were entered into a multicentre, multinational, randomised open-label comparative parallel-group study of target glycaemic control and the incidence of documented symptomatic hypoglycaemia in insulin naive subjects with type 2 diabetes failing on oral hypoglycaemic agents and treated with either Lantus or Levemir insulin (L2T3). This trial is completed and another one assessing the efficacy and safety of a basal plus regimen with insulin glargine and insulin glulisine in type 2 diabetes in everyday practice is recruiting (Basal Plus).

Inhaled pre-prandial human insulin with the AERx iDMS plus glimepiride versus rosiglitazone plus glimepiride in type 2 diabetes.

This was a 26-week open-label, multicentre, randomised, parallel trial to investigate safety and efficacy. While a lot of effort went into this and related trials of inhaled insulin in type 1 diabetes, the AERx device was eventually withdrawn worldwide as commercially non-viable.

Satavaptan

One trial in hyponatraemia was investigated. This was a double-blind, randomised, placebo controlled, multicentre study evaluating the efficacy and safety of two doses of satavaptan versus placebo in patients with dilutional hyponatraemia due to the syndrome of inappropriate anti-diuretic hormone secretion. Endocrinology had increasing concerns about this agent which is an ADH receptor blocker. Subsequently the trial was abandoned.

Involvement in three diabetes trials continued in association with the Clinical Trials Unit. The DREAM (Diabetes reduction assessment with ramipril and rosiglitazone medication) trial was completed and showed very little after the drugs were washed out. The DIRECT trial (Diabetic retinopathy candesartan trial) was also completed and showed some benefit in terms of prevention of retinopathy in type 1 diabetes but little effect on its progression. The NAVIGATOR (Nateglinide and Valsartan in impaired glucose tolerance outcomes research trial) trial continues into 2009.

FUNDING

2007

$50,000 The Canberra Hospital Private Practice Fund. A/Prof J Dennis Wilson, Prof Chris Parish and Dr Charmaine Simeonovic

Heparanase as a target for Type 1 Diabetes treatment.

2008

$13,000 (Approximately). The Canberra Hospital Private Practice Fund. Dr Sumathy Perampalam, A/Prof Chris Nolan and A/Prof Peter Hickman. Vitamin D Deficiency in Pregnancy – a pilot study.

PUBLICATIONS

Transient transmission of porcine endogenous retrovirus (PERV) to fetal lambs after pig islet tissue xenotransplantation, Popp, SK; Mann, DA; Milburn, PJ; Gibbs, AJ; McCullagh, PI; Wilson, JD; Tonjes, R. and Simeonovic, CJ (2007), Immunology and Cell Biology, 85, 238–248
Cushing’s syndrome in a diabetic clinic population, Newsome, S; Chen, K; Hoang, J; Wilson, JD; Potter, JM; Hickman, PE (2008), Internal Medicine Journal, 38, 178-182

Research Update – Sitagliptin and other Gliptins, Wilson, JD (2007), Diabetes Management, 20, 6

PRESENTATIONS/ABSTRACTS


CANBERRA HOSPITAL

Endocrinology and Diabetes Research Group

STAFF

A/Prof Christopher J Nolan, Head Endocrinology and Diabetes Research Group and Senior Specialist, Endocrinology, Canberra Hospital, A/Prof ANU Medical School
Dr Alexandra Funkat, Postdoctoral Scientist
Dr Paula Maña, PharmD, Postdoctoral Scientist
Ms Kavitha Kugathas, Laboratory Technician
Ms Lorraine Elkerbout, Laboratory Technician
Ms Stephanie Cheung, Laboratory Technician

Dr Leili Madad, MSc Student, ANU
Ms Amie Rieseberg, Medical Student, ANU
Mr Milan Radojevic, Medical Student, ANU
Ms Rushanthi Pereira, Medical Student, ANU
Ms Anne-Gaelle Bedhet, Health Science Student, French Exchange Program
Ms Virginie Cogneras, Health Science Student, French Exchange Program

STUDENTS

Dr Luis Socha, PhD Student, Awarded Degree-Dec 2007, ANU
Dr Arjuna Pathmaperuma, PhD Student, ANU
Ms Jee-Hye Kim, PhD Student, ANU

COLLABORATIVE ASSOCIATES

ACT

Prof Geoff Farrell, Liver Research Group, Canberra Hospital
Prof Jane Dahlstrom, Anatomical Pathology, Canberra Hospital
Prof David Ellwood, Fetal Medicine Unit, Canberra Hospital

Jee-Hye Kim, Leili Madad, Associate Professor Chris Nolan, Arjuna Pathmaperuma
RESEARCH PROJECTS

Biochemical basis of islet-beta cell compensation and failure in normal pregnancy and gestational diabetes melitus.

A/Prof Christopher Nolan. Gestational diabetes develops due to failure of beta-cell adaptation to the insulin resistance of pregnancy. This NHMRC funded project is focussed on the molecular/biochemical mechanisms of beta-cell compensation processes in normal pregnancy and beta-cell failure in gestational diabetes within rodent models.

Glucolipotoxicity in the Pathogenesis of Diabetic Fetopathy.
A/Prof Christopher Nolan, Prof Jane Dahlstrom, Prof David Ellwood, A/Prof Alison Kent. Diabetic pregnancy is associated with disordered lipid as well as glucose metabolism. This collaborative project between the Canberra Hospital Departments of Endocrinology, Anatomical Pathology, Fetal Medicine and Neonatology is investigating the importance of interaction of hyperglycaemia and hyperlipidaemia in the development of fetal abnormalities in diabetic pregnancy. Initial studies have focussed on effects of elevated glucose, elevated fatty acids and the combination of both on trophoblast cells isolated from human placenta.

Mechanisms of disordered hepatic lipid partitioning in non-alcoholic steatohepatitis.

Prof Geoff Farrell and A/Prof Christopher Nolan. The Liver Research Group and Endocrinology and Diabetes Research Groups are collaborating at both the basic and clinical science levels on the factors that determine the development of non-alcoholic steatohepatitis in obesity and type 2 diabetes.

Non-immune islet β-cell susceptibility factors in the NOD mouse model of type 1 diabetes.
A/Prof Christopher Nolan and Prof Christopher Goodnow. This work is funded by a NHMRC and the Juvenile Diabetes Research Foundation Special Program Grant in Type 1 Diabetes with collaborators at the Garvan Institute. Drs Shane Grey, Jenny Gunton, Trevor Biden, Ross Laybutt and the University of Melbourne Department of Medicine, Dr Sofianos Andrikopoulos. Non-immune islet β-cell susceptibility factors may contribute to the initiation of β-cell damage and triggering of autoimmune attack in the pathogenesis of type 1 diabetes (T1D). This hypothesis is supported from data generated by the work of Dr Luis Socha during his PhD candidature. Determination of these factors may lead to novel preventative strategies for subjects at risk of developing T1D. The aim of this project is to determine non-immune islet β-cell susceptibility factors in the NOD mouse model of T1D.

CLINICAL TRIALS (NATIONAL & INTERNATIONAL MULTICENTRE):

2005–2008

ADVANCE (Action in Diabetes and Vascular Disease), Institute for International Health, Sydney NSW Nolan CJ, Principal Investigator, Canberra, ACT Site.
2005–2007

OPTIONS (Obesity Protocol Targeting an Investigational Option for a New Weight Loss Solution), Metabolic Pharmaceutical Limited, Melbourne, Australia Nolan CJ, Principal Investigator, Canberra, ACT Site.

2007–2008

Pfizer Protocol A5251022.
A 1-year, randomized, double-blind, placebo-controlled phase 3 study to evaluate the efficacy and safety of CP-945,598 in the treatment of overweight, oral agent-treated subjects with Type 2 Diabetes. Nolan CJ, Principal Investigator, Canberra, ACT Site.

Roche Protocol BC20799.
Multicentre, double-blind, randomized, placebo-controlled, dose ranging phase 2 study to investigate efficacy, safety, tolerability and pharmacokinetics of the DPP-IV inhibitor RO4876904 in patients with Type 2 Diabetes (BC20779). Nolan CJ, Principal Investigator, Canberra, ACT Site.

2007–2009

REASSURE
A randomized, double blind, placebo controlled, parallel-group, fixed dose, Rimonabant (20 mg), multicentre study on HbA1c in overweight or obese patients with type 2 diabetes not adequately controlled on two antidiabetic agents. Nolan CJ, Principal Investigator, Canberra, ACT Site.

2008–2010

Novo Nordisk Protocol NN304-1687.
A randomised, parallel-group, open-labelled, multinational trial comparing the efficacy and safety of insulin detemir (Levemir®) versus human insulin (NPH insulin), used in combination with insulin aspart as bolus insulin, in treatment of pregnant women with type 1 diabetes. Nolan CJ, Principal Investigator, Canberra, ACT Site.

FUNDING

2006–2007

Nolan C, Ellwood D The Canberra Hospital Private Practice Major Grant. Glucolipotoxicity in the Pathogenesis of Diabetic Fetopathy. $86,000 per annum for 2 years

2007–2009

Nolan CJ NHMRC Project Grant. Biochemical basis of islet-beta cell compensation and failure in normal pregnancy and gestational diabetes mellitus. $154,000 per annum for 3 years

Farrell G and Nolan CJ. NHMRC Project Grant. Mechanisms of disordered hepatic lipid partitioning in non-alcoholic steatohepatitis. $146,000 per annum for 3 years

2008–2012

Grey S, Andrikopoulos S, Biden T, Gunton J, Laybutt R, Nolan C NHMRC/JDRF Special Program Grant in Type 1 Diabetes. β-Cell Mass and Function in Type 1 Diabetes and Islet Transplantation. $607,550 per annum for 5 years

PUBLICATIONS


**PRESENTATIONS/ABSTRACTS**


Kugathas, K, Le-Picard, A, Pathmaperuma, A, Funkat, A, and Nolan, CJ. Overweight but normal glucose tolerance in the offspring of pregnant rats that have gestational diabetes mellitus. *Australasian Diabetes in Pregnancy Society Annual Scientific Meeting.* 2007


Nolan CJ. Failure of islet beta-cells to compensate in the pathogenesis of gestational diabetes and type 2 diabetes. *Concord Hospital, Endocrinology Unit, Sydney, NSW.* 2007


Nolan CJ. Importance of intrinsic beta-cell susceptibility in both type 1 and 2 diabetes. *Baker Institute of Medical Research, Melbourne, VIC.* 2008

Nolan CJ. Islet beta-cell dysfunction and diabetes in pregnancy. *Royal North Shore Hospital, Endocrine Unit, Sydney, NSW.* 2008

Nolan CJ. The placental trophoblast – not a beta-cell. *Montreal Diabetes Research Center, Quebec, Canada.* 2008

**AWARDS**

CANBERRA HOSPITAL

Centre for Advances in Epidemiology and IT

STAFF
Dr Bruce Shadbolt, Director

STUDENTS
Ruiduan Wang, PhD Student

COLLABORATIVE ASSOCIATES
University of Wollongong, Australian Health Outcomes Collaboration
Jan Sansoni
Astoria Barr

ACTIVITIES
The Centre’s main activity is the provision of a research support service. The type of support includes advice on research study and clinical trial design, biostatistical advice and analysis, grant submissions, student supervision, and instrument assessment.

During 2007–08 the Centre contributed broadly across health research activities in the ACT. The stand out contributions included research support in neonatology, pediatrics, oncology, hematology, pathology, orthopedics, neurology, respiratory health, rheumatology, gastroenterology, and endocrinology.

The Centre supports the ANU Medical School providing tutorial support in the evidence-based medicine sub program.

In April 2008 the Centre co-convened the 13th Australian Health Outcomes Conference with the University of Wollongong. The conference theme was facilitating knowledge exchange and transfer for a dynamic future.

In October 2008 the Centre collaborated with the Pain Management Unit to jointly win the 2008 ACT Health Quality award for consumer participation. The prize was given for our work on an innovative self-managed education program for chronic pain patients.

PEER REVIEWED JOURNAL PUBLICATIONS


CANBERRA HOSPITAL
Gastroenterology and Hepatology

STAFF
Assoc. Prof. Lybus Chester Hillmani, Director Mugga Wara Endoscopy, Director Brindabella Endoscopy, Director Tarbolton Pty Ltd for GastrotrACT, Clinical Associate Professor Australian National University

STUDENTS
Third year medical student, Ashish Srinivasan

COLLABORATIVE ASSOCIATES
GEHU and Pathology Depts. TCH and Brindabella and Mugga Wara Endoscopy
Prof. Douglas Rex, Assoc. Prof. Tony Clarke
Dr Stuart Miller, Sleep Physician

RESEARCH PROJECTS
Continuing data acquisition for Barrett’s oesophagus database and standardisation of data acquisition between TCH and private endoscopy facilities.
Involvement in multinational assessment of Propofol for sedation for endoscopy procedures.
Initial overnight studies assessing the relationship between gastro-oesophageal reflux and obstructive sleep apnoea.

FUNDING
No grants (Research supported by gastrotrACT and Brindabella and Mugga Wara Endoscopy Centres).

PUBLICATIONS
Papers published in peer-reviewed journals:


EDITORIALS, REVIEWS AND LETTERS

Targeting surveillance in Barrett’s oesophagus. J. Gastroenterol Hepatol. 2008; 23:1311–1312

PRESENTATIONS/ABSTRACTS
Invited speaker
Practice Management – Research in Private Practice
Australian Gastroenterology Week, Brisbane Australia 2008


Hassam Ajamieh
CANBERRA HOSPITAL

Inflammatory Bowel Disease Research Group

STAFF

Associate Professor Paul Pavli, Senior Staff Specialist, Canberra Hospital and Associate Professor, ANU Medical School

Dr Peter Tyrer, Post-Doctoral Fellow, Canberra Hospital, Visiting Fellow ANU Medical School, Adjunct Professional Associate, Cell Biology, Immunology and Biochemistry, University of Canberra

Anna Powell, Research Assistant (to January 2008)

Jennifer Kerrigan, Research Assistant (from May 2008)

STUDENTS

Jennifer Kerrigan, Upstream Signalling to Nod2. University of Canberra, BSc Hons. Supervisors: Ruth Foxwell, Peter Tyrer and Paul Pavli

Claire O’Brien, Molecular microbiology of IBD. PhD ANU. Supervisors: Paul Pavli, Gwen Allison, Jane Dahlstrom; Advisor: Peter Tyrer

Michelle Nelson, Protein Bound 3,4-Dihydroxyphenylalanine as a Signal for Enhanced Antioxidant Defences PhD University of Canberra. Supervisors: Peter Tyrer, Roger Dean and Ruth Foxwell (completed March 2008)

COLLABORATIVE ASSOCIATES

Dr Gwen Allison, School of Biochemistry & Molecular Biology, ANU

Associate Professor Ruth Foxwell, Faculty of Applied Science, University of Canberra

Professor Jane Dahlstrom, Anatomical Pathology, Canberra Hospital and ANU Medical School

RESEARCH PROJECTS

The overall research program is directed at clinical and basic scientific aspects of inflammatory bowel diseases (IBD)

Clinical trials in IBD

Paul Pavli

The GEHU has participated in international multicentre drug trials of the following agents: interleukin 11, CDP571 (anti-TNF agent), onercept (anti-TNF agent), natalizumab (anti-integrin agent), infliximab (for ulcerative colitis), CDP870 (certolizumab), OPC6535, abatacept and anti-mycobacterial agents (rifabutin, clarithromycin and clofazamine).

Crohn’s Disease Associated Intracellular Signalling in Monocytes/ Macrophages

Peter C Tyrer, Paul Pavli, A Ruth Foxwell, Anna Powell, Jennifer Kerrigan

The demonstration that the first genetic abnormality described in Crohn’s disease affects a monocyte lineage-specific gene, NOD2, has given considerable impetus to the further development of techniques to study intestinal macrophage and blood monocyte function. Current research has focussed on the downstream signalling event after activation of NOD2, but nothing is known of the events that lead to NOD2 activation and its regulation. We are using highly enriched populations of blood monocytes and monocytic cell lines to study the function of NOD2. We have used immunoprecipitation and fluorescence
deconvolution microscopy with image analysis to show that NOD2 interacts with a known innate immune system receptor, cell-surface calreticulin, in a muramyl dipeptide-dependent manner, suggesting that calreticulin operates upstream of NOD2. We have examined the effects of the anti-inflammatory cytokine, transforming growth factor-β (TGF-β), which is found at elevated levels within the gut, to regulate NOD2. Immunofluorescence microscopy of isolated monocytes shows that TGF-β downregulates the expression of NOD2 protein in monocytes from normal subjects, but fails to do so in monocytes from Crohn’s disease patients. In addition, fluorescence deconvolution microscopy shows that NOD2 interacts with components of the TGF-β signalling cascade in the human monocytic THP1 cell line. We have shown that TGF-β inhibits lipopolysaccharide and muramyl dipeptide induced NF-κB signal transduction. MDP/NOD2 signalling has been found, by our group, to be influenced by the Smad, PI3K/Akt and MEK1 pathways. This work is beginning to reveal the events that lead to the activation and regulation of NOD2 and has the potential to identify targets for therapeutic intervention in Crohn’s disease.

Interaction between intestinal epithelial cells and peripheral blood monocytes
Peter C Tyrer, Paul Pavli, A Ruth Foxwell

Intestinal macrophages exist in a state of relative ‘unresponsiveness’ to activating stimuli when compared to peripheral blood monocytes. We have developed a unique model of human monocyte-epithelial cell interactions. The model consists of freshly isolated peripheral blood monocytes cocultured with the human enterocyte-like Caco-2 cells separated by a semi-permeable polycarbonate membrane. This model displays the features of intestinal monocytes, for example reduced expression of pro-inflammatory markers, such as CD14. We used the model to examine the pathophysiological effects of two bacterial pathogen-associated molecular pattern molecules, lipopolysaccharide and muramyl dipeptide. Both molecules increased the number of monocytes that were able to migrate across the membrane barrier, increased the expression of CD14, induced apoptosis, and reduced the integrity of the epithelial barrier. This model shows promise for the study of intestinal disease, oral tolerance, and drug and vaccine delivery.

Use of laser capture microdissection to identify bacteria in lymph nodes of Crohn’s disease patients
Gwen Allison, Jane Dahlstrom, Kathy Francki, Paul Pavli

The proposed study aims to determine whether bacteria can be identified in draining lymph nodes of patients who suffer from Crohn’s disease using new culture-independent techniques.

Genetic studies of the inheritance of IBD
Paul Pavli

The Australian Familial IBD Register, established in 1991 with assistance of the Australian Crohn’s and Colitis Association and colleague gastroenterologists, now includes details of over 350 multiplex IBD families. There are >700 affected individuals. Studies are being performed on extracted DNA to find susceptibility genes for IBD.

Role of Protein-Bound DOPA in Antioxidant Defences
Roger T Dean, A Ruth Foxwell, Michelle Nelson, Peter C Tyrer

Proteins are continually exposed to damaging free-radicals, resulting in the production of oxidised protein, a process that has been implicated in the initiation and progression of many age-related diseases. DOPA (3,4-dihydroxyphenylalanine) is a product of protein oxidation, formed through the oxidation of tyrosine residues and is currently the major treatment for Parkinson’s disease. DOPA, a redox active molecule, is involved in various pathologies, including neurodegenerative disorders, cataracts and atherosclerosis. Due to its chemical nature, DOPA is capable of acting as a either a pro-oxidant or an antioxidant and we propose that under physiological conditions, DOPA is likely to act as an antioxidant, and may act as a signalling molecule, triggering the enhancement of cellular antioxidant defence systems. In support of this hypothesis, we have determined that in human monocytes, DOPA at physiological concentrations, is incorporated into cellular proteins, does not exhibit cytotoxicity, and able to protect cells from oxidative stress. Additionally, exposure to DOPA...
alters the expression of proteins involved in antioxidant defences, cytoskeletal organisation, protein chaperoning, metabolism and innate immunity. This work shows that DOPA has significant anti-oxidant effects on cells and has the potential to allow the use of DOPA in diseases such as atherosclerosis and cataracts.

FUNDING
2006–2007
The Canberra Hospital Private Practice Fund
$99,000 Identification of Signal Transduction Abnormalities of Monocytes in Crohn’s Disease Dr Peter C Tyrer, Associate Professor Paul Pavli, Associate Professor A Ruth Foxwell

PUBLICATIONS

PRESENTATIONS/ABSTRACTS
TGF-β Regulates the Crohn’s Disease-Associated Protein, Nod2 Peter C. Tyrer, Anna Powell, Elaine G Bean, Jennifer Kerrigan, A. Ruth Foxwell and Paul Pavli 38th Australian Society for Immunology Conference, Canberra, December 2008 (poster presentation)
Function of Nod2: The Role of TGF-β Peter Tyrer, Mater Medical Research Institute Mucosal Disease Symposium, Brisbane, October 2008 (invited speaker)
Upstream Signalling to, and Negative Regulation of, Nod2 Peter C Tyrer, Anna C Powell, Elaine G Bean, Jennifer L Kerrigan, A Ruth Foxwell, Paul Pavli Canberra Regional Health and Medical Research Conference, May 2008 (speaker)
Pathophysiological Effects of Muramyl Dipeptide in a Novel Coculture Model of Intestinal Epithelium and Monocyte Interactions. Peter C Tyrer, Elaine G. Bean, Anna C. Powell, A. Ruth Foxwell, Paul Pavli 13th International Congress of Mucosal Immunology, Tokyo, Japan, July 2007 (poster presentation)
Pathophysiological Effects of Muramyl Dipeptide in a Novel Coculture Model of Intestinal Epithelium and Monocyte Interactions. Peter C Tyrer, Elaine G. Bean, Anna C. Powell, A. Ruth Foxwell, Paul Pavli Australian Society for Medical Research Young Investigator of the Year Forum, Canberra, June 2007 (winner of Guan Chong Young Investigator of the Year Award)

AWARDS
Dr Peter Tyrer, Guan Chong Young Investigator of the Year Award 2007 Canberra Regional Health and Medical Research Conference, and Australian Society for Medical Research Young Investigator of the Year Forum, Canberra, June 2007
CANBERRA HOSPITAL
Liver Research Group, Gastroenterology and Hepatology Unit

STAFF
Professor Geoff Farrell, Director
Gastroenterology and Hepatology Unit, Canberra Hospital, Professor of Hepatic Medicine, ANU Medical School
Dr Narci Teoh, Senior Lecturer in Medicine and Senior Staff Specialist, Gastroenterology and Hepatology Unit, Canberra Hospital
Dr Shiv Chitturi, Senior Staff, Specialist, Gastroenterology and Hepatology Unit, Canberra Hospital
Dr Claire Larter, Post-doctoral Scientist
Dr Pawan Pyakurel
JY (Helen) Hou
Sydney Hodge
Jacqueline Williams
Derrick van Rooyen
Leah Maddocks
Matthew Clyne
John Brooling

Distinguished Visitors
Sabbatical leave, August 2007–July 2008: Professor Jiangao Fan, Center for fatty liver disease, Shanghai First People’s Hospital, Jiaotong University, Shanghai, China
Professor Henry Chan, collaborating senior investigator, Chinese University of Hong Kong (October 2008)
Dr Usha Dutta, Postgraduate Institute for Medical Research, Chandigarh, India

STUDENTS
Déborah Heydet, PhD, ANUMS
Supervisors: Geoff Farrell, Claire Larter, Carol Hill
Sharon Pock, PhD, ANUMS
Supervisor: Narci Teoh
Kamalijit Ghatora, year 1 medical student, ANUMS (research project)
Marianna Heales, summer vacation student (medicine, University of Tasmania)

COLLABORATIVE ASSOCIATES
Professor Anthony C. Allison, ‘Alavita’ Biotechnology Inc, San Francisco
Professor Phillip Board, JCSMR, ANU
Professor Chris Parish, JCSMR, ANU
Dr Gerard Hoyne and Professor Chris Goodnow, JCSMR, ANU
Associate-Professor Chris Nolan, Endocrinology, TCH and ANU Medical School
Dr Carol Hill, JCSMR, ANU
Professor Jenny Graves and Dr Amber Alsop, RSB, ANU; and Peter MacCallum Institute, Melbourne
Professor Robert S. McCuskey, University of Arizona, Tucson
Professor Henry Chan, Chinese University of Hong Kong, Hong Kong
Professor Paul Lai, Chinese University of Hong Kong
Dr Jun Yu, Chinese University of Hong Kong, Hong Kong
Professor Jiangao Fan, Shanghai First People’s Hospital, Jiaotong University, Shanghai, China
Dr Lisa Sedger, University of Technology, Sydney
Dr Matthew Yeh, University of Washington, Seattle
Dr Geoffrey Haigh, Gastroenterology Unit, VA Hospital, UW (Seattle)
Professor Sum Lee, Gastroenterology Unit, VA Hospital, UW (Seattle)
Dr George Ioannou, Gastroenterology Unit, VA Hospital, UW (Seattle)
RESEARCH PROJECTS

Main Fields of Study

Liver carcinogenesis (Narci Teoh): Role of DNA repair mechanisms in the pathogenesis of hepatocellular carcinoma. Two major papers have resulted from this work in 2007–08, respectively showing accelerated onset of liver cancer in Ku70-gene-deleted mice (published in Hepatology 2007), and abrogation of hepatocarcinogenesis in ATM gene-deleted mice (provisionally accepted by Gastroenterology). This has led to several promising leads in pro-cancer pathways (identified by comparative genomic hybridization), the significance of which is now being tested in primary cultures of murine liver cancer cells.

Liver ischaemia-reperfusion injury: Novel hepatoprotective strategies against hepatic ischaemia reperfusion injury in murine models. This has led to a pivotal article in Gastroenterology 2007, which was editorialised, showing that the novel therapeutic protein diannexin (an annexin V dimer) confers hepatoprotection against ischaemia-reperfusion injury. Other work has characterized ways to protect fatty livers against this serious form of injury incurred during surgery or liver transplantation, as we reviewed in Anatomical Record.

Obesity-related liver disease: Microvascular dysfunction and predisposition to liver cancer. This is an exciting new field of research that is critically relevant to our clinical research program in diabetes and non-alcoholic fatty liver disease (NAFLD).

Mechanisms of non-alcoholic fatty liver disease: This has been a very productive area of research, with the earlier emphasis being on the role of fatty acids in development of steatohepatitis (NASH) (2 articles in 2008). During the last 18 months, we have characterised the role of dietary fat content on development of NASH in obese mice (foz/foz - mutation of Alstrom gene) with diabetes and metabolic syndrome. New directions are hypothalamic dysregulation of appetite (Deborah Heydet), factors determining hepatic...
lipid partitioning (Claire Larter), and role of cholesterol accumulation in onset of liver injury, hepatic inflammation and fibrogenesis (Derrick van Rooyen).

Role of TRAIL in liver biology: In collaboration with Dr Lisa Sedger, we have observed what appears to be a highly novel role for the TNF superfamily member, TRAIL in liver biology – the regulation of cell survival during chronic liver injury and after partial hepatectomy.

Why does cirrhosis occur in type 2 diabetes, and how can it be prevented? [Geoff Farrell, Shiv Chitturi, Chris Nolan]. This project was started in 2007 by Shiv Chitturi with input from Dr Sally Newsome (ANU Research Fellow of TCH), and has been ably carried forward by Ms Sydney Hodge (project officer) in 2008. The aims are to identify factors associated with severe liver scarring (cirrhosis) in patients with diabetes, and to evaluate the impact of lifestyle measures (dietary intake, physical activity) on the prevention and treatment of non-alcoholic fatty liver disease (NAFLD) in these patients. The two cohorts being studied are a Community cohort consists of newly diagnosed type 2 diabetic patients recruited from peripheral Diabetes education centres, and a Liver clinic cohort of patients referred to The Canberra Hospital Liver clinic for assessment of their abnormal liver tests. Data analysis will commence 2009.

FUNDING
2005–2009
NHMRC Program Grant #358398
GC Farrell CIA, G McCaughan CIB; NC Teoh PI. The molecular and cellular basis of liver disease. $4,700,000 over 3 centres

2007–2009
NHMRC Project Grant #418101
GC Farrell, CJ Nolan. Mechanisms of disordered hepatic lipid partitioning in non-alcoholic steatohepatitis. $432,000

NHMRC Project Grant #418100
NC Teoh; AIA: Jenny Graves; AIB: Amber Alsop; AIC: Geoff Farrell. DNA repair mechanisms in the pathogenesis of hepatocellular carcinoma. $326,250

2008–2010
Philip Bushell Foundation, Why does cirrhosis develop in diabetes, and how can it be prevented? CI. Geoff Farrell

2007
Narci Teoh. Arnott Fellowship in Cancer Research, RACP. Pathogenesis of hepatocellular carcinoma
PUBLICATIONS

2007


Farrell GC Déjà vu, mais pas en anglais! Precautionary notes on publishing the same article in two Languages. (Editorial) J Gastroenterol Hepatol 2007;22:699–700


Chan HL, de Silva HJ, Leung NW, Lin SG, Farrell GC, the Asia-Pacific Working Party on NAFLD. How should we manage patients with non-alcoholic fatty liver disease in 2007; J Gastroenterol Hepatol 2007;22:801–8


2008


Fan JG, Farrell GC Epidemiology of non-alcoholic fatty liver disease in China, J Hepatol 2008 (in press)
Fan JG, Farrell GC. VAT fat is bad for the liver, SAT fat is not! (Editorial), J Gastroenterol Hepatol 2008;23:829–32
Farrell GC. Primary biliary cirrhosis in Asians: less common than in Europeans, but just as depressing, (Editorial) J Gastroenterol Hepatol 2008;23:508–11
Farrell GC. A feast of new offerings from JGH in the year of the rat! (Editorial) J Gastroenterol Hepatol 2008;23:169–70
Teoh NC, Bowden FJ. Bring out your dead—the return of the long case? BMJ 2008;336:1250

INTERNATIONAL INVITED LECTURES

Narci Teoh
Hepatology State of the Art Lecture: Advances in Current Therapy for patients with Chronic Hepatitis C

New Zealand Gastroenterology Society Meeting, Christchurch 2007
Management of Hepatocellular Carcinoma: Novel Protective Strategies against Hepatic Ischaemia Reperfusion Injury
International Liver Congress, Hong Kong, June 2008

Geoff Farrel
Gastroenterology Society of New Zealand, Annual Scientific Meeting, Christchurch: 21-23 October: Keynote lecture – Better management of chronic hepatitis B; Liver injury from drugs and herbal medicines
Haemophilia Society of Australia and New Zealand, Canberra, 5 October. Keynote speaker: Advances in treatment of hepatitis C
Singapore National University Hospital and NUS Visiting Expert in field of Fatty Liver Disease and Drug-Induced Liver Injury. April 22–27 [6 lectures].
Asia-Pacific Digestive Week, Kobe, October 2007. Pathogenesis of NAFLD: insights from man and mouse
Feb International Liver Congress (Hong Kong – Shanghai meeting), February – 3 lectures.
Asia-Pacific Digestive Week, Delhi, September 2008. Pathogenesis of insulin resistance in NAFLD

PRESENTATIONS

Other than listed as published abstracts — all of which were presented at the indicated meeting


Teoh NC, Williams J, Larter CZ, McCuskey RS, Farrell GC. Increased susceptibility of steatotic and steatohepatitic livers To hepatic ischaemia reperfusion injury
**Poster presentation** at The Asia Pacific Digestive Week, Kobe, Oct 2007.

Teoh NC, Williams J, Larter CZ, McCuskey RS, Farrell GC. Increased susceptibility of steatotic and steatohepatitic livers from foz/foz mice to hepatic ischaemia reperfusion injury

**Oral presentation** at NZ Gastroenterology Society meeting, Christchurch, Nov 2007

**ABSTRACTS**


Teoh NC, Williams J, Larter CZ, McCuskey RS, Farrell GC. Increased susceptibility of steatotic and steatohepatitic livers from foz/foz mice to hepatic ischemia reperfusion injury. J Gastroenterol Hepatol 2007; 22(Suppl. 3):A237

Farrell GC. Pathogenesis of non-alcoholic fatty liver disease (NAFLD). J Gastroenterol Hepatol 2007;22(Suppl. 3):A30 *Australian Gastroenterology Week 2008 [October, Brisbane, Qld]*


Larter CZ, Yeh MM, Teoh NC, Farrell GC. High fat-feeding saturates adipose stores, decreasing Serum adiponectin and causing steatohepatitis in obese mice: implications for NASH. J Gastroenterol Hepatol 2008;23:A269

*Liver Week 2008; American Association for the Study of Liver Disease (November, San Francisco, CAL)*


Larter CZ, Yeh MM, Teoh NC, Farrell GC. Dietary intervention attenuates metabolic abnormalities and improves liver histology in obese mice with steatohepatitis: Mechanistic implications for NASH. Hepatology 2008;48:1175: 831A


**AWARDS**

2007 Inaugural Geoff Farrell Journalism Award for Hepatitis C by Hepatitis Australia. Narci Teoh: Prize for Best Laboratory Science Oral Presentation 2008

*Canberra Region Annual Scientific Meeting, Canberra*. Claire Larter: Prize for Best Poster 2008. Canberra Region Annual Scientific Meeting, Canberra
STAFF
Dr Imogen Mitchell, Director, Intensive Care
Dr Anne Leditschke, Director of Research
Rebecca Ashley, Research and Data Coordinator
Andrew Bailey, Research and Data Coordinator
Elise Crowfoot, Research and Data Coordinator
Jamie Ranse, Research and Data Coordinator

STUDENTS
Gavin Williams, ANU Medical School
Laura Wise, ANU Medical School
Parul Bali, ANU Medical School
Joseph Kim, ANU Medical School
Lola Kurimalawai, Postgraduate student, University of Canberra

COLLABORATIVE ASSOCIATES
Associate Professor Paul Smith, Trauma and Orthopaedic Research Unit
Dr Rachel Li, Trauma and Orthopaedic Research Unit
Professor Julia Potter, Professor of Pathology, ANU Medical School
Associate Professor Peter Hickman, Director of Chemical Pathology, ACT Pathology
Professor Peter Collignon, Director of Infectious Diseases/Microbiology, Canberra Hospital
Dr Karina Kennedy, Department of Infectious Diseases/Microbiology, Canberra Hospital
Dr Carolyn Hawkins, Canberra Hospital

RESEARCH PROJECTS
Australia & New Zealand Intensive Care Society Clinical Trials Group Research
2008 saw the conclusion of 2 large multi-centre clinical trials endorsed by the Australia & New Zealand Intensive Care Society Clinical Trial Group (ANZICS CTG).

The NICE Study (Normoglycaemia in Intensive Care Evaluation) was a huge undertaking, funded by the National Health and Medical Research Council, examining the effects of two blood glucose targets (4.5–6.0mmol/L and 8–10mmol/L) on 90 day all-cause mortality in Intensive Care patients. Of a total 6104 patients randomised, the Canberra Hospital Intensive Care Unit recruited 307 (5%). Preliminary results will be presented in February 2009 and are eagerly awaited by the Intensive Care community.

The RENAL Study (Randomised Evaluation of Normal Vs Augmented Level of Renal Replacement Therapy in ICU) compared the effect of a higher continuous renal replacement therapy (CRRT) flow rate (40mls/kg/hr) with a lower CRRT flow rate (25mls/kg/hr) on 90-day all-cause mortality in Intensive Care Unit patients with severe acute renal failure. This study reached the recruitment target of 1510 patients ahead of schedule, and preliminary results are also expected in February of 2009.

Currently, we are working towards commencing another ANZICS CTG study in 2009. ARISE (The Australasian Resuscitation in Sepsis Evaluation) is a Randomised Controlled Trial of Early Goal Directed Therapy in Patients with Severe Sepsis, an international collaboration which has received significant financial support from the National Health & Medical Research Council.

In 2007, Canberra Hospital Intensive Care Unit participated in 3 Point Prevalence Projects conducted on behalf of the ANZICS CTG. VTE was a Point Prevalence Survey of Venous Thromboembolism Prophylaxis Management in the critically ill. The one day snapshot project aimed to identify current practices in deep vein thrombosis prophylaxis among intensive care units throughout Australia and New Zealand.
VTE Sepsis studied the same practices, specifically in Critically Ill patients with sepsis, over a 4 week period during May and June 2007.

The Saline Albumin Fluid Evaluation Translation of Research into Practice Study SAFE TRIPS was a follow up to the Saline Albumin Fluid Evaluation, whose results were published in the New England Journal of Medicine in 2004. This point prevalence project, conducted in June 2007, aimed to assess fluid resuscitation practice in Intensive Care patients in as many countries as possible worldwide to:
- Document current practice in fluid resuscitation
- Determine identifiable patient characteristics that influence choice of fluid
- Determine whether there are identifiable regional or national variations in choice of resuscitation fluid not explained by patient characteristics

Clinical Excellence Commission and Intensive Care Coordination and Monitoring Unit (ICCMU) Research
The Central Venous Line associated bacteraemia in ICU (CLAB-ICU) or CLAB project builds on work commenced through the ‘Safer Systems Save Lives’ Project. Designed to reduce Central Venous Catheter blood stream infections in Intensive Care Units across NSW, CLAB is being conducted by the Clinical Excellence Commission in collaboration with the Intensive Care Coordination and Monitoring Unit (ICCMU) and with the assistance of the NSW Department of Health Quality and Safety Branch.

Pharmacology and Industry Sponsored Research
CAPtivate, a study that aimed to evaluate the safety and efficacy of Tifacogin (Recombinant Tissue Factor Pathway Inhibitor) administration in patients with severe Community-Acquired Pneumonia, has just completed recruitment in the latter part of 2008. Results from the study should be available mid-2009.

PROWESS SHOCK investigates the safety and efficacy of Drotrecogin Alfa (activated) in adult patients with severe septic shock commenced at the Canberra Hospital in October 2008.

ART – 123 examines the safety and efficacy of Recombinant Human Thrombomodulin in patients with sepsis and disseminated intravascular coagulation.
Intensive Care Unit Generated Research
Recognition of the Deteriorating Patient
A prospective controlled trial of effect of the use of the Modified Early Warning Score on Morbidity and Mortality Rates
Principal Investigators: Dr Imogen Mitchell, Mr Chris Van Leuvan, ANU Medical School; Ms Heather McKay, Patient Safety and Quality Unit, ACT Health; Ms Judy Gosper, Patient Safety and Quality Unit, ACT Health; Dr Tracey Bessel, Patient Safety and Quality Unit, ACT Health
Research Grant: ACT Health Project Grant received

Inspiratory Muscle Training
A randomised trial of inspiratory muscle training as an adjunct to ventilatory weaning in prolonged mechanical ventilation.
Principal Investigators: Ms Bernie Bissett Senior Physiotherapist; Dr Anne Leditschke
Research Grant: Allied Health Scholarship ($5000) received.

Acute Renal Failure in Critical Illness
An audit of acute renal failure in critical illness, with a focus on contrast nephropathy.
Principal Investigator: Dr Anne Leditschke

Burnout: Experiences of Emotional Exhaustion in Critical Care Nurses
This research aims to highlight the awareness of burnout, which is essential to recognize symptoms and prevent it from occurring. Formulated strategies, resulting from this project may help, minimise and prevent emotional exhaustion (burnout).
Principal Investigator: Lola Kurimalawai

Cortisol Physiology in Critical Illness
An observational study of cortisol physiology in critical illness.
Principal Investigators: Dr Anne Leditschke; Associate Professor Peter Hickman, Director of Chemical Pathology; Professor Julia Potter, Director of Pathology

Intramedullary Pressure Monitoring in Long Bone Instrumentation
Investigation of the effects of monitoring and controlling intramedullary pressure in long bone instrumentation in a sheep model.

Principal Investigators: Dr Paul Smith, Trauma and Orthopaedic Research Unit; Dr Rachel Li, Trauma and Orthopaedic Research Unit; Dr Anne Leditschke

Impact of a Pandemic Triage Tool on Intensive Care Admissions
Considers impact of a pandemic triage tool on intensive care admissions.
Principal Investigators: Mr Andrew Bailey; Mr Jamie Ranse; Dr Anne Leditschke

Lymphopenia in Critically Ill Trauma Patients
Lymphopenia has been described as a marker of sepsis. This study investigates the frequency of lymphopenia in non-septic trauma patients.
Principal Investigators: Professor Peter Collignon, Department of Infectious Diseases and Microbiology; Dr Karina Kennedy, Department; Dr Anne Leditschke

PUBLICATIONS


PRESENTATIONS/ABSTRACTS
Ranse J. In-hospital resuscitation: graduate nurses’ lived experience in the non-critical care environment – a hermeneutic phenomenological approach [abstract]. ACT Health, Nursing and Midwifery, 2nd Compendium of Research and Evidence Based Practice. 2007
Ranse J. Medical emergency teams: graduate nurses interactions, attitudes and perceptions during resuscitation events in the non-critical care environment [abstract]. Australian Critical Care. 2008;21(1):54
Ranse J, Taylor N. Mountain biking events: presentation characteristics and medical needs; paper presented at the 8th Rural Critical Care Conference. Batemans Bay, Australia, 23rd August 2008
Ranse J, Taylor N. Medical needs at the world largest mountain biking event; paper presented at the St John Ambulance Australia National Conference, Adelaide, Australia, 20th June 2008
Ranse J, Carter S. Engaging volunteers in emergency services: the St John Ambulance Australia perspective; paper presented at the St John Ambulance Australia National Conference, Adelaide, Australia, 20th June 2008
Mitchell I. Early recognition of the deteriorating patient reduced unplanned ICU admissions; paper presented at the ANZICS/ACCCN Intensive Care Annual Scientific Meeting, Rotorua, New Zealand, 27th October 2007

Leditschke IA. Dead is Dead. Invited presentation at ‘Why Organ Donation? – a seminar for health professionals’ Parliament House, Canberra, 15th October 2007


Ranse J. Medical emergency teams: graduate nurses interactions, attitudes and perceptions during resuscitation events in the non-critical care environment; paper presented at the ANZICS/ACCCN Intensive Care Annual Scientific Meeting, Rotorua, New Zealand, 26th October 2007


Ranse J. Exploring the volunteer first aiders’ experience post-resuscitation; paper presented at the St John Ambulance Australia National Conference, Canberra, Australia, 22nd June 2007

Arbon P, Zeitk K, Ranse J, Wren H, Driscoll K, Elliott R. Multi-casualty triage – putting triage theory into practice at the scene of multiple casualty vehicular accidents; paper presented at the 15th World Congress on Disaster and Emergency Medicine, Amsterdam, the Netherlands, 14th May 2007

**AWARDS**

Mitchell I. Guan Chong Award for Best Clinical Oral Presentation. Canberra Region Annual Scientific Meeting and ASMR Young Investigator Forum. Early recognition of the Deteriorating Patient reduces unplanned admissions to the intensive care unit.

STAFF
Prof Graham Buirski, Director Medical Imaging
Canberra Hospital. Professor of Radiology ANU Medical School
Dr Rajeev Jyoti, Deputy Director (Academic) Medical Imaging, Clinical Senior Lecturer Radiology ANU Medical School
A/Prof Ross O’Neil, Supervisor of Training, RANZCR, Clinical A/Prof Radiology ANU Medical School

STUDENT
Dr Yi Song Wong, Advanced trainee in vascular and interventional Radiology

CURRENT RESEARCH PROJECTS
A diffusion tensor magnetic resonance imaging (DT-MRI) study of depression and cognition in type 2 diabetics: a pilot study. Research proposal in submission, pending review outcome. Dr R Jyoti. Collaboration: Department of Psychological Medicine and Endocrinology the Canberra Hospital

Ultrasound assessment of brachial artery in patients on low carbohydrate diet. Double blind RCT. Data collected. Writing up. Dr R Jyoti. Collaboration: Department of Gastroenterology the Canberra Hospital

General practice based musculoskeletal pain imaging plan. Dr R Jyoti. A research project in planning for grant submission to NHMRC. The specificity and sensitivity of ultrasound in identifying the medial collateral ligament of the ankle in patients with Weber b and C fractures. Buirski g, Orifice R, Scarvell J, Smith P. Collaboration: Orthopaedics department the Canberra Hospital


FUNDING
Private Practice Fund the Canberra Hospital grant of $15,200.00. Size of kidneys in premature infants (SKIPI study). Dr R Jyoti, A/Prof A. Kent, Dr M Falk

PUBLICATIONS


PRESENTATIONS/ABSTRACTS

Kent AL, Jyoti R, Robertson C, Gonsalves L, Meskell S, Shadbolt B, Falk MC. Are renal volumes measured by magnetic resonance imaging and three-dimensional ultrasound in the term neonate comparable?

Accepted abstract for the 13th Annual Congress of The Perinatal Society of Australia and New Zealand (PSANZ09), to be held at the Darwin Convention Centre, Northern Territory.

Kent AL, Jyoti R, Robertson C, Gonsalves L, Meskell S, Shadbolt B, Falk MC. Does extreme prematurity affect kidney volume at term corrected age?

Jyoti R, Wong Yii Song
Cost effective use of MR Urography in Evaluation of complex renal tract conditions-a pilot study. Published abstract in Journal of medical Imaging and radiation Oncology Poster presentation RANZCR 2005

Rao Prashanth, Jyoti R, Khurana G, Kirk H
STAFF
Assoc Professor Zsuzsoka Kecskes
Assoc Professor Alison Kent
Dr David Todd CMO, Department of Neonatology
Assoc Prof William McGuire
Mrs Margaret Broom, Research Nurse, Department of Neonatology
Dr Manbir Chauhan, Previous Fellow Neonatal Unit, Department of Neonatology
Ms Kelly Cameron, Neonatal Nurse, Department of Neonatology
Dr Sascha Meyer, Previous Fellow Neonatal Unit, Department of Neonatology
Dr Blessy Charles, Current Fellow Neonatal Unit, Department of Neonatology

STUDENTS
Ms B Schiller, PhD student (Co-supervisor with Prof R Martin) at School of Biochemistry and Molecular Biology ANU
ANU Medical Student Research Projects
Ms Carly Neller
Ms Jennifer Porteus
Mr Alex Dillon
Ms G Riley
Ms M Stilianos
Ms K Barrett
Ms P Moore
Ms M Maddock
Mr T Gleeson
Ms Bianca Preo
Ms Hui Ying Chow
Ms Deborah Moran

Cathy Ringland, Associate Professor Zsuzsoka Kecskes, Dr David Todd, Margaret Broom
COLLABORATIVE ASSOCIATES

Professor John Bertram, Head, Department of Anatomy and Developmental Biology, Monash University, Melbourne, Australia

Rebecca Douglas-Denton, Department of Anatomy and Developmental Biology, Monash University, Melbourne, Australia

Dr Mary Jane Black, Monash University, Melbourne

Prof Jane Dahlstrom, Dept of Anatomical Pathology, Canberra Hospital

Dr Mark Koina, Dept of Anatomical Pathology, Canberra Hospital

Linda Brown, Dept of Anatomical Pathology, Canberra Hospital

Prof David Ellwood, Dept of Obstetrics and Gynaecology, Canberra Hospital

Assoc Prof Chris Nolan, Dept of Endocrinology, Canberra Hospital

Dr Michael Falk, Dept of Nephrology, Canberra Hospital

Dr Rajeev Jyot, Dept of Medical Imaging, Canberra Hospital

Dr Ross O’Neill, Dept of Medical Imaging, Canberra Hospital

Dr Gwen Allison, Dept of Microbiology, Australian National University

Prof Peter Collignon, Dept of Microbiology and Infectious Diseases, Canberra Hospital

Dr Bruce Shadbolt, Clinical Epidemiology Unit, Canberra Hospital

Professor Rosemary Martin, School of Biochemistry and Molecular Biology (BAMBI), Australian National University

Professor Paul Colditz, Perinatal Research Centre, School of Medicine, University of Queensland

Dr Barbara Lingwood, Perinatal Research Centre, School of Medicine, University of Queensland

A/Prof David Croaker, Paediatric Surgery, Australian National University Medical School

Audrey Wright & Dr Marilyn Rochefort, Westmead Hospital, Westmead, Sydney, NSW

Dr Luke Jardine & Dr Alice Stewart, Royal Brisbane and Women’s Hospital, QLD

Dr Srinivas Ramakrishnan, John Hunter Hospital, Newcastle, NSW

Prof Marjan Kljakovic & Ms Karen Ciszek, ANU Medical School Canberra

Dr Laurel Teoh, Paediatrics, Canberra Hospital

Mr Mat Harris & Mr Christian Saville, Fisher and Paykel Health Care

RESEARCH PROJECTS

Bacterial PRIMers, Neonatal Infection and Premature Labour (PRIMIP Study). Assoc Prof Kent, Drs W Seliem, G Allison, P Collignon, D Ellwood, JE Dahlstrom

To compare bacterial primers with current microbiological techniques for determining infections in premature labour and the early neonatal period

The role of glucolipotoxicity in the pathogenesis of diabetic fetopathy (GLTxIP study). A/Prof C Nolan, Prof JE Dahlstrom, Dr P Scott, Ms Kugathas & Assoc Prof Kent

To Examine the effect of glucolipotoxicity in pregnancy on the placenta and the subsequent fetus and neonate

Study of indomethacin and ibuprofen and glomerular development in an animal model (SING II study). Assoc Prof Kent, Dr MC Falk, Prof JE Dahlstrom, Dr M Koina, Dr D Willenborg, Prof John Bertram, R Douglas-Denton

Further study to determine whether indomethacin and ibuprofen impair glomerular development during glomerulogenesis.

Glomerular Urinary Podocytes in Premature Infants (GUPPI study). Assoc Prof A Kent, Prof JE Dahlstrom, Dr L Brown

To determine whether administration of indomethacin or gentamicin results in glomerular injury in the premature neonate as evidenced by excretion of podocytes in the urine

Post mortem glomerular study of premature neonates. Assoc Prof A Kent, Prof JE Dahlstrom, Dr MJ Black, Prof J Bertram.

To determine whether extreme prematurity and exposure to a number of insults can decrease the number of glomeruli
Renin and aldosterone levels in neonates (RENAL study). Assoc Prof A Kent, Prof Jane Dahlstrom, Assoc Prof Chris Nolan, Dr Peter Hickman. To determine whether maternal hypertension and diabetes results in elevated neonatal renin and aldosterone levels and blood pressure.

Predicting neonatal and infant morbidity after perinatal hypoxic-ischaemic injury. In this multi-centre study, prospectively collected data will be analysed and scoring systems used for predicting long-term outcome applied to the dataset to determine, which system is most predictive.

Amplitude integrated EEG (aEEG) as a monitoring tool in neonatal stroke. The use of aEEG for neonates has mainly focussed on definition of brain damage after asphyxia. In this study, the value of aEEG in defining abnormalities after neonatal stroke is assessed.

Normative values for passage of meconium in preterm and term infants. This collaborative study evaluates time to first passage of meconium in neonates to gather normative data. Results of this study will guide clinicians in determine which infants need further investigations for Hirschsprung’s disease.

Cerebral impedance following hypoxia/ischaemia in the human infant. Impedance measurements are mainly known for assessment of fluid status in adults. In this multi-centre trial, cerebral impedance is measured and correlated with long-term neurological outcome in babies following perinatal asphyxia.

Effects of early discharge of premature infants on parent satisfaction. The Centre for Newborn Care has instigated an early discharge program, in which parents are trained to do gastric feeding by gavage of their premature infant in the home environment. This quality assurance project investigates parental satisfaction with this program.

Effect of home gavage feeding of premature infants on short-term outcomes. The Centre for Newborn Care has instigated an early discharge program, in which parents are trained to do gastric feeding by gavage of their premature infant in the home environment. This quality assurance project investigates safety and short-term outcomes of this program.

Oxygen for resuscitation of preterm infants. Traditionally neonates are resuscitated with 100% oxygen. Recommendations for term infants now state to use 21% oxygen instead as there are concerns about long-term effects of pure oxygen. The best concentration of oxygen to be used for preterm infants is unknown. As oxygen for resuscitation is blended and tailored to the needs of the baby at Canberra Hospital, this quality control project assesses the efficacy and safety of this practice.

Does early extubation (<6 hours) reduce the incidence of chronic lung disease in very premature infants? Obstetric and Neonatal practice have changed dramatically over the last decade. The effects of changed practice result in shorter duration of ventilation of premature infants. This project assesses the effects of duration of ventilation (<6 hours vs. >6 hours) in babies born <28 weeks gestation at Canberra Hospital on short-term (duration of oxygen requirement, duration of CPAP) as well as long-term (need for re-intubation, CLD) outcomes.
INIS (International Neonatal Immunotherapy Study) A multicentre randomised trial to assess efficacy and long term outcomes of immunoglobulin in neonatal sepsicaemia. A two year follow up is in progress - developmental assessment continues to five years. NHMRC and UK MRC funded trial.

CAP (Caffeine for Apnoea of Prematurity) Multicentre - randomised trial to assess effectiveness and long term developmental outcome of caffeine used to treat apnoea in preterm infants. A five year follow up is in progress. Canadian and Australian NHMRC funded trial.

BOOSTII (the Benefits of Oxygen Saturation Targeting Study) A comparative study which examines exposure of severely premature infants (< 28wks) to lower and higher oxygen levels. Developmental follow-up to be conducted at two years - funded by NHMRC.

Training in Cochrane methodology

Methods of weaning CPAP in infants <30 weeks gestational age: A multicentre randomised controlled trial.

— Canberra Hospital Co-ordinating centre: Dr David Todd, Mrs Margaret Broom, Ms Kelly Cameron, Dr Mambir Chauhan, Dr Bruce Shadbolt
— Westmead Hospital Sydney: Mrs Audrey Wright, Mrs Carol Cameron, Dr Marilyn Rochefort
— Royal Brisbane and Women’s Hospital: Dr Luke Jardine, Dr Alice Stewart, Sandy Meskell

Inspired Humidity and temperature with the Stephanie Ventilator
— Ms Bianca Preo (Med student), Dr David Todd, Dr Bruce Shadbolt

Inspired Humidity and temperature with the F&P MR850
— Dr David Todd, Mr Mat Harris, Mr Christian Saville

Inspired humidity and temperature with the WILAmed PMH 5000 humidifier
— Ms Hui Ying Chow (Med Student), Dr David Todd

The Placement of central lines and endotracheal tubes in neonates <30 weeks gestation
— Ms Deborah Moran (ANU Med Student), Dr David Todd

Pulmonary follow up survey in preterm infants < 29 weeks gestation in conjunction with the ACT Kindergarten Asthma and allergies survey ANU Medical School.
— Dr David Todd, Cathy Ringland, Margaret Broom, Dr Blessy Charles, Prof Marjan Kljakovic, Ms Karen Ciszek, Dr Laurel Teoh

Non-invasive cardiac Output study using the USCOM monitor in preterm infants <36 weeks gestation
— Dr David Todd, Dr Sascha Meyer, Dr Bruce Shadbolt

FUNDING

2006
The Canberra Hospital Private Practice Trust Fund: $37,203.28; CPAP weaning trial.
The Canberra Newborn Intensive Care Foundation: $2,200.00; Perpetual Treronic licence for CPAP weaning trial.

2007
The Canberra Hospital Private Practice Trust Fund: $9,900.00; USCOM cardiac output monitor trial.
The Canberra Newborn Intensive Care Foundation: $2,500.00; Humidity and Temperature probe.


2008

Renin and Aldosterone in neonates (RENA study). The Canberra Hospital Private Practice Fund. $16,500 (PI – A Kent) AL Kent, D Ellwood, P Hickman, C Nolan, JE Dahlstrom.
PUBLICATIONS


PRESENTATIONS/ABSTRACTS

Kent AL, Dahlstrom JE, Ellwood D. Postmortem and placental pathology in perinatal deaths. PSANZ, Melbourne, Australia, 2007


Kent AL, Kecskes Z, Shadbolt B, Falk MC. Blood pressure readings in term neonates – normative values in the current era. PSANZ, Melbourne, Australia, 2007

Kent AL, Williams J. Increasing ambient room temperature in the operating theatre and plastic wrap improves admission temperature in premature infants. ESPR, Prague, Czechoslovakia, 2007


Sелием W, Shadbolt BS, Falk MC, Kent AL. Antenatal and postnatal risk factors for neonatal hypertension and infant follow-up. ESPR, Prague, Czechoslovakia, 2007

De Cure N, Myers R, Shadbolt B, Kent AL. Time to regain birth weight as a predictor of poor somatic growth at discharge in extremely premature infants. PSANZ, Gold Coast, Australia, 2008


Kent AL, Dahlstrom JE, Bourne M, Freebairn L, Ellwood DA for the ACT Perinatal Mortality Committee. Perinatal mortality in the ACT – A 5-year review. PSANZ, Gold Coast, Australia, 2008


Kent AL, Jyoti R, Robertson C, Gonsalves L, Meskell S, Shadbolt B, Falk MC. Are renal volumes measured by magnetic resonance imaging and three-dimensional ultrasound in the term neonate comparable? The Canberra Region Annual Scientific Meeting, Canberra, Australia, 2008


Gubhaju, L, Stamp, L, Moore, L, Kent, AL Black, MJ. Pre-term Birth: Effects on Nephrogenesis in the Human Kidney. ANZSN Meeting, Newcastle, Australia, 2008


Z Kecskes, K Gardner. Amplitude integrated EEG (aEEG) as a monitoring tool in neonatal stroke. 48th Annual Meeting of the European Society for Paediatric Research, Prague, Czech Republic Spain, October 6–8, 2007

Li J, Nahon I, Kecskes Z, Croaker GDH. Paediatric Constipation: it’s not all bad diet and poor toilet training. Paediatric Colorectal Club, York, UK, July 14 – 16, 2007


M Stilianos, Z Kecskes. Effects of early discharge of premature infants on parent satisfaction. 12th Annual Congress of the Perinatal Society of Australia and New Zealand; 2008; April 21–24, Goldcoast, Australia

Barrett, Kecskes Z. Effect of home gavage feeding of premature infants on short-term outcomes. 12th Annual Congress of the Perinatal Society of Australia and New Zealand; 2008; April 21–24, Goldcoast, Australia

Ringland CP. Posttraumatic stress disorder and the NICU graduate mother. 12th Annual Congress of the Perinatal Society of Australia and New Zealand; 2008; April 21–24, Goldcoast, Australia

Hanzic M. Education program for home gavage feeds for preterm infants. 12th Annual Congress of the Perinatal Society of Australia and New Zealand; 2008; April 21–24, Goldcoast, Australia

Pini G. Programs that promote the initiation and maintenance of lactation for mothers of preterm and/or LBW/VLBW infants in neonatal intensive care units. 12th Annual Congress of the Perinatal Society of Australia and New Zealand; 2008; April 21–24, Goldcoast, Australia

Z Kecskes, M Stilianos. Effects of early discharge of premature infants on parent satisfaction. 49th Annual Meeting of the European Society for Paediatric Research, Nice, France, October 24 to 28, 2008


Todd DA, Wright A & Ramakrishnan S: Methods of weaning CPAP in infants <30 weeks gestational age: A multicentre randomised controlled trial. Fetal and Neonatal Physiology Meeting Melbourne, 2007

Todd DA. Invited Talk: Retinopathy of prematurity (ROP): The incidence, pathophysiology and treatment. Special Care Neonatal Study day. The Calvary hospital, ACT, 2007


Todd DA, Harris M and Saville C. Inspired temperature variations with the F&P MR850 humidity base. Annual PSANZ meeting: Gold Coast, Australia, 2008

Todd DA, Harris M and Saville C. Inspired humidity variations with the F&P MR850 humidity base. Annual PSANZ meeting: Gold Coast, Australia, 2008

Meyer S, Todd DA, Shadbolt B. Assessment of cardiac output with portable continuous wave Doppler ultrasound (USCOM) in the Neonatal intensive care unit. Annual PSANZ meeting: Gold Coast, Australia, 2008


Todd DA. NEC and the neonate. Invited talk: Special Care Neonatal Study day. The Calvary hospital, ACT, 2008


Todd DA, Harris M and Saville C. Inspired temperature variations with the F&P MR850 humidity base. The Canberra Annual Scientific meeting, Australia, 2008

Todd DA, Harris M and Saville C. Inspired humidity variations with the F&P MR850 humidity base. The Canberra Annual Scientific meeting, Australia, 2008
STAFF
Associate Professor Christian J Lueck, Head of Department and Senior Staff Specialist
Dr Andrew Hughes, Senior Staff Specialist
Dr Craig McColl, Senior Staff Specialist
Dr Chandi Das, Senior Staff Specialist
Dr Colin Andrews, Visiting Medical Officer
Dr Roger Tuck, Visiting Medical Officer
Ms Angela Borbelj, Senior Neurophysiology Technologist
Ms Kate Martin, Neurophysiology Technologist
Ms Isabel Harvey, Stroke Liaison Nurse
Dr Omar Ahmad, Advanced Trainee in Neurology

STUDENTS
Ms Diana M Perriman, NH&MRC Dora Lush Scholar, PhD Student
Several ANU medical students have been involved with student projects

COLLABORATIVE ASSOCIATES
Professor Richard Lindley, Department of Geriatrics, Westmead Hospital, Sydney
Professor Craig Anderson, Department of Neurology, The George Institute, Sydney
Professor Philip Bath, Department of Medicine, University of Nottingham, UK
Professor Nancy J Newman, Department of Neuro-Ophthalmology, Emory University, Atlanta, Georgia, USA
Professor Valérie Biousse, Department of Neuro-Ophthalmology, Emory University, Atlanta, Georgia, USA
Professor Elsdon Storey, Neurologist, Alfred Hospital and Monash University, Melbourne
Professor Rosemary Martin, School of Biochemistry and Molecular Biology, Australian National University, Canberra
Professor John Morris, Neurologist, Westmead Hospital, Sydney
Associate Professor Ted Maddess, Research School of Biological Sciences, Australian National University, Canberra
Associate Professor Isla M Williams, Neuro-ophthalmologist, Monash University, Melbourne
Associate Professor Andrew Neely, Department of Engineering, University of New South Wales at the Australian Defence Force Academy, Canberra
Associate Professor Paul Smith, Trauma and Orthopaedic Unit, Canberra Hospital and Australian National University, Canberra
Dr Ross O’Neil, Department of Medical Imaging, Canberra Hospital and Australian National University, Canberra
Dr Lavinia Hallam, Department of Pathology, Canberra Hospital and Australian National University, Canberra
Dr Andrew James, Research School of Biological Sciences, Australian National University
Dr Jennie Scarvell, Trauma and Orthopaedic Unit, Canberra Hospital and Australian National University, Canberra
Dr Larry Abel, Royal Victorian School of Optometry, Melbourne
Dr Elizabeth Pepper, Neurologist, Westmead Hospital, Sydney
Mr Gawn McIlwaine, Consultant Ophthalmologist, Mater Hospital, Belfast, UK
Dr Chen Ming Sheng, Neurologist, Longyan No. 1 Hospital, Fujian, China
**RESEARCH PROJECTS**

The use of eye movement measurement as a potential tool to study aging and degenerative disorders of the brain (A/Prof Christian Lueck in association with A/Prof Isla Williams and Dr Larry Abel).

*The department has a research interest in looking at changes in eye movement parameters with aging, aiming to try to develop a useful biological marker of aging and degenerative diseases.*

Multifocal visual evoked potentials in multiple sclerosis and other neurological disease (A/Prof Christian Lueck in association with A/Prof Ted Maddess and Dr Andrew James).

*The department is collaborating with the research school of biological sciences to determine whether mfVER might be a useful adjunct to, or even a replacement for, MRI in the management of multiple sclerosis and other neurological disorders. (See Presentation 20).*

The timing of anticoagulation in acute stroke presumed to result from an embolus from the heart in patients with atrial fibrillation (A/Prof Christian Lueck, Dr Andrew Hughes, Dr Omar Ahmad).

*The department is in the process of setting up a multicentre trial (ACES) to try to determine the optimum timing of anticoagulation in this setting – a common clinical problem without an evidence-based answer. (See Presentations 3 and 9).*

An audit of the management of optic neuritis by Australian and New Zealand ophthalmologists and neurologists (A/Prof Christian Lueck in association with Prof Nancy Newman, Prof Valérie Biousse and others).

*This questionnaire survey was performed as part of a large-scale international study in conjunction with a group of neuro-ophthalmologists based in Atlanta, Georgia, USA. (See Publications 4 and 5, and Presentations 1, 2, and 4).*

A study of neurological advanced training in Australia (A/Prof Christian Lueck in association with Prof John Morris and Dr Elizabeth Pepper).

*This questionnaire survey was performed in conjunction with neurologists at Westmead Hospital, and demonstrated considerable variation in training at different sites across the country, generating discussion at a National level which will hopefully result in improved training in neurology. (See Publication 3, and Presentation 6).*
Finite element modelling of compression of the optic chiasm (A/Prof Christian Lueck in association with A/Prof Andrew Neely, Mr Gawn McIlwaine, Dr. Ross O’Neil, Dr. Lavinia Hallam and others).
The department is involved with a group of engineers at the Australian Defence Force Academy and an ophthalmologist in Belfast, UK, looking at finite element modelling of the process of compression of the optic chiasm by tumours in an effort to understand the phenomenon better. We are also involved in related pathological and radiological studies. (See presentation 18).

Spinocerebellar Ataxia (A/Prof Christian Lueck in association with Prof. Elsdon Storey and others).
The department has been involved with a group in Melbourne which has described a new dominantly-inherited spinocerebellar ataxia (SCA 30). (See Publication 6, and Presentation 12).

Investigation into thoracic kyphosis in stroke and normal aging (A/Prof Christian Lueck, Dr Andrew Hughes, in association with A/Prof Paul Smith, Dr Jennie Scarvell, Ms Diana Perriman and others).
The department is collaborating with the Trauma and Orthopaedics Unit at the Canberra Hospital to study the development of increased kyphosis with ageing and stroke, and how this might be treated. (See presentations 16).

The Use of Coaguchek as a tool for measuring coagulation urgently in thrombolysis patients (A/Prof Christian Lueck, Dr Andrew Hughes, Ms, Isabel Harvey).
The department is investigating the possibly use of this tool in the emergency setting.

Clinical Audit (A/Prof Christian Lueck, Dr Andrew Hughes, Dr Omar Ahmad, Ms. Isabel Harvey, Ms Angela Borbelj, Ms Kate Martin, in association with various medical students, registrars and Dr Chen Ming Sheng).
The department is actively engaged in various audits looking at different aspects of the management of stroke and other neurological conditions. This has generated several presentations and publications at National and International Meetings and peer-reviewed journals. (See Publications 1and 7, and Presentations 5,7,11,13,14).

Case reports (A/Prof Christian Lueck, Dr Andrew Hughes, Dr. Omar Ahmad, in association with various registrars and other Canberra Hospital clinicians).
Members of the department have presented a number of case reports to various scientific meetings, and are at various stages in the process of preparing written papers for submission to peer-reviewed journals. (See presentations 10,15,17,19).

Other Clinical Research (A/Prof Christian Lueck, Dr Andrew Hughes, Ms Isabel Harvey in association with Prof Richard Lindley, Prof Craig Anderson, Prof Philip Bath and others).
The department is involved in several investigator-led clinical trials including IST-3, INTERACT, and ENOS. (See Publication 2, and Presentation 8).

Pharmaceutical Company Research (A/Prof Christian Lueck, Dr Craig McColl, Dr Omar Ahmad in conjunction with the Clinical Trials Unit).
The department is involved in a small number of clinical trials funded by pharmaceutical companies, specifically PERFORM, MAZE, CogniMS and BEGIN.
FUNDING

<table>
<thead>
<tr>
<th>Date</th>
<th>Source</th>
<th>Investigator/Grantee</th>
<th>Title</th>
<th>Amount</th>
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<tr>
<td>October, 2006</td>
<td>The Canberra Hospital Private Practice Fund</td>
<td>Lueck CJ</td>
<td>Evaluation of the management of Optic Neuritis.</td>
<td>$7,999</td>
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<tr>
<td>October, 2006</td>
<td>NH&amp;MRC, 457343</td>
<td>Lindley R, Levi C, Read S, Parsons M, Hand P, Lueck C</td>
<td>Project grant: The third international stroke trial.</td>
<td>$210,000</td>
</tr>
<tr>
<td>January, 2007</td>
<td>NH&amp;MRC Dora Lush Scholarship Grant 41027</td>
<td>Lueck CJ, Perriman D</td>
<td>Electrogoniometric measurement of kyphosis in stroke.</td>
<td>$90,000</td>
</tr>
<tr>
<td>January, 2007</td>
<td>Rsbs, Biotechnology Research Centre</td>
<td>Maddess T, James AC, Lueck CJ, Caetano T</td>
<td>Neurodegenerative Diseases and Vision.</td>
<td>$156,904</td>
</tr>
<tr>
<td>December, 2007</td>
<td>The Canberra Hospital Private Practice Fund</td>
<td>Hughes A</td>
<td>Kyphosis in stroke: electrogoniometric measurement and evaluation of a rehabilitation strategy</td>
<td>$34,909</td>
</tr>
<tr>
<td>September, 2008</td>
<td>ACT Health</td>
<td>Lueck CJ</td>
<td>The Anticoagulation in Cardioembolic Stroke (ACES) Trial.</td>
<td>$45,940</td>
</tr>
<tr>
<td>December, 2008</td>
<td>The Canberra Hospital Private Practice Fund</td>
<td>Lueck CJ</td>
<td>Correlation of eye movements with peripheral neuromuscular parameters in health and disease</td>
<td>$65,844</td>
</tr>
</tbody>
</table>

PUBLICATIONS


O Ahmad, K Ahmad, KBG Dear, I Harvey, A Hughes, CJ Lueck. Atrial Fibrillation and Anticoagulation in a Stroke Unit Population. *Internal Medicine Journal* (in press)
PRESENTATIONS/ABSTRACTS


O Ahmad, I Harvey, K Ahmad, A Hughes, CJ Lueck. Atrial fibrillation and anticoagulation in a stroke unit population. Poster presented at 1st Annual Scientific Meeting of Australian and New Zealand Association of Neurologists, Alice Springs, 21–25th May, 2007


DM Perriman, JM Scarvell, A Hughes, CJ Lueck, PN Smith. Which is the best exercise to train the thoracic erector spinae? A surface EMG study. Poster presented at the Health and Medical Research in the Canberra Region Conference, Canberra, June, 2008


AWARDS


This won the NOSA prize for best registrar presentation at the meeting