



MENZIES RESEARCH INSTITUTE
Annual Report 2008



Menzies
Research
Institute





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CHAIRMAN'S AND DIRECTOR'S REPORT

The Menzies Research Institute (Menzies) strengthened its unique place in Australian medical research with a period of unprecedented growth during 2008.

Strategy and Growth

In 2008, Menzies' total income increased from \$12.1 million in 2007 to \$17.4 million – a 56 per cent growth rate. Research income grew to \$12.9 million, a 51 per cent growth from 2007 and competitive grant income increased to \$8.7 million, a remarkable 60 per cent growth rate from the previous year. This success in attracting significant competitive funding highlights the growing strength of our team.

As a result of the huge increase in research projects being undertaken by Menzies, staff and student numbers increased significantly from 160 in 2007 to 277 in 2008.

In 2008, Menzies further increased its involvement in a number of commercialisation activities, including the formation of TasTherapeutics Pty Ltd, a company spun-out of Menzies. In addition, a number of provisional

and international patent applications for discoveries that have commercial potential were filed by Menzies.

With sound strategies and governance arrangements in place, we are optimistic that we will continue to grow and build high quality medical research at Menzies.

Research Highlights

There were many commendable research highlights and awards during the year. A few examples include:

- Over 70 research grants were awarded to Menzies' researchers during 2008, through government grants and philanthropic bodies, testimony to the high quality of research Menzies is generating.
- Menzies exceeded the national average success rate with seven National Health and Medical Research Council (NHMRC) project grants awarded for 2009.

- Menzies lifted its average and median publication impact factor by 12 per cent in 2008, signifying the increase in the quality of research publications.
- A number of Menzies' staff members were invited to deliver keynote addresses or to present refereed papers at major national and international conferences.
- Professor Simon Foote was invited to speak at the National Institutes of Health in the United States of America in November 2008.
- Professor Mike Clark was appointed an Emeritus Professor of the University of Tasmania.
- Clare Smith was the Tasmanian winner of AusBiotech's Student Excellence Awards. This is a national event that encourages students to think about the potential commercial outcomes of their research. Clare is



researching a new antimalarial therapy and is supervised by Professor Simon Foote.

- Heather McGee was awarded the best student presentation in the Mutagenesis and Experimental Pathology section of the Australian Health and Medical Research Congress in Brisbane. Her presentation was titled "Early changes in the skin immune system following neonatal exposure to ssUVR".
- Dr Kristy Sanderson was elected to the national executive committee of the Australasian Society for Psychiatric Research (ASPR), Australasia's foremost society for psychiatric and mental health researchers.

Young Researchers

Providing a stimulating and rewarding learning environment that is responsive to student needs is an important focus of Menzies. In 2008 we had 51 students enrolled in postgraduate degrees.

Menzies is committed to educating the medical researchers of tomorrow. We showed commitment to developing the top researchers of the future, by providing professional development opportunities throughout the year. Students took part in seminars, teaching opportunities and received travel grants with support from Menzies and the University of Tasmania.

Key Partners

Our success has been the result of great co-operative effort involving a number of key Menzies' stakeholders including, the University of Tasmania, especially the School of Medicine, The Menzies Foundation, the Tasmanian Government and a number of organisations directly supporting our research, such as The Atlantic Philanthropies, Australian Cancer Research Foundation, the Royal Hobart Hospital Research Foundation, the Royal Hobart Hospital, Cancer Council Tasmania, Arthritis Australia and the Masonic Centenary Medical Research Foundation.



Dr Dan Norton

Our work is not possible without the continuous support and generosity of the whole community that enables us to carry out vital research. We thank all our generous donors and volunteers who contributed to our success in 2008 for their commitment to research.

Our New Building

This year we watched with great enthusiasm, as the new Menzies' building unfolded into an architectural splendour. Staff were consulted and provided ongoing input into the design to ensure a world class facility upon completion.

We eagerly await completion of the new building in late November 2009 and look forward to moving into our new home in early December.

The building will boast research equipment and technology designed to take advantage of recent developments in engineering and biological advances. To accommodate the rapid expansion of Menzies, a Stage Two project is required. Menzies is currently campaigning to raise the required \$90 million and secured \$44.7 million from the Commonwealth in the May 2009 budget.

2009 and Beyond

While Menzies grew considerably in 2008, the tough economic times may have an impact on Menzies



Professor Simon Foote

in 2009. We will be in a position to continue with our core activities, nevertheless, continued support from our donors will be even more vital if we are to maintain the pace and quality of our research.

With the ongoing dedication of our researchers and staff, visionary guidance from our board and senior management team, and support from corporate and individual donors, we are confident that 2009 will be a positive year for the Menzies Research Institute.

Dr Dan Norton
Chairman

Professor Simon Foote
Director

The Board

The Board is the governing body of the Menzies Research Institute.

The Board brings a diverse range of expertise across business and finance, health and research.

Board Directors:

Dr Dan Norton (Chairman)

Dr David Boadle

Professor Simon Foote

Sir Guy Green AC KBE CVO

Mr Damon Thomas

Professor Jonathan West

Professor Judith Whitworth AC

MANAGEMENT

Menzies' Board is responsible for the overall corporate governance of the Menzies Research Institute.

The Director is empowered to manage the operations of Menzies in conformity with agreed plans, policies and procedures, and is accountable to the Board for operational performance.

The role of the Senior Management Team is to advise the Director on issues arising during the course of the operation of Menzies.

Members of the Senior Management Team in 2008 were:

- Professor Simon Foote (Director)

- Professor Michael Clark (Senior Member)
- Associate Professor Alison Venn (Deputy Director)
- Professor Graeme Jones (Senior Member)
- Professor Haydn Walters (Senior Member)
- Associate Professor Inn Chuah (Senior Member)
- Professor James Vickers (Deputy Director)
- Dr Roger Chung (Member)
- Mark Bennett (General Manager)

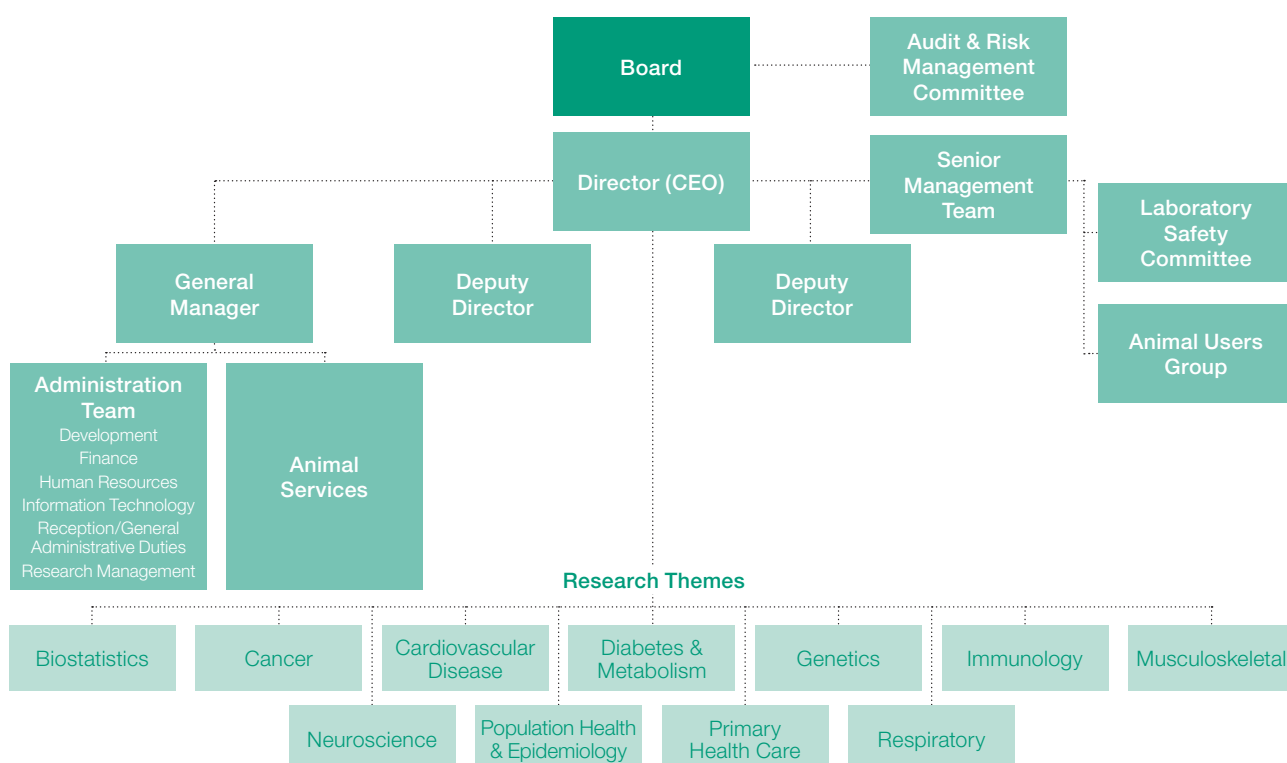
Menzies' research themes are consistent with our objectives and

build on Menzies' foundation in population health research.

Supporting the research programs is the Administration Team, including research management, information technology, human, financial, communication and physical resource management. Development activities promote Menzies' research and facilitate the development of beneficial relationships with government, industry and the community.

Honorary researchers, scientific advisers and volunteers also provide invaluable support.

ORGANISATIONAL STRUCTURE



RESEARCH

Senior Members

Associate Professor Leigh Blizzard
Associate Professor Steve Cheung
Associate Professor Inn Chuah
Professor Michael Clark
Professor Simon Foote
Professor Graeme Jones
Professor Mark Nelson
Associate Professor
Stephen Rattigan
Professor David Small
Associate Professor Bruce Taylor
Associate Professor Alison Venn
Professor James Vickers
Professor Haydn Walters
Associate Professor Adrian West

Members

Dr Roger Chung
Dr Tracey Dickson
Dr Changhai Ding
Dr Adele Holloway
Associate Professor David Johns

Dr Michelle Keske
Dr Stephen Richards
Dr Kristy Sanderson
Dr Jim Stankovich
Dr Ingrid van der Mei
Dr Tania Winzenberg
Associate Professor Greg Woods
Dr Jane Zochling

Honorary Researchers

Honorary Research Professors

Professor Terry Dwyer
Professor Anne-Louise Ponsonby

Honorary Associates

Professor Marianne Berwick
Dr Liesel Fitzgerald
Mrs Dace Shugg
Dr Velandai Srikanth

Honorary Fellows

Dr Trevor Beard
Professor David Hosmer
Mr Barry Moore
Dr Fiona Scott

Honorary Members

Professor Michael Ashby
Dr Melanie Bahlo
Dr John Burgess
Professor Don Chalmers
Professor Peter Dargaville
Dr Shyamali Dharmage
Dr Matthew Jose
Professor Ray Lowenthal
Dr Katherine Marsden
Professor Andrew Palmer
Dr David Reid
Professor Andrew Robinson
Professor Terry Speed
Professor Jeff Summers
Associate Professor Paul Turner
Dr Chris Ward
Dr Michael Wiese
Associate Professor
Richard Wood-Baker

RESEARCH



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BIOSTATISTICS – GENETIC

MEMBER:

Dr Jim Stankovich

RESEARCH TEAM:

Dr Russell Thoon, Genetic Statistician

Dr Devindri Perera, Genetic Statistician

Edward Doddridge, UROP Student

INTERNAL COLLABORATORS:

Professor Simon Foote, Senior Member

Associate Professor Bruce Taylor, Senior Member

Dr Ingrid van der Mei, Member

Dr Joanne Dickinson, Senior Research Fellow

Dr Brendan McMorran, Senior Research Fellow

Annette Banks, Genealogist

Dr Briony Patterson, Research Fellow

Andrea Polanowski, Research Assistant

Clare Smith, PhD Student

Dr Elizabeth Tegg, PhD Student

Bradley Wray, Student

EXTERNAL COLLABORATORS:

Associate Professor Patcharee Lertrit, Mahidol University, Thailand

Bussaraporn Kunhapan, Mahidol University, Thailand

Dr Taisei Mushiroda, RIKEN, Japan

Dr Timothy Thornton, University of California Berkeley

Dr Justin Rubio, Howard Florey Institute, University of Melbourne

Dr Melanie Bahlo, Walter and Eliza Hall Institute of Medical Research

Dr Sharon Browning, Department of Statistics, University of Auckland

Dr Brian Browning, Department of Statistics, University of Auckland

Professor Matthew Brown, Diamantina Institute, University of Queensland

The Australia and New Zealand Multiple Sclerosis Genetics Consortium

Dr Helmut Butzkueven, Howard Florey Institute, University of Melbourne

Dr Anneke van der Walt, Royal Melbourne Hospital

Associate Professor David Amor, Murdoch Children's Research Institute, Melbourne

FUNDING BODIES:

Australian Research Council

Cancer Australia

Cancer Council Tasmania

David Collins Leukaemia Foundation

Multiple Sclerosis Research Australia

National Health and Medical Research Council

Royal Hobart Hospital Research Foundation

The Genetics of Multiple Sclerosis

Multiple sclerosis (MS) is a progressive neurodegenerative condition that afflicts young adults. It is triggered by a complex mixture of genetic and environmental factors.

We are performing statistical analyses to identify genetic risk factors for MS by analysing genetic variants measured in thousands of individuals with MS. This study is a collaboration with a large consortium of Australian and New Zealand genetics researchers.

We are also investigating whether certain genetic variants are associated with severity of MS.

In a study of Tasmanians with MS, we found no association between the gene CTLA4 and risk of disease. In studies of over 1000 Tasmanians



and Victorians with MS, we confirmed that the genes KIAA0350, IL2RA, RPL5 and CD58 influence susceptibility to disease.

We commenced analysis of a larger dataset involving around 4000 Australians and New Zealanders with MS to search for new MS genes. We also commenced studies investigating

whether certain genes are associated with severity of disease.

The Genetics of Hyperplastic Polyposis Syndrome

Hyperplastic polyposis syndrome (HPS) is a rare form of hereditary bowel cancer. It is characterised by large numbers of hyperplastic polyps



Dr Jim Stankovich

in the bowel. The syndrome may be caused by a recessive gene, and it appears to be more common in the Tasmanian population than in other parts of Australia. We are analysing data to try and identify a mutation causing the disease.

We obtained funding from the Royal Hobart Hospital Research Foundation to support this project, led by clinical geneticist Associate Professor David Amor.

We have genotyped DNA samples from a number of Tasmanians with HPS, and commenced analysis of this genetic data.

The Genetics of Leber's Hereditary Optic Neuropathy

Leber's Hereditary Optic Neuropathy (LHON) is a rare form of visual impairment which occurs in young adults, particularly men. It is caused

by the degeneration of retinal ganglion cells, which leads to loss of central vision.

LHON is maternally inherited, and is primarily caused by mutations in the mitochondria, the energy powerhouses of cells. However there are other genetic factors involved in LHON, and we are searching for these factors by studying families with LHON from Thailand.

Thai PhD student Bussaraporn Kunhapan visited Hobart for seven months to work on statistical analysis of genetic data from this project.

Genetic statistician Dr Timothy Thornton from the USA also visited briefly, and made valuable contributions to this project.

We commenced writing up results for publication in 2008.

Patterns of Human Genetic Variation and Evidence of Selection

Patterns of human genetic variation reflect forces of natural selection acting over thousands of years.

In particular, malaria has exerted strong evolutionary pressures, increasing the frequencies of genetic variants which protect against malaria. We are studying patterns of genetic variation to identify genes which may affect susceptibility to malaria, and may hence be suitable targets for anti-malarial therapies.

We identified a number of genes expressed in red blood cell progenitors which show evidence of selection, and therefore may influence susceptibility to malaria.

A database of these genes was prepared, for use by laboratory-based malaria researchers to identify possible targets for anti-malarial therapies.

BIostatistics, NEUROepidemiology of AGEING, INTERNATIONAL HEALTH AND OTHER PROJECTS

SENIOR MEMBER:

Associate Professor Leigh Blizzard

RESEARCH TEAM:

Biostatistics

Dr Devindri Perera,
Biostatistician/Genetic Statistician

Dr Russell Thomson,
Biostatistician/Genetic Statistician

Dr Stephen Quinn, Biostatistician

Dr Karen Wills, Biostatistician

Petr Otahal, Statistical Officer

Jana Canary, PhD Candidate

Neuroepidemiology of Ageing

Dr Velandai Srikanth,
Chief Investigator

Associate Professor Alison Venn,
Senior Member

Dr Sue Pearson, Research Fellow

Zoe Perry, Psychologist

Emma Rouse, Psychologist

Jan Stacey, Psychologist

Sally Merritt, Ultrasound Radiography

Jason Little, Psychologist

Glenna Harvey, Project Coordinator/
Retinal Photography

Kate Butorac, Project Coordinator

Alfonso Ayesa, Research Officer

Costan Magnussen, Research Officer

Charlotte McKercher,
Research Officer

Stella Foley, Research Officer

Gloria Lawson, Nurse

Keryl Houlgrave, Participant Liaison

Michele Callisaya, PhD Candidate/
Gait Assessments

Kara Martin, PhD Candidate

Georgie Boon,
Administrative Assistant

Pam McDonald,
Administrative Assistant

Kate Probert, Administrative Assistant

Wendy Davidson, Volunteer –
Clinics and Administration, Data Entry

Kate Rutherford, Volunteer

Marie Steele, Volunteer

Bob Uren, Volunteer

Marylyn Uren, Volunteer

International Health

Associate Professor Alison Venn,
Cancer Registration

Dr Velandai Srikanth,
Stroke Surveillance

Dr Michael Schmidt, Research Fellow

Dr Tran Hoang Mai, Honorary Fellow

Dr Phung Ngoc Hai, Project Manager

Dr Tran Quoc Bao, Project Officer –
Surveillance System (Hanoi)

Dr Tran Thanh Huong,
Project Officer (Hanoi)

Dr Do Khang Chien, Project Officer –
Clinical Services (Hanoi)

Mr Petr Otahal, Statistical Consultant

Kate Butorac, Survey Consultant

Catrina Boon, Survey Consultant

Mr Costan Magnussen,
Survey Consultant

Dr Seana Gall, Stroke Surveillance

Pham Diem Hao,
Project Assistant (Hanoi)

Dr Tran Thanh Thu,
Project Assistant (Hanoi)

Le Thanh Hai,
Project Assistant (Hanoi)

Mark Bennett, Project Administration

Tim Albion, IT Consultant

Dr Au Bich Thuy, PhD Candidate

Other Projects

Dr David Reid, Chief Investigator

Professor Graeme Jones,
Senior Member

Professor Haydn Walters,
Senior Member

Associate Professor Richard
Wood-Baker, Honorary Member

Dace Shugg, Honorary
Project Adviser

Ceri Flowers, Project Officer

Peta Hitchens, PhD Candidate

INTERNAL COLLABORATORS:

Dr James Fell, School of Human
Life Sciences, UTAS

EXTERNAL COLLABORATORS:

Professor Ron Barry,
University of Alaska, Fairbanks

Dr Lesley Day, Monash University
Accident Research Centre

Professor Terry Dwyer, Murdoch
Childrens Research Institute

Dr Robert Granger,
Royal Hobart Hospital

Professor David Hosmer,
University of Massachusetts

Dr Pham Hung Luc, Can Tho
University of Medicine and Pharmacy

FUNDING BODIES:

National Health and Medical
Research Council

The Atlantic Philanthropies Inc

Goodness-of-Fit Testing of Log-Link Models for Categorical Outcome Data

Statistical methodology for the study of diseases and medical conditions

We have contributed to recent advances in statistical methodology that have made relative risk estimation possible for follow-up data with continuous covariates. The mathematical models are the log binomial model for binary outcomes, and the log multinomial model for multinomial outcomes. The aim of this project is to investigate whether the fit of a log binomial model can be assessed using goodness-of-fit tests developed for the binary logistic model, and whether the fit of a log multinomial model can be assessed using goodness-of-fit tests developed for the multinomial logistic model.

Work in 2008 focused on writing the programming code required to fit the models and calculate the

test statistics required under each of the goodness-of-fit tests. This is a straightforward task in the simplest cases (e.g. Pearson chi-squared statistic) but is complex and time-consuming in other cases particularly those for which the test statistics are applied to weighted or smoothed functions of the residuals and require pre-estimation of the weights and tuning parameters. This has been completed for the log binomial model, and simulation studies have commenced to assess the adequacy of the goodness-of-fit tests for this model.

Survey of Risk Factors for Cardiovascular Diabetes in Can Tho, Viet Nam

Non-communicable diseases

The aims of this study are to assess the cardiovascular diabetes (CVD) risk profile of the population of the Can Tho province in the Mekong Delta region of Viet Nam, compare

the reliability and validity of alternative questionnaire measures of physical activity, assess the feasibility and validity of pedometer estimates of physical activity, and to examine the associations of physical activity and CVD risk indicators.

Work in 2008 focused on analysis of the data and preparation of manuscripts for publication. We expect to have four papers accepted for publication in international journals in 2009.

Project to Develop an Integrated Surveillance System for Non-Communicable Diseases in Viet Nam

Non-communicable diseases

The aim of this project is to develop a sustainable system for surveillance of non-communicable disease (NCD) in Viet Nam. The focus of initial action is on heart disease and stroke, diabetes mellitus and cancer. Primarily what



Left to Right: Associate Professor Leigh Blizzard (back row), Petr Otahal, Jana Canary, Dr Karen Wills and Dr Stephen Quinn

is sought is a nationally coordinated system for assembling information on the incidence/prevalence of those chronic diseases and their modifiable risk factors, enabling these to be tracked over time in response to national strategies to prevent and manage NCD. The project has two further arms of healthy lifestyle intervention and monitoring clinical outcomes of NCD management.

Work in 2008 focused on training local collaborators to undertake surveys of risk factors for NCD. In May, we conducted training workshops in Hanoi, Hue and Ho Chi Minh City. In November/December, we returned to conduct further training and supervise pilot studies in Bin Dinh, Can Tho, Dak Lak, Hue, Hanoi, Hoa Binh, Ho Chi Minh City and Thai Nguyen.

Cigarette Type and Lung Function Study

Obstructive lung disease

The premise for monitoring and regulating tar yields as part of Australia's comprehensive tobacco control strategy was that cigarettes with lower tar delivery would be less hazardous. The study seeks to determine whether there are differences in lung function between people who smoke low-yield cigarettes, and those who smoke cigarettes that have higher yields. To shed light on the causal pathways involved, the lungs of participants are scanned to determine whether the pattern of deposition of smoke-like particles differs between smokers of lower-yield and higher-yield cigarettes.

Analyses of the data using conventional measures of lung function – including forced expiratory volume in 1 second, forced vital capacity and mid-flow forced expiratory flow – is complete. We now only await data from the experimental multiple breath nitrogen washout test. The software provided to interpret the output of this test has failed, and we have contracted computer programming support to recover it.

Jockey Falls and Performance Attributes

Falls and injuries to jockeys in thoroughbred horse racing

This study is using a database of 3,360 jockey falls resulting in 861 injuries from 748,367 rides in 75,434 races and 10,373 race meetings in Australia during 2002-06 to identify potentially modifiable factors that are associated with falls and injuries to jockeys. A second arm of the study is to trial measurements of the physiological and performance attributes of jockeys and track-work riders licensed to ride in Tasmania.

Compilation of the database has been completed and analysis of the data commenced. A first paper, reporting the incidence of falls, injuries and fatalities was accepted for publication in the Medical Journal of Australia in August 2008. Physiological and performance assessments of 28 jockeys and track-work riders were completed in May 2008. Peta Hitchens, the PhD candidate working on this study, suspended her candidature in September to assist the Tasmanian racing industry during its re-structure.

Tasmanian Study of Cognition and Gait (TASCOG)

Falls and dementia in older people

TASCOG is a study of cerebrovascular mechanisms underlying gait, balance and cognition in a population-based sample of Tasmanian people aged at least 60 years. The primary aim is to measure brain structural changes identified by magnetic resonance imaging (MRI), and to examine in detail the effect of their volume and location on key aspects of brain function (gait, balance and cognition). A further aim of the study is to discover factors that can be modified or treated in order to prevent dementia and falls, and thus contribute in a significant way to improving the health of older Australians.

This has been a very successful year for this cross-sectional study of brain ageing, its effects and determinants. Overall 425 participants were recruited with 400 having MRI scans. There have already been five papers published or accepted for publication, including four in international high-ranking journals in the fields of cerebrovascular disease and ageing. Cerebral white matter lesions (WML) and brain atrophy have been found to be correlated with several gait and balance variables and, for the first time, were shown to predict the future risk of falls. Other analyses have focused on age-related factors responsible for poorer gait and balance. Three manuscripts are currently in submission or under revision, and several more are in preparation. There have been several presentations at key national and international scientific meetings.

Cognition and Diabetes in Older Tasmanians (CDOT) Study

Type 2 Diabetes Mellitus and Dementia

CDOT is a study aimed at studying the reasons for the development of cognitive decline in people with Type 2 Diabetes, with important roles postulated for cerebrovascular disease, neurodegeneration and advanced glycation endproducts (AGEs). The findings may assist in delaying or preventing dementia in people with Type 2 Diabetes.

This project is well on the way to completion in 2010. Additional recruitment sources were identified including the Tasmanian Diabetes Registry and the Endocrinology Clinics at the Royal Hobart Hospital. We have recruited 245 participants and completed all measures on 200 of them. The remaining 45 participants will be measured by mid 2009, following which data cleaning and analyses will begin. There have already been two publications arising from this study.

CANCER AND IMMUNOLOGY

SENIOR MEMBER:

Dr Adele Holloway

RESEARCH TEAM:

Dr Fiona Poke,
Junior Postdoctoral Fellow
Alison West, Research Assistant
Owen Sprod, PhD Student
Abeer Qadi, PhD Student

EXTERNAL COLLABORATORS:

Professor Frances Shannon, John
Curtin School of Medical Research,
Australian National University

FUNDING BODIES:

David Collins Leukaemia
Foundation

National Health and Medical
Research Council



Dr Adele Holloway specialises in cancer and immunology

Deregulation of Gene Expression by RUNX1 Fusion Proteins in Leukaemia

Leukaemia commonly arises due to genetic changes to the RUNX1 (or Acute Myeloid Leukaemia 1) gene.

Whilst reversing these genetic changes remains a long term goal, this is currently not possible. However, we have shown that the altered forms of RUNX1 found in leukaemic cells cause changes, referred to as epigenetic changes, to target genes.

These epigenetic changes are thought to contribute to the development and progression of leukaemia. For example, we have shown that altered forms of RUNX1 cause epigenetic changes to the GM-CSF gene, leading to its silencing. However we have found that these epigenetic changes can be reversed by pharmacological intervention, allowing the GM-CSF gene to be switched back on.

In addition we have identified a number of new targets of RUNX1. The expression of these genes is altered in cells containing the leukaemic forms of RUNX1, and we are currently investigating whether this contributes to the development of leukaemia.

Switching Genes on in Immune Cells: How does Basal Chromatin Structure Predict Cytokine Gene Responses?

Cells within the immune system are activated to fight infection by producing a host of signalling molecules called cytokines. Immune diseases arise when these genes are not switched on at the correct time and place.

This project aims to determine how particular marks or 'tags' associated with the DNA encoding cytokine genes controls their ability to be switched on in response to immune signals.

The DNA environment of a gene can be changed by the presence of different epigenetic marks or 'tags'.

We have identified a number of epigenetic 'tags' that mark the GM-CSF cytokine gene in a particular way only in cells in which it can be switched on. We have found that GM-CSF becomes overproduced if we increase the amount of these 'tags' associated with the gene.

Furthermore, by adding these 'tags' to the gene in other cell types we are able to switch the gene on in cells where it is not normally produced.

We are now in a position to determine how the underlying DNA sequence generates these 'tags' and whether the inappropriate expression of GM-CSF in immune diseases is associated with changes in these 'tags'.

CANCER AND IMMUNOLOGY

MEMBER:

Associate Professor Greg Woods

RESEARCH TEAM:

Jill Chuckowree, Technical Officer
Mark Cozens, Technical Officer
Narelle Phillips, Technical Officer
Nicholas Casey, PhD Student
Alexandre Kreiss, PhD Student
Dr Roslyn Malley, PhD Student
Heather McGee, PhD Student
Deborah Scott, PhD Student
Cesar Tovar, PhD Student

Gabriella Brown, Honours Student

Flora Cheung, Honours Student

LOCAL COLLABORATORS:

Emeritus Professor H Konrad Muller,
School of Medicine, UTAS

Dr Silvana Bettiol,
Lecturer in Microbiology,
School of Medicine, UTAS

EXTERNAL COLLABORATORS:

Professor Mary Norval,
University of Edinburgh

Dr Kathy Belov, University of Sydney

Dr Vanessa Hayes,
Children's Cancer Institute Australia
for Medical Research

Dr Elizabeth Murchison,
The Wellcome Trust Sanger Institute

FUNDING BODIES:

Australian Research Council

Cancer Council Tasmania

Clifford Craig Medical Research Trust

University of Tasmania Foundation
Inc, The Dr Eric Guiler Tasmanian
Devil Research Grant

The Effect of UV Radiation and Vitamin D Deficiency on the Development of the Skin Immune System

Sunshine is important for the production of vitamin D but severe sunburn in children promotes an increased risk of skin cancer in later life.

We propose that exposure to sunshine and vitamin D influences the development of the immune system and that vitamin D can protect against the deleterious effects of UVB-radiation. The outcomes from this research will indicate the importance of the developmental period for the skin immune system and how a balance of exposure to UVB and vitamin D production can influence these outcomes. This will have implications for skin cancer development.

We determined that vitamin D, obtained from the diet, can protect against UVB-radiation induced DNA damage.

The significance of this is that vitamin D could protect against the development of skin cancer.

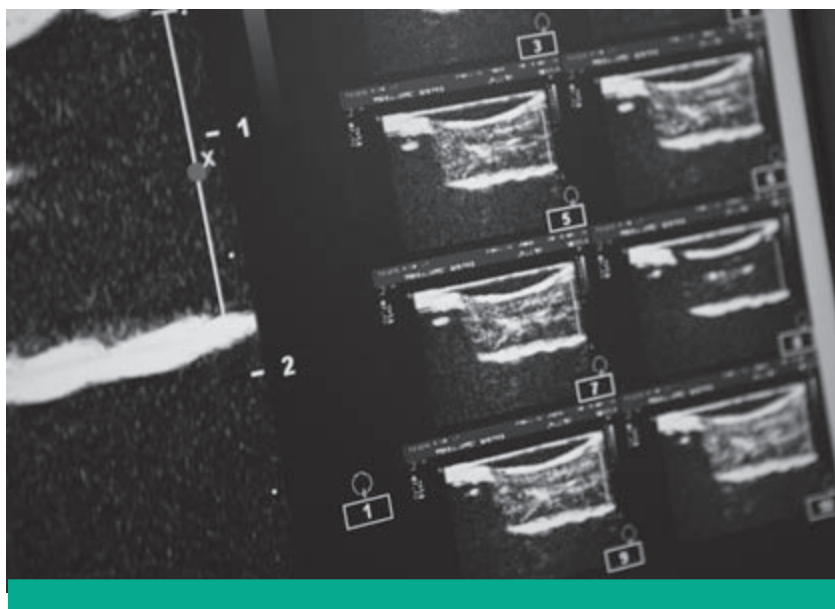
Interestingly, females responded more effectively than males. This may partly provide an explanation why males are more susceptible to skin cancer than females. Exposure of neonatal mice to sunlight, in the form of solar simulated radiation, altered the development of the skin immune system and increased the production of T regulatory cells.

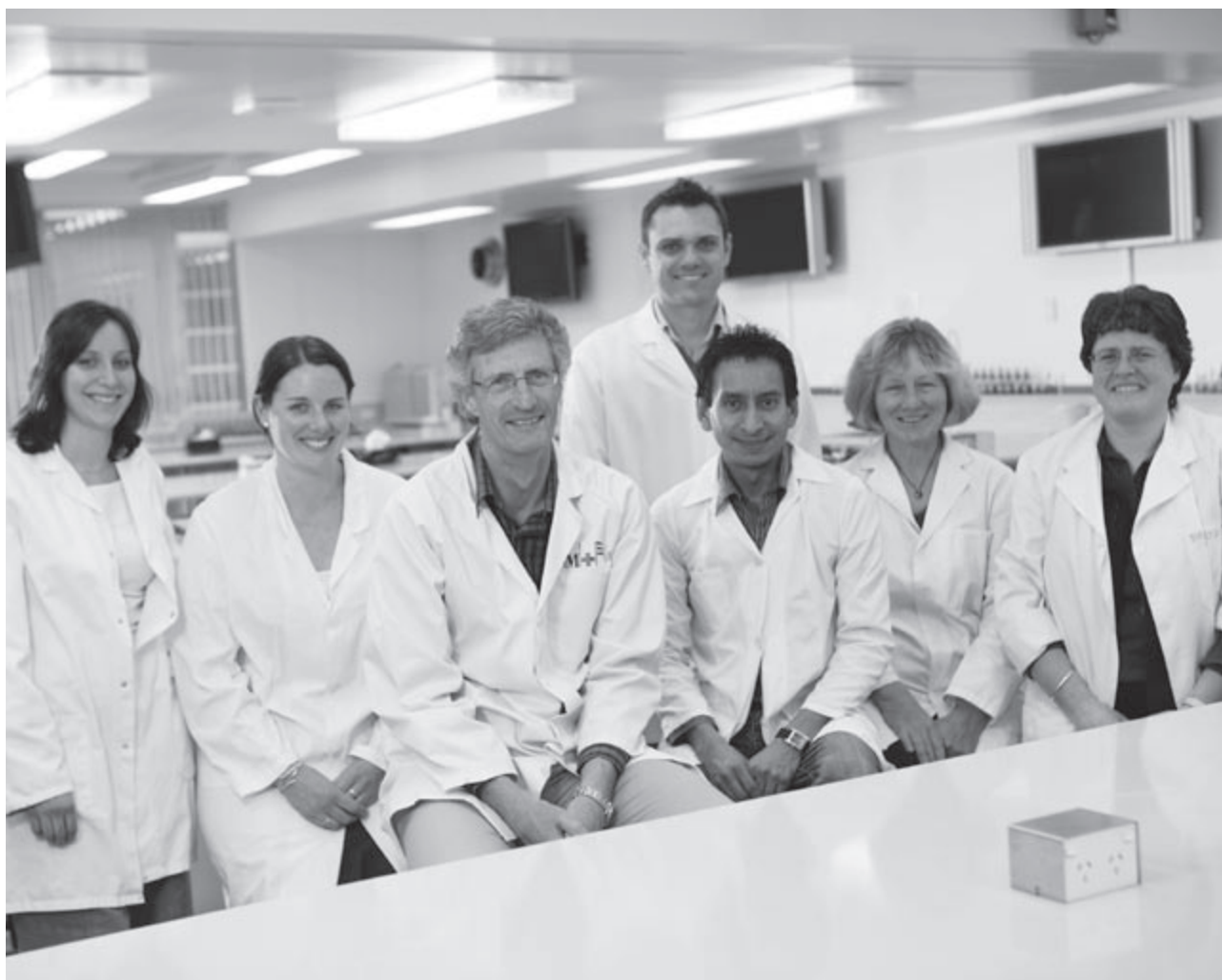
This resulted in an increased level of immunosuppression when the mice reached adulthood.

The Immune Responses of the Tasmanian Devil and the Devil Facial Tumour Disease

The Tasmanian devil is currently under threat from a devastating disease known as Devil Facial Tumour Disease (DFTD). A remarkable feature of this disease is that it is directly transferred between devils.

There has been no evidence of resistance against DFTD in the wild population. In order to evaluate





Associate Professor Greg Woods (third from left) and his team

how this transmissible cancer can avoid detection by the devil's immune system, we have undertaken a thorough analysis of the immune response of the Tasmanian devil, including immune responses against DFTD.

We have undertaken a range of studies on the structure and function of the immune system of the Tasmanian devil and remain convinced that devils have a competent immune system.

We also discovered that devils can produce an immune response that can protect devils against this disease, but the protection appears to be short lived.

A preliminary study on the effectiveness of chemotherapy indicated that DFTD could be killed

by cytotoxic drugs but when trialled on diseased devils the chemotherapy was partially effective. Analysis of the tumour has revealed that it is a rare peripheral nerve cell tumour.

Silencing the AML1/ETO Fusion Gene as a Treatment Strategy for Acute Myeloid Leukaemia

Acute myeloid leukaemia is a cancer of white blood cells. One cause is an alteration in the cell's DNA to produce a new gene called AML1/ETO. This gene alters the cell's regulatory mechanisms, resulting in uncontrolled growth.

If we could inactivate this gene we have a therapy that specifically targets the leukaemic cells. This study aimed at inactivating this cancer-causing gene with "RNA

interference". Our approach was to develop RNA sequences that would specifically bind and inactivate the AML1/ETO cancer gene, causing the cancer to stop growing.

"Short interfering" RNA molecules were added to cancer cells expressing the AML1/ETO cancer causing gene. Some encouraging results were initially obtained as two of the "short interfering" RNA that we designed, reduced the growth of the cancer cells but when the experiments were repeated, there were inconsistent results.

It was therefore decided to evaluate an alternative set of "short hairpin" RNA molecules. It would appear that "short hairpin" RNA molecules could be more effective at inactivating cancer cells than "short interfering" RNA molecules.

DIABETES AND METABOLISM

SENIOR MEMBERS:

Professor Michael Clark
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FUNDING BODIES:

Australian Research Council

National Health and Medical
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National Heart Foundation,
Australia

National Institutes of Health, USA

Central and Peripheral Actions of Insulin for the Control of Muscle Capillary Recruitment

The overall goal of the proposed studies is to explore the hypothesis that insulin controls microvascular perfusion of muscle by a central neural mechanism ending at terminal arterioles on the vasculature, and endeavour to identify the details of this control.

In-house novel techniques will be used for examining both the role of central control mechanisms involving the brain, as well as peripheral mechanisms, by local infusion of various agents likely to enhance or block insulin's microvascular action.

We have demonstrated that centrally administered insulin failed to show any increase in muscle capillary recruitment, glucose uptake, limb blood flow or capillary recruitment, until the amount administered began to spill-over into the systemic blood and raise plasma insulin concentrations.

However it was found that central administration (i.e. ICV) of a NOS inhibitor, L-NMMA, had no effect on blood pressure or heart rate, but blocked systemic insulin-mediated microvascular perfusion and femoral blood flow.

Additionally we have shown that a locally applied NOS inhibitor in the epigastric artery of the test leg blocked systemic insulin-mediated capillary recruitment.

Together these findings are suggesting that systemic insulin-mediated increases in limb blood flow and muscle microvascular perfusion may be regulated by a central pathway that is NO-dependent but not directly mediated by insulin.

In addition, both a central and peripheral NO-dependent component of systemically administered insulin is regulating muscle microvascular perfusion.



Associate Professor Stephen Rattigan and Dr Stephen Richards

Blood Flow Routes in Muscle

The overarching aim of this project is to use high-resolution imaging technology (contrast enhanced ultrasound, CEU) in vivo and tissue sectioning to characterise the role of nutritive and non-nutritive flow routes in muscle in relation to insulin action, insulin resistance, and exercise.

The central hypothesis is that non-nutritive blood flow in muscle constitutes a major proportion of flow under basal conditions and thus is a reservoir for the redistribution to nutritive capillaries in insulin action and exercise.

We are exploring whether the non-nutritive flow route is located in connective tissue within the muscle, and if this is where adipocytes proliferate in states of low physical activity, obesity and insulin-resistance.

Further, we are determining if insulin exerts both a vasodilatory (to dilate arterioles at the entry to capillary units) and a vasoconstrictor action (to constrict entry to the non-nutritive route) in muscle.

This project commenced in 2008 and therefore progress is still in its

infancy. However, we have already demonstrated that insulin-mediated microvascular perfusion is blunted in the high-fat fed rat, thus linking a dietary model of type 2 diabetes to a defect in the vascular action of insulin in muscle.

Further we have shown that an acute microsphere injection into rats in vivo causes insulin-resistance and decreased microvascular perfusion.

This model will be useful to demonstrate the chronic effects of impaired microvascular perfusion on insulin action in muscle.

Additionally preliminary findings suggest that acute exercise (electrical stimulations at different frequencies) causes a frequency-dependent increase in muscle microvascular perfusion but this effect is impaired during high fat feeding.

These findings were presented at the European Association for the Study of Diabetes (EASD), held in Rome 8–11 September, 2008 and the European Society of Microcirculation, held in Budapest, Hungary August, 2008.

Endothelin-1, Type 2 Diabetes and Hypertension

Endothelin-1 is a relatively recently discovered peptide hormone that is released by cells that line the blood vessels and is elevated in the blood of diabetics who have high blood pressure. Since this hormone constricts blood vessels and prevents full perfusion of muscle, delivery of insulin and glucose to the muscle cells becomes limited.

We propose that the diminished delivery of insulin and glucose contribute to insulin resistance, an early change that invariably precedes the development of type 2 diabetes.

We also propose that the vasoconstriction by endothelin-1 that causes the poor perfusion of muscle contributes to the high blood pressure of these individuals.

Our aims are to explore these relationships using animal models.

The most important finding from this study demonstrates that endothelin-1, a hormone principally released by the endothelial cells that line all of the blood vessels, markedly inhibited insulin action, particularly its vasodilatory action on blood vessels to increase delivery.

The findings suggest that elevated endothelin-1 levels that have already been reported by others in diabetics, may contribute to the insulin resistance of muscle by increasing vascular resistance and limiting insulin and glucose delivery.

Additionally elevated endothelin-1 levels also reduce aerobic exercise activity in muscle in association with an effect to increase blood pressure. These findings may help to explain the reduced aerobic exercise capacity of hypertensive patients that has been reported by other researchers.

Furthermore the novel fat cell hormone, adiponectin is able to oppose endothelin-1 action. This raises the possibility that adiponectin may be the body's means of counteracting raised endothelin-1 levels in obese patients, those with diabetes and cardiovascular disease.



GENETICS

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The Role Platelets Play in a Malarial Infection

Malaria is a parasitic disease that infects some 300 million people annually and kills more than one million children each year. It is a disease that has moulded the genome of humans with many mutations in the red cell genes co-localising with areas of high malarial endemicity. We are interested in the defence mechanisms the host employs to combat the disease.

Malaria is transmitted by mosquitoes and is common in third-world tropical countries. While the sporozoites, injected by the mosquito, infect liver cells, the rest of the infection centres on the red cell. Malarial parasites invade red cells, multiply, cause the cell to burst then repeat their cycle in

other red cells. People infected with the virulent *P. falciparum* form die from either severe anaemia, or from a syndrome called cerebral malaria. Cerebral malaria is caused by infected red cells sticking to the lining of blood vessels in the brain, causing the release of a cascade of highly active biological molecules called cytokines. This, and the decreased amount of oxygen arriving at brain cells, causes this disease, which has a high mortality rate.

Not all children infected with malaria die from the disease, despite being infected with similar parasites. We believe there are significant genetic differences between individuals that protect some people from the more severe consequences of the disease.

One potential host defence mechanism involves platelets. These cells normally regulate blood haemostasis, especially blood clotting, but also have an appreciated importance in immune defence. Our group has discovered that platelets can bind to infected red blood cells and kill the parasite inside. We believe this is a very important early defence against the parasite and this effect can modulate the level of parasites in the blood in the period before the adaptive immune system can mount a specific defence against the parasite. This is a novel observation that has been accepted for publication in *Science*.

Ongoing work on this project aims to understand the molecular mechanism behind the ability of platelets to kill the malarial parasite.



Dr Brendan McMorran and Professor Simon Foote in the genetic research laboratory

The most immediate outcome of this work is the reassessment of the use of aspirin in the treatment of malaria. This drug inhibits the activation of platelets and therefore renders them incapable of killing the parasite in the red cell. This drug is widely used to relieve inflammation and fever, as well as specifically treat the fevers and chills associated with malarial infections.

We use mouse models of malaria and cultured human malarial parasites to study these issues. We employ methodologies in immunology, biochemistry and microscopy to study the parasite-host interaction. The Institute is well positioned to carry out these studies.

Protective Role for Platelets in Malaria Infection

Malaria is caused by the plasmodium parasite, which grows and replicates within circulating red blood cells. The project investigates how platelets bind to parasite-infected red blood cells and kill the parasites inside.

Achievements:

- Awarded best poster at the Keystone Symposia: Malaria Immunology and Vaccine Development, Austria June 2008.
- Paper accepted in 2008 and to be published in the journal, *Science* in early 2009, showing that platelets are important in protecting against malaria infection: *Platelets kill intra-erythrocytic malarial parasites and mediate survival to infection*.

The Search for Novel Antimalarial Drugs Using Host Targets

Treatments for malaria have existed for thousands of years. Some modern day treatments derive from these ancient natural compounds. For example, the bark of the Cinchona tree contains quinine, an effective drug introduced in the 1920s. Chinese medicines included the fever-relieving herb Qinghaosu, from which was isolated artemisinin, an antimalarial that has recently come onto the market commercially. In the years after the second world

war, chloroquine was developed. This was a very effective, cheap antimalarial and was used extensively for the next 40 years.

However, with the possible exception of artemisinin, all antimalarial drugs have become increasingly ineffectual due to the development of resistance by the parasite. The parasite has two major mechanisms of resistance, it can exclude the drug and it can mutate the gene encoding the target.

We are looking for new antimalarial compounds that avoid the problem of resistance by targeting host molecules. The advantage of this approach is that the targets are not under the control of the parasite genome, therefore the parasite cannot mutate the target. Also, the site of action of these drugs is likely to be outside the parasite and therefore the parasite will be unable to modulate the concentration of drug. We call this approach "Host Directed Therapy" or HDT.

We have been using a bioinformatics approach to identifying pathways of

the host red cell that are used directly by the parasite. We have identified one such pathway where the parasite actively imports enzyme from the red cell and then uses these enzymes for its own metabolic support. There are some commercially available inhibitors for some of these enzymes and we have demonstrated these can prevent the growth of *P. falciparum* malarial parasites in culture. One of these compounds is an irreversible inhibitor. We can show that blocking the human enzyme exclusively is sufficient to prevent the growth of the parasite. There is also an enzyme in this pathway that appears to be absent from the parasite. We are synthesising substrate analogues of this enzyme with the view to developing a range of small molecular inhibitors.

We use a range of technologies in this project including, basic parasitology, both *in vitro* and *in vivo* models of the disease. We use recombinant DNA technology to express target molecules in bacteria. There is a considerable amount of synthetic chemistry involved in the production of the inhibitors and this is done in collaboration with the School of Chemistry, UTAS.

The Identification of Genes Mediating Resistance to Malaria Using Large-Scale Mouse Mutagenesis

We know that human populations living in malarial endemic regions have acquired a large number of mutations that render them more resistant to malaria. Thalassaemias, G6PD deficiency and the Duffy Blood Group are all examples of mutations that affect the red cell found in areas endemic to malaria. We also know platelets play a role in the host response to malaria (Project 1). There is a large amount known about the adaptive immune system and its role in protective immunity. However, despite this, we still do not understand why some children die from malaria, whereas others from the same family/village survive a very similar infection.

We are trying to identify the mechanisms underlying the human response to malarial infection. In the course of this study we also

hope to uncover targets from novel approaches to malarial infection using the host directed therapy approach described in Project 2.

Our approach is to use the mouse malaria, *P. chabaudi* as a model for human malarias. This malaria affects mice in a very similar fashion to human malarias. Gene mutations that affect the rate of growth of human malarias have similar effects in the mouse.

We are conducting a large-scale mutagenesis experiment in mice, causing mutations in the germ-line of mice and then challenging their progeny with malaria. We are looking for mice that have a better capacity to resist the malarial infection than other mice. These mice may carry mutations that protect them against malaria. We will use modern genetic tools to identify these mutations. At present we have several mice carrying mutations that protect them from a *P. chabaudi* infection.

The identification of these genes will increase our knowledge of the host response to malarial infection and will also provide additional targets for host directed therapy and be directed towards our drug-discovery pipeline (Project 2).

We use classical mouse genetics, DNA sequencing, parasitological, immunological and haematological technologies as part of this project.

The Identification of Naturally-Occurring Mutations in a Gene Mediating Resistance to Malaria

As described in previous projects, we still do not completely understand how some children succumb to a malarial infection whereas others survive. In other words, we do not understand the host's defence mechanisms against the malarial parasite. This is important if we are to develop new ways of treating this nasty disease.

Over the past decade, we have been using the mouse as a model for malarial infections, infecting them with the rodent malarial parasite *P. chabaudi*. When different strains of mouse are infected with this parasite,

there are very different responses seen. Some strains are resistant to infection and appear completely unaffected throughout a brief period of infection whereas others die rapidly from the infection. Therefore there are genetic differences between these mice strains that explain their response to infection.

We have performed a number of genetic crosses between these strains and have mapped genetic loci conferring either susceptibility or resistance. Some of these loci are very complex with numerous sub-regions containing genes that affect outcome to infection. We are continuing to map some of these genes with a view to identifying them.

We have generated congenic animals for some of these loci that allow the study of the biology of the loci.

We use a variety of techniques, including classical genetic linkage and QTL analysis, the generation of congenic animals, microarray and DNA sequencing techniques. We also study the biology of our congenic animals using immunological, parasitological and haematological techniques. Eventually we will use transgenic mouse models.

The Identification of Genes Underlying a Familial Susceptibility to Blood Cancers

Haematological malignancies (blood cancers) are a relatively common form of cancer and have enjoyed a remarkable degree of therapeutic success over the past 40 years. However they still kill many patients every year and current treatments are associated with considerable risks. Many of these cancers have a genetic basis to them that can be inherited from one generation to the next. This can cause these cancers to be more common in some families than others.

We are trying to identify some of these inherited risk genes using large families from Tasmania. We have identified certain families where there is an increase in incidence of blood cancers. This may be limited to a small number of different types of tumour but in many families there is

a general increase in the incidence of many blood cancers. We propose this is due to a genetic predisposition that affects early haematopoietic stem cells that can subsequently give rise to malignancies in any blood cell type.

The families we have found are very large. Some of them have hundreds, if not thousands of individuals, all descended from common, early immigrants to Tasmania. This gives two major advantages. Firstly, if there is a genetic determinant then we can isolate the location using classical genetic mapping. This work is ongoing in the laboratory and is the major focus of this project. However the presence of such large families in Tasmania provides a second distinct advantage. Many of these genes will contain a rare genetic alteration, or polymorphism that is associated with an increased risk of developing the cancer, however presence of this genetic alteration will not always result in disease. These sorts of genetic changes are very difficult to identify and are likely to be quite common in cancers. Having large pedigrees means that even if only a small number of people carrying the genetic change get cancer, given the size of these families, we would expect to see several cancers due to a common mutation.

In this project we use classical genetic mapping, PCR, statistics, high-throughput genotyping, DNA sequencing, mutation detection, cell culture and microarrays.

Achievements:

- David Collins Leukaemia Foundation Project Grant
- Dr Liz Tegg (PhD Student) was awarded the HOTT COSA Roche Fellowship (\$50,000) and the Royal Hobart Hospital Research Foundation Clinical Fellowship (\$100,000 per year for three years)

Identifying a Genetic Basis of Multiple Sclerosis

Multiple sclerosis (MS) is a progressive disease affecting the central nervous system. The myelin sheath encompassing nerve fibres

is destroyed, resulting in a loss of neuronal function. It tends to occur in circumscribed areas, causing a specific neurological deficit and a focal "patch" that can be seen on MRI scans of the brain. MS has several different forms. The most common is the relapsing, remitting variety where patients experience worsening of symptoms followed by full to partial recovery. Unfortunately for most patients the course for this variety is progressively downwards. Primary progressive MS has no such variation and there is a steady decline in function.

MS is more common in Tasmania than other states and there appears to be a latitudinal gradient which may be explained by a decreasing exposure to sunlight. However there is definitely a significant genetic component to MS with siblings of affected individuals having a 40-fold higher risk of contracting the disease than others in the population. We know that the MHC region of the genome contributes significantly to disease with the DR15 haplotype being enriched in MS patients. This does not explain all the genetic contribution to disease. There are likely to be many more loci involved. We are trying to find these loci.

We have been working on this for a number of years and up until recently the technology has not been sufficiently sensitive to identify these genes. We can now survey the entire genome with high density arrays. This has recently been done as a consortium of most MS researchers in Australia with some interesting results emerging.

We are following up some of these results.

This project requires sophisticated statistical analysis, high throughput genotyping and careful clinical analysis.

A Host-Directed Therapy for Malaria

Current anti-malarial drugs are aimed at inhibiting parasite enzymes or processes. Widespread parasite

resistance has developed too many of these. This project seeks to use an alternative approach where drugs are being developed that inhibit red blood cell enzymes known to be utilised by the parasite during intraerythrocytic infection. Such drugs will be essentially resistance-proof since they target molecules outside the genetic control of the parasite.

Achievements:

- Tasmania (\$75,000 pre-seed grant)
- Awards to PhD student, Clare Smith, who works on this project: Glaxo-Smith-Kline postgraduate support grant (\$25,000) and AusBiotech-GlaxoSmithKline student excellence award, Tasmanian winner and national finalist.

The Genetics of Renal Failure

Renal disease is much more common in many Australian Aboriginal populations than in Australians of European ancestry. Prevalence has increased as more people have adopted a Western diet. We are searching for genes that increase risk of renal failure in Aboriginal populations.

We have assessed the quality of DNA samples that were collected over 10 years ago, and prepared samples for genotyping at the Australian Genome Research Facility. We commenced preliminary analyses of these genotype data.

The Identification of Genes Underlying Susceptibility to Prostate Cancer

Prostate cancer is the most commonly diagnosed cancer in men other than skin cancers. Almost one man in ten will develop prostate cancer during his lifetime.

It is well established that family history of disease is a strong risk factor for prostate cancer, indicating that genes contribute to risk of this disease.

Knowledge of the genes underlying the development of prostate cancer is important in understanding this disease and is likely to have wide

ranging benefits through facilitating the development of new diagnostic tools, screening tests to identify those at risk, and the ability to better tailor available therapies.

The genetic study of large families has proven to be a powerful approach to discovering the genes contributing to disease. We propose to utilise this approach to identify genes important in the development of prostate cancer through the genetic study of Tasmanian families with multiple cases of disease.

Achievements:

- Publications in international journals including *Prostate* and *European Journal of Human Genetics*.
- Award of a Cancer Australia Grant \$515,000 over three years.
- Invitation to join the international prostate cancer genetics research consortium (PRACTICAL).

Characterisation of Alpha 2 Integrin: A Potential Biomarker for Prostate Cancer

Our team has identified a gene (integrin alpha 2) significantly associated with risk of developing prostate cancer. Two genetic alterations within this gene are associated with increased prostate cancer risk. There is also evidence provided by other researchers, which supports a role for this gene in tumour development and tumour spread.

This project aims to examine the genetic alterations associated with disease and how they may influence expression of this gene. Further we will examine why this may result in differences in the development of prostate tumours and their propensity to spread to other parts of the body, most frequently to the bone.

The outcomes of this research may have direct application to the development of novel biomarkers for prostate cancer detection and to the discovery of new therapeutic targets.

Achievements:

- Cancer Council Tasmania grant for 2009



NEUROSCIENCE AND MULTIPLE SCLEROSIS

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FUNDING BODIES:

Australian Research Council

MS Research Australia

MS Tasmania

National Health and Medical Research Council

National MS Society of the USA



Associate Professor Bruce Taylor and Dr Ingrid van der Mei

ANZGENE Collaboration

This project was developed to undertake a genome wide association scan for genes that confer susceptibility to Multiple Sclerosis (MS). During 2008 the consortium including the MRI collected nearly 4000 genetic samples from cases with MS in Australia and New Zealand that were subsequently genotyped in Australia and also as part of the Wellcome Trust study of MS genes. Analysis of the large data set is currently underway with submission of manuscripts to high citation index journals.

Achievements:

Collection of DNA samples and phenotype data from over 400 people with MS in Tasmania.

MS Genes and Prevalence Study

This study ran in conjunction with the ANZGENE DNA collection and collected data on the environmental factors that may be important in the development of MS in Tasmanian people with MS.

Achievements:

Collected phenotype data on over 500 people with MS in Tasmania.

Completed full data collection on all cases of MS in Southern Tasmania allowing comparisons of prevalence and incident data with previous MRI datasets for 2001 and previously published datasets from 1981 and 1961 producing one of the world's longest MS epidemiological datasets. Analysis is nearing completion for presentation in 2009 and publication.

Longitudinal Cohort Study of MS in Southern Tasmania

This project followed 198 people with MS between 2002 and 2005 in Southern Tasmania to assess the effect of personal behaviour on the rate of progression of MS with a particular focus on personal sun exposure and vitamin D.

Achievements:

This study generated three publications in 2008 describing the detrimental effects of smoking on MS development and progression, the role of vitamin D on relapses at the population level, and the role of missing doses of immunomodulatory therapy on the risk of progression and relapse.

Effect of Epstein-Barr Virus (EBV) and Human Herpes Virus 6 (HHV-6) Latent Infection or Reactivation on MS Activity: A Prospective Clinical Cohort Study

This study used the Longitudinal Cohort Study of MS in Southern Tasmania as a platform and examines the effect that Epstein-Barr Virus and Human Herpes Virus 6 can have on the accumulation of clinical disability, increase in brain lesion load, and onset of relapses of MS.

Study samples have been analysed at Westmead Hospital for antibody levels and viral DNA load for Epstein-Barr Virus and Human Herpes Virus 6.

The Ausimmune Study

This multicentre case control study of environmental factors in the prediction of development of MS completed the final follow up assessments of all cases and data analysis commenced with the completion of two papers for publication in early 2009.

Achievements:

- Completion of case follow up to the two-three year time point.
- Completion of two manuscripts.

- Presentation of data at the World Congress of MS in Montreal in September.

AUSLONG Project

In 2008 we were successful in obtaining NHMRC funding for an extension study of the Ausimmune study. This study will particularly look at factors that predict conversion to clinically definite MS following a first central nervous system demyelinating event. Additionally the role of environmental and genetic factors in the rate of progression of MS following conversion will be studied.

The New Zealand Prevalence Study

This is a cross sectional study that aimed to capture and phenotype all cases of MS resident in NZ on census day March 2006 – to determine their level of disability and their MS phenotype.

Achievements:

- Completed data collection on over 2900 cases of MS. Database completed.
- First analyses completed.
- Data presented at the World Congress of MS Montreal 2008.



NEUROSCIENCE

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Alzheimer's Australia Foundation

ANZ Charitable Trust
(JO and JR Wicking Trust)

Australian Research Council

Australian Rotary Health
Research Fund

Motor Accident Insurance Board

Motor Neuron Disease Research
Institute of Australia Inc

National Health and Medical
Research Council

Royal Hobart Hospital Research
Foundation

Tasmanian Department of Health
and Human Services

Tasmanian Masonic Centenary
Medical Research Foundation

University of Tasmania Foundation
(Brian Marks Bequest)

Using Metallothioneins as a Model for Understanding Cellular and Biochemical Interactions between Neurons and Astrocytes within the Brain

Our work has highlighted a complex
system of interactions between
neurons and the major supporting
cell within the brain, astrocytes.

We have developed models
for understanding some of the
signals that are generated by
injured neurons, and how they are

received by astrocytes. In turn,
we have identified how astrocytes
upregulate the expression of
the neuroprotective protein
metallothionein in response to
neuron injury, and actively secrete
metallothionein so that it can act
protectively upon neurons.

This bi-directional interaction
between neurons and astrocytes
highlights an important
neuroprotective mechanism
within the injured brain.

Identifying the Specific Structural Features of Metallothionein that Regulate its Ability to Modulate Astrogliosis

We have identified an unsuspected
neuroprotective mechanism
in the brain, which involves a
neuroprotective molecule acting
upon astrocytes, and causing them
to change their function.

Astrocytes rapidly respond to injury
by changing their size, shape and

expression of molecules, which is a process termed astrogliosis. Generally this process is inhibitory, in that astroglial astrocytes express molecules that block regeneration of neurons.

We have found that the neuroprotective protein metallothionein can switch on some features of astrogliosis, but in doing so, it changes astrocytes from being inhibitory to neuron regeneration to a periventricular phenotype.

We have now characterised the specific parts of the metallothionein molecule that induce this change in astrocytes, and the signalling pathways that are responsible for this change in astrocyte behaviour.

We are using this approach to develop a better understanding of how the brain attempts to heal itself following injury.

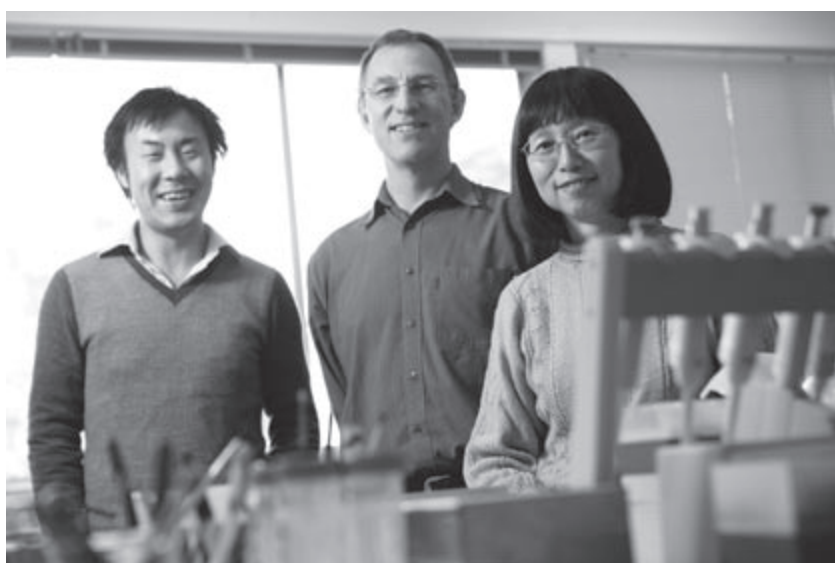
Developing Metallothioneins as a Therapeutic Agent for Promoting Neuronal Recovery from CNS Injury or Neurodegenerative Disease

Neuronal dysfunction as a consequence of injury or disease has a significant impact upon the entire community. Unfortunately there are no clinical therapies currently available to either protect neurons from dying or promote neuronal recovery following CNS (central nervous system) injury or disease.

We have conducted trials using metallothionein to treat animals with a genetic predisposition to two major neurodegenerative diseases, motor neuron disease and Alzheimer's disease.

In particular, we have investigated the biochemical mechanism by which metallothionein reduces the toxicity of a protein associated with Alzheimer's disease and prevents the formation of aggregates which are seen in the brains of sufferers with this disorder.

We have also developed a screening model for rapid identification of molecules with therapeutic potential.



Dr Roger Chung, Associate Professor Adrian West and Associate Professor Meng Inn Chuah

Protection of the Brain from Infection: Immune Properties of Olfactory Ensheathing Cells

This project aims to understand how tissues in the nose play a role in protecting the brain from infection. In particular, we are interested in how olfactory ensheathing cells, the supporting cells of the olfactory nerves, are able to dispose of harmful bacteria.

The data show that olfactory ensheathing cells produce nitric oxide that can kill bacteria and also cytokines that activate cells of the adaptive immune system.

We are currently examining how olfactory ensheathing cells prevent infection of the brain by viruses in collaboration with scientists overseas.

Cellular Degeneration in Alzheimer's Disease and Related Dementias

Alzheimer's disease is a neurodegenerative disease that progresses over the course of many years and has several pathological hallmarks, namely, β -amyloid plaques, neurofibrillary tangles and neuropil threads.

Although much is now known about Alzheimer's disease there is still considerable controversy over

which of the pathological hallmarks causes the disease, why only certain populations of nerve cells die and how these nerve cells degenerate in this condition.

The aim of this project is to study the pathological hallmarks of Alzheimer's disease in human brains and to utilise *in vivo* and *in vitro* models to investigate the crucial cellular changes underlying the neurodegeneration in this condition.

Our studies utilising human brain tissue and transgenic mouse models of Alzheimer's disease have identified the earliest neuronal changes associated with amyloid plaque formation. These investigations have provided new insights into potential therapeutic interventions that target the early brain changes of the disease, before substantial nerve cell degeneration has occurred.

We have also determined the particular characteristics of the pathological changes that occur in strongly inherited forms of Alzheimer's linked to mutations in the 'presenilin' genes.

The Cause of Neural Degeneration in Motor Neuron Disease

Motor neuron disease involves the selective degeneration of the

nerve cells involved in movement in the spinal cord and the cortex of the brain. The reasons for this selective degeneration and the cellular alterations resulting in nerve degeneration are unknown.

The aim of this project is to investigate the mechanisms involved in neurodegeneration in the main form of motor neuron disease, amyotrophic lateral sclerosis (ALS).

Our laboratory has developed novel cell culture models that replicate key intracellular changes which lead to ALS-like degeneration of spinal neurons. These studies demonstrated that filamentous (cytoskeletal) proteins within nerve cell processes are susceptible to abnormal accumulation in this disease, which may then trigger a gradual degeneration of the neuron.

Our investigations also showed that overstimulation of excitatory receptors, known as excitotoxicity, can cause the disruption and accumulation of cytoskeletal proteins in distinct segments of the axon.

Axon Regeneration in the Mature Central Nervous System

Brain and spinal cord injury are major causes of death and disability. The aim of this project is to determine how nerve cells in the brain respond to injury, utilising unique cell culture models.

Our research is aimed at determining the cellular features that characterise the adaptive response of nerve axons to damage in the adult brain and comparing and contrasting these with developmental events. It may then be possible to manipulate this axonal response to injury to help damaged brains to repair themselves.

Our studies have determined key similarities and differences between how mature nerve cells respond to injury as compared to the cellular features of developing neurons. This investigation showed that damaged axons of mature neurons can sprout, but this regenerative response is undirected and not responsive to growth factor cues important in initial axon growth.

We have also developed a new cell culture model that involves transient stretch injury to axons, modelling the forces that impinge on nerve cells in closed brain trauma. These studies have identified key cellular changes that are linked with secondary degeneration of stretched axons.

Nerve Cell Plasticity and the Neuropathology of Parkinson's Disease

Parkinson's Disease (PD) is one of the most common neurodegenerative disorders. Its incidence increases steadily with age affecting approximately one per cent of the population at age 65 and up to five per cent by the age of 85 years.

At the time of diagnosis, patients suffer from a range of motor impairments that worsen over time. Pathologically these patients are characterised by the accumulation of a protein known as alpha-synuclein in specific types of nerve cells in their brain. However, the function of this protein is unknown.

This research aims to clarify the role of alpha-synuclein in PD and normal CNS function and provide new potential therapeutic targets for the treatment of PD and other neurodegenerative disorders in which oxidative stress, excitotoxicity and central nervous system trauma have been implicated.

Our studies found that the protein alpha-synuclein is upregulated in neurones, in response to chronic oxidative stress, and is associated with neuroprotection.

Furthermore, we have determined that a similar response occurs in response to neuronal physical trauma, which is a risk factor for PD and also occurs across a range of nerve cell types including those that are selectively vulnerable to PD.

We have established two colonies of transgenic mice, one that models a genetic mutation in alpha-synuclein that is present in some cases of PD and another that does not produce the protein at all, therefore introducing a range of experimental possibilities for these investigations.



Dr Tracey Dickson

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FUNDING BODIES:

National Health and Medical
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Studies on the Mechanism of Neurodegeneration in Familial Amyloidotic Polyneuropathy

Familial amyloidotic polyneuropathy is a disease frequently caused by mutations in a gene encoding the protein transthyretin (TTR) or prealbumin. Our studies have shown that oligomeric forms of TTR bind to anionic lipids in the plasma membrane of peripheral neurons, thereby disrupting membrane fluidity.

This disruption results in the activation of a nonselective voltage-insensitive cation channel which causes membrane depolarization. The subsequent influx of calcium may be a key trigger for neurodegeneration. Our current work is aimed at identifying the voltage-insensitive cation channel.

Awarded National Health and Medical Research Council project grant.

The Mechanism of Neurodegeneration in Alzheimer's Disease

Alzheimer's disease is caused by the build-up of oligomeric forms of

beta-amyloid protein (Abeta) in the brain. Abeta is derived by proteolytic cleavage of the beta-amyloid precursor protein. Oligomers of Abeta disrupt the normal function of neurons by disrupting calcium homeostasis.

Our current work is aimed at:

- 1) identifying the molecular species of Abeta that are responsible for this effect,
- 2) identifying the ion channels and receptors that mediate Abeta-induced calcium disruption and
- 3) understanding the role of calcium in neuritic dystrophy and cognitive decline.

Regulation of the Beta-Secretase of Alzheimer's Disease by Glycosaminoglycans

The beta-secretase (also known as BACE1) is an aspartyl protease that catalyses the first step in the production of Abeta, the protein which causes Alzheimer's disease.

BACE1 cleaves the beta-amyloid precursor protein to yield a proteolytic fragment called C99, which is subsequently broken down into Abeta. BACE1 is generally considered to be one of the best targets for developing a drug which can be used to prevent the disease. However, progress on developing a drug has been slow, owing to the difficulty of identifying low molecular weight inhibitors of BACE1 that can cross the blood-brain barrier.

Our studies have shown that glycosaminoglycans may be involved in regulating the assembly and normal function of BACE1 in the brain. By targeting the BACE1-glycosaminoglycan interaction, it may be possible to block beta-secretase cleavage of the beta-amyloid precursor protein *in vivo*.

Post Synaptic Density Scaffold Proteins in the Growth Cone: Homer and Shank, Crucial for Calcium Signalling

Homer and Shank are post-synaptic density scaffold proteins, known for their role in learning and memory.

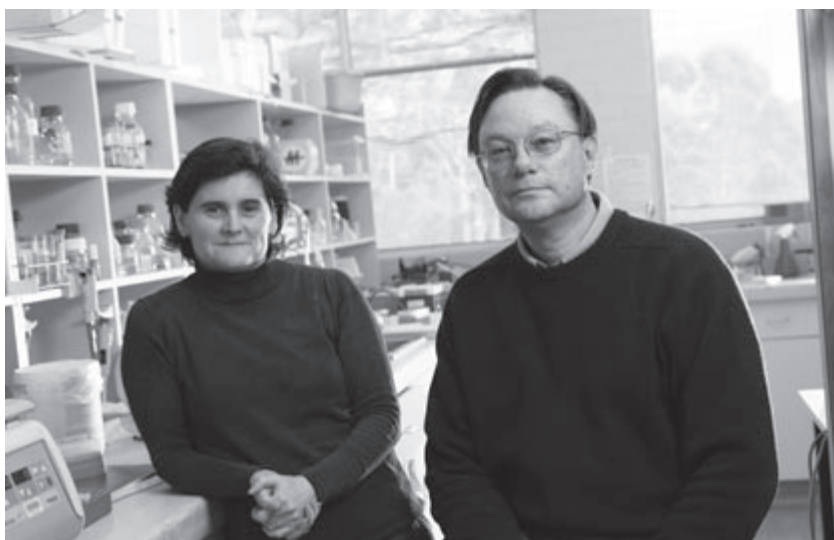
Exciting novel data from Dr Foa's laboratory demonstrates that Homer in particular, is also crucial during brain development, where Homer acts to regulate fluctuations in calcium levels within the cell.

This is particularly important in growing neurons as they send out long processes to connect with other cells and "wire" neurons into the electrical circuit that ultimately forms the brain.

Calcium Regulation in Development and Alzheimer's Disease

Calcium is known to be crucial to all aspects of neuronal function. The Foa lab exploits the simple developmental model of the growing, turning neuron to examine the mechanisms that regulate calcium.

Understanding calcium signalling during development is a fundamental



Dr Lisa Foa and Professor David Small work in the area of neuroscience

step in understanding calcium dysregulation in neurodegenerative diseases. Indeed it has been suggested that diseases such as Alzheimer's disease may "hijack" developmental signalling mechanisms.

Hence Dr Foa and Professor Small have entered into a joint initiative, combining and complementing their laboratories, aiming to improve current understanding of neuronal calcium regulation in development and disease.

NEUROSCIENCE

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EXTERNAL COLLABORATORS

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FUNDING BODIES:

National Health and Medical Research Council

Deciphering how PTEN Phosphatase Mediates Excitotoxic Neuronal Death

Our main objective is to decipher the mechanism by which PTEN (phosphatase and tensin homologue)

is recruited by the over-stimulated glutamate receptor to enhance excitotoxic neuronal death.

The specific aims are:

- 1) Ascertain how calpain-catalysed truncation modulates PTEN subcellular localisation and activity;
- 2) Determine the effect of phosphorylation of each of the C-terminal tail sites (S380, T382, T383 and S385) on PTEN subcellular localisation and activity;
- 3) Decipher the role played by nuclear PTEN in excitotoxic neuronal death;
- 4) Design of a cell-permeable peptide derived from the calpain-cleavage sequence in PTEN, and examine this peptide for potential neuroprotective effect.

We have found that calpain-catalysed C-terminal tail truncation



Associate Professor Steve Cheung

enhances PTEN localisation in the nucleus. However, the truncation has no effect on its phosphatase activity.

We are in the process of generating recombinant lentivirus directing the expression of this truncated form of PTEN in neurons.

MUSCULOSKELETAL

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FUNDING BODIES:

Arthritis Australia

Pharmaceutical Industry

National Health and Medical
Research Council

Tasmanian Community Fund

Tasmanian Government



Professor Graeme Jones heads up the musculoskeletal team at Menzies

The year 2008 was a very busy and rewarding year in the Musculoskeletal Unit. A total of 20 publications were made and a number of these are worth highlighting.

Firstly, we provided the first robust long term evidence that **physical activity in childhood has a long-term impact of bone strength in adult life**. This was published in the top *Bone* journal.

We also published work showing that a **number of measures of bone strength correlate with fracture risk in children**.

Low levels of inflammation in the blood also predict bone loss in healthy elderly suggesting targeted anti-inflammatory therapy may prevent osteoporosis.

In collaboration with Matthew Brown, we developed a novel study design which should lead to new insights into the **genes involved in osteoporosis**.

A number of important presentations were made in 2008. Professor Jones presented at both The European League Against Rheumatism

(EULAR) and the Australian Research Council on **tocilizumab**. This is an exciting new treatment for rheumatoid arthritis.

Dr Changhai Ding presented a talk at the Australian Research Council suggesting **certain anti-inflammatories known as COX-2 agents may protect against cartilage loss in the knee**.

The Tasmanian Older Adult Cohort (TASOAC) study is ongoing with study participants coming back for their five year visits. This stage will be finished in May 2009 when major data analysis is planned. Measurement of bone density in the knee, MRI assessment of knee and hip joints, and assessment of spinal fractures is a major and time consuming exercise but the results will be worth the effort.

There are also a number of clinical trials ongoing in rheumatoid arthritis, fibromyalgia, osteoarthritis and osteoporosis.

New grants were received for additional substudies in **TASOAC** including genetic studies and two new studies from the National Health and Medical Research Council (NHMRC).

MUSCULOSKELETAL

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FUNDING BODIES:

Arthritis Australia

National Health and Medical
Research Council

Tasmania Community Fund

levels, change in vitamin D levels over 2.9 years, baseline radiographic osteoarthritis, baseline cartilage volume, and change in cartilage volume over 2.9 years.

We have found that sunlight exposure and serum 25-(OH) D are both associated with decrease knee cartilage loss (assessed by radiograph or MRI). This is best observed using the whole range of 25-(OH) D rather than predefined cut-points and implies that achieving vitamin D sufficiency may prevent and/or retard cartilage loss in knee osteoarthritis.

A paper from this finding has been published in *Arthritis and Rheumatism*.



Dr Changhai Ding

knee cartilage defects, tibial bone area and cartilage volume in young adults 20 years later. These knee structural changes are assessed by MRI in the participants of Childhood Determinants of Adult Health (CDAH) study located in metropolitan Melbourne and Sydney.

This study commenced in March 2008. We commenced recruitment of participants in Sydney and 149 have completed Computer Assisted Telephone Interview (CATI) and 65 have completed knee MRI scan (target 150 participants). We have also recruited participants in Melbourne and 89 have completed CATI and 36 have completed knee MRI scan (target 250 participants). The MRI scans are being read by a research assistant. The study is due for completion at the end of 2009.

Vitamin D Status over Time: Association with Knee Structural Change Assessed by MRI in Older Adults

We determined the associations between baseline serum vitamin D

Are Serum Inflammatory Markers and Leptin Predictive of Knee Structural Changes in the Elderly?

We determined if serum levels of inflammatory markers [interleukin (IL)-6, tumour necrosis factor (TNF)- α] and leptin were associated with radiographic changes of hip and cartilage loss of knee over 2.9 years.

We have found that serum levels of IL-6 and TNF- α are positively associated with knee cartilage loss (assessed by radiograph or MRI) in older people implying inflammatory response may play a role in the pathogenesis of knee osteoarthritis.

Furthermore, serum levels of leptin and IL-6 are positively associated with hip JSN (an indirect measure of cartilage), but not osteophytes in older people suggesting metabolic and inflammatory mechanisms may play roles in the aetiology of hip OA via an effect on cartilage.

Does Childhood Physical Activity, Fitness and Fatness Impact on Knee Structural Change 20 Years Later?

The aim of this study is to determine the associations between physical activity and fatness in childhood, and

MUSCULOSKELETAL

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FUNDING BODIES:

Abbott Australasia

Arthritis Australia

Royal Australian College
of Physicians/Australian
Rheumatology Association



Dr Jane Zochling who has a keen research interest in Ankylosing spondylitis, scleroderma and psoriatic arthritis

determine the best way to improve early diagnosis (recognised as a hurdle in this disease) to thus enable early intervention.

Recruitment has been slow but steady throughout 2008, with ongoing data collection as the cohort is established. Early disease has proved more difficult to attract, and GP education and targeting and media strategies are planned for early 2009.

Patient feedback has been extremely positive, and involvement of patient support groups will greatly enhance the study.

Tasmanian Systemic Sclerosis Epidemiology (TASSiE) Study

Cohort study of scleroderma (systemic sclerosis) and mixed connective tissue disease in Tasmania. This connective tissue disease can be mild, however, in its most aggressive form can cause significant mortality from pulmonary hypertension, pulmonary fibrosis or renal failure.

There has long been the clinical impression that the disease was more prevalent here than in other Australian centres. Prospective studies on circulation and prognosis are being considered in collaboration with the cardiology unit at the

Royal Hobart Hospital (RHH) and a novel approach to measuring that circulation is being discussed with the Hyperbaric Medicine Unit (RHH).

Results to date confirm the impression that Tasmania has a high prevalence of scleroderma, four times that of other (published) cohorts in the country.

Initial results also show that the incidence of clinically significant pulmonary hypertension is close to 50 per cent, higher than reported nationally or internationally. The reasons for these observations are now being addressed.

GRACE

A collaboration with the International Group for Research in Psoriasis and Psoriatic Arthritis (GRAPPA), clinical data is being collected in patients with psoriatic arthritis and linked to treatment decisions, in particular change in treatment, in order to establish the best measurement tools to reflect the need for treatment change in this disease. Tasmanian patients are being included in this international initiative.

2008 saw our commitment to collaborate with this project; patient enrolment will start in January 2009.

Tasmanian Ankylosing Spondylitis Study (TASS)

Cohort study of patients with ankylosing spondylitis (AS), a type of arthritis affecting the spine and big joints, which begins in early adulthood and causes progressive pain and disability.

The study aims to describe the epidemiology of the disease in Tasmania which has not been previously described, to look at the potential genetic and environmental aspects of the disease. People with suspected or early disease are also being specifically targeted to

MUSCULOSKELETAL AND PRIMARY HEALTH CARE

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THEME AREA:

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Heart Foundation of Australia

Masonic Centenary Medical
Research Foundation

National Health and Medical
Research Council

Royal Australian College
of General Practitioners,
Cardiovascular Research
Grants in General Practice

Royal Hobart Hospital
Research Foundation



Dr Tania Winzenberg

The Assessment of Physical Activity in General Practice

This project aims to improve knowledge in the area of physical activity (PA) assessment by general practitioners (GPs), as little is known about PA assessment in general practice.

The first part of the study, investigating how GPs describe their current practice of assessing the PA of their patients, has been completed. Fifteen GPs were interviewed and the data from the interviews analysed. A manuscript has been completed and is being considered for publication.

The second part of the study aims to determine whether or not PA measured by GPs obtaining self-report from their patients is an accurate way of determining whether patients meet recommended PA levels. It compares GPs assessments with an objective PA measure made using an accelerometer. This measures the frequency, duration and intensity of PA. Data collection

for the study is complete and analysis underway.

The results of these studies will improve current knowledge of how GPs assess PA, and will be used to guide further research into developing innovative ways to promote PA in the general practice setting.

The Effects of Vitamin D Supplementation Bone Density in Vitamin D Insufficient Teenagers: A Randomised Controlled Trial

Osteoporosis is a condition where bones become weaker and more prone to fracture. Fractures from osteoporosis in the elderly are common, costly and cause significant death and disability. They may be reduced by improving the amount of bone laid down in childhood. Childhood vitamin D deficiency is common and is harmful for bone development.

The use of vitamin D supplements in children to improve bone health needs further investigation.

This is a pilot study to test the feasibility of a large scale trial to determine what effect vitamin supplementation has on bone development in adolescents who have mild to moderate vitamin deficiency. The pilot study is underway and will be completed in 2009.

Lifestyle Outcomes of Absolute Risk Feedback: A Pilot Randomised Trial of a General Practice-Based Behavioural Intervention (LOAF)

Much cardiovascular disease could be prevented if GPs could encourage their patients to improve their diet, physical activity and smoking behaviour. Communication of risk to patients may change their behaviour but the effectiveness of individualised cardiovascular risk feedback in general practice is not yet known.

This study aims to determine whether feedback of their cardiovascular risk to patients in general practice can improve lifestyle behaviours associated with cardiovascular disease.

Funding was obtained for the study in late 2008, and it is due to begin in mid-2009.

Ankle Brachial Index Determination by oscillometric method IN General practice (ABIDING)

People who have peripheral arterial disease (PAD) have blockages of the circulation to their legs. If you have PAD you have blood vessel disease throughout the body and are very likely to have a heart attack or experience a stroke. PAD can be diagnosed simply by comparing the blood pressure in the arms and legs. Until now this needed a special costly instrument. New blood pressure machines can do this without this instrument. ABIDING is a study to determine how reliably this can be done by practice nurses in general practices. We have obtained National Health Committee (NHC) funding for this study, which will be undertaken in 2009–10.



POPULATION HEALTH

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FUNDING BODIES:

Department of Health and Human
Services Tasmania

National Health and Medical
Research Council



Dr Ingrid van der Mei

AusD: Assessment of Solar UV Exposure for Vitamin D Synthesis in Australian Adults

This study aims to examine what predicts vitamin D levels in healthy adult populations in four locations across Australia (Hobart, Canberra, Brisbane and Townsville) and assesses how much sun exposure is required for vitamin D sufficiency.

The study will examine the vitamin D status of each participant with a blood sample and measure factors such as recent sun exposure, skin type, amount of skin exposed when outside in the last month and the use of vitamin D supplements.

The National Health and Medical Research Council grant is important for the translation of the beneficial effects of vitamin D on health into Australian Public Health Recommendations.

This new study was in the set up phase during 2008. All questionnaires and forms have been designed and prepared for administration. Protocols have been developed for every aspect of the study, databases have been set up and research officers recruited.

TasD: Vitamin D Status in Healthy Tasmanians and Recommendations for Public Health

This study focuses on five Tasmanian studies involving healthy participants. The studies cover the full life span, including schoolchildren, teenagers and young, middle-aged and older adults. Ambient UV data has become available for the first time and this is analysed to describe the seasonal patterns in ambient UVR in Hobart.

The study focuses on the prevalence of vitamin D deficiency, predictors of vitamin D levels and the use of this data to assist new recommendations for public health messages on sun exposure and vitamin D sufficiency.

The data has been analysed and the results have been written up in a report.

POPULATION HEALTH, CANCER AND CARDIOVASCULAR DISEASE

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FUNDING BODIES:

National Health and Medical
Research Council

National Heart Foundation

Tasmanian Community Fund

The Cancer Council Tasmania

Veolia Environmental Services

The Childhood Determinants of Adult Health (CDAH) Study

The CDAH study is a follow-up of 8,498 children who participated in the 1985 Australian Schools Health and Fitness Survey when they were aged between seven and 15 years. Extensive measures of body composition, fitness and lifestyle were collected in 1985 and again 20 years later. At follow-up 2,410 participants attended one of 34 study clinics Australia-wide and a further 1,585 completed questionnaires.

The study aims to examine associations between childhood factors and the risk of cardiovascular disease and type 2 diabetes in adulthood. Factors associated with depression and bone health are also being explored.

Following the completion of data collection in 2006, data analysis

remained the main focus of our work in 2008.

Recent results from the study have shown that declining physical fitness from childhood to adulthood is associated with adult obesity and insulin resistance; that depression is less common in young adults with higher leisure-time physical activity; and that consuming take-away food twice a week or more is associated with poorer overall diet quality and obesity.

An analysis of data from CDAH and the Tasmanian Older Adult Cohort (TASOAC) study has investigated the relationship between pedometer measures of steps/day and risk factors for heart disease and diabetes. In both younger and older adults, those in the most sedentary category (less than 5000 steps/day) had the highest prevalence of risk factors.

International Collaboration on Cardiovascular Disease Risk from Childhood to Adulthood

Very few studies internationally have the capacity to examine the contribution of childhood factors to the risk of cardiovascular disease in adulthood. Those that do have extensive measures of physical and lifestyle characteristics at multiple time points, and large numbers of participants followed since childhood.

This international collaboration has been established to pool data from three such studies: the Childhood Determinants of Adult Health (CDAH) Study conducted at Menzies, the Cardiovascular Risk in Young Finns Study from Finland, and the Bogalusa Heart Study from the USA.

By pooling data, we have greater ability to examine rare outcomes and, when findings are consistent across the three cohorts, more confidence in the results.



Associate Professor Alison Venn (left) and her team

Work on our second collaborative project was completed in 2008. Using measurements from ultrasound images of the carotid artery (carotid artery intima-media thickness (IMT)), it investigated the utility of two currently recommended paediatric dyslipidaemia classifications (for blood cholesterol and triglycerides) in predicting early signs of atherosclerosis in young adults.

The study found that the two classifications performed equally well and that overweight or obese adolescents with dyslipidaemia were at greatest risk of having high carotid IMT in adulthood. These findings will help inform clinical guidelines for managing paediatric dyslipidaemia.

Tall Girls Breast Density Study

While uncommon in recent years, estrogen treatment to reduce growth in tall girls has been available since the 1950s. This study aims to find out whether this treatment has had any long-term effects on breast tissue.

One of the features of breast tissue is the proportion of dense tissue that appears on a breast x-ray

(mammogram). This feature, referred to as mammographic density is recognised as a risk factor for breast cancer. Mammographic density is known to be affected by hormones such as estrogen, but it is not known whether hormone levels in adolescence have any long-term effects on the breast.

Women aged 40 years and over, who had been assessed or treated for tall stature as adolescents, and had participated in a previous follow-up study of the effects of treatment, were invited to participate in this study.

Data collection was completed in 2007 with 169 treated and 142 untreated tall women having telephone interviews and providing a mammogram for breast density measurements.

Analysis completed in 2008 found that high-dose estrogen exposure during adolescence appeared to have curtailed growth of mammographically dense tissue and is unlikely to have increased breast cancer risk through mechanisms related to mammographic density.

The Tasmanian Parkinson's Disease Research Project

Parkinson's disease is a common brain disease, second only in frequency to Alzheimer's disease in people over the age of 60. It is estimated that at least 100,000 Australians suffer from Parkinson's disease.

The Tasmanian Parkinson's Disease Research Project is part of a wider Australian study examining the genes that cause Parkinson's disease and aims to discover other genes that have not been linked to the disease before. Identifying inherited risk factors will provide a better understanding of the way Parkinson's disease develops and is an important step towards preventing and treating the disease.

DNA and medical information have been collected from two groups of Tasmanians: (1) Those with a strong family history of Parkinson's disease, and (2) Those with Parkinson's disease who are being treated with the drug L-Dopa.

In 2008, further genetic testing of the DNA samples from L-Dopa treated patients was carried out by our collaborators in Victoria.

POPULATION HEALTH

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Associate Professor
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Professor Brian Oldenburg,
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FUNDING BODIES:

National Health and Medical
Research Council

Victorian Health Promotion
Foundation



Dr Kristy Sanderson discusses her research work on depression

health outcomes of working while ill
versus work absence.

We designed a new approach to
address this important question,
which draws on existing and
published data to develop
descriptive epidemiological and
economic models. These models
are being developed throughout
2008-09 with the support of
a National Health and Medical
Research Council project grant.

We hope to better inform
employees, employers and clinicians
on how to manage these common
health conditions.

An overview of this project was
presented by invitation at the Work,
Stress and Health 2008 conference,
a major international conference
convened by the American
Psychological Association and
Centers for Disease Control. It was
also presented at the Australasian
Society for Psychiatric Research
and a meeting of the Victorian and
Tasmanian Chapter of the Australasian
Epidemiological Association.

Estimating the Economic Benefits of Eliminating Job Strain as a Risk Factor for Depression

This study is estimating the
economic benefits that might accrue
from reducing the number of people
suffering from depression related to
stress at work.

These estimates are being
conducted for the Victorian
population, and will be applicable
to other States and Territories,
with appropriate adjustment for
differences in population. Applying
the estimated proportions of
depression among working
Victorians that are attributable to
job stress (and therefore could be
prevented), we are estimating job
strain-attributable depression costs
and health outcomes among working
Australians from three perspectives:
societal, individual, and employer.

To explore a potentially important
factor in the apportionment of costs
between society, individuals, and
employers, we will compare costs

Depression and Anxiety in the Workplace: The Costs and Outcomes of Working While Ill

Depressive and anxiety disorders
are common in the working
population and potentially costly.
Individuals can continue working
while ill, or take an absence from
work. Whichever of these actions
is taken has potential health
and economic consequences
for themselves, co-workers and
employer.

This study is systematically
evaluating the economic cost and

for employees with paid sick leave versus those employed casually or self-employed without paid sick leave.

This study is funded by the Victorian Health Promotion Foundation.

The Costs of Chronic Disease in the Workplace from Employee and Employer Perspectives

Chronic disease is associated with loss to the Australian workforce of around half a million productive person years. The health benefits of workplace health promotion are well-demonstrated; however the development of methods to assess the key organisational benefit of improved productivity has been much slower. Improving the health and productivity of the workforce through greater engagement of business has potential benefits for individuals, businesses, and society.

In 2008, we began a pilot study to investigate a new method for costing lost productivity based on the managers' perspective, and development of this study will continue throughout 2009. This new approach has the potential to encourage greater engagement of business with workplace health promotion.

We were also part of a UTAS-funded collaboration that hosted a well-attended workshop on establishing the research agenda in Tasmania on health and productivity in the workplace.

Mental Health Promotion in the Workplace

We conducted a quantitative analysis of previous research to determine whether the current interest in promoting health in workplaces (e.g. physical activity programs) could potentially also be having a flow-on effect to mental health. We found that general health promotion has

the potential for small but significant improvements in mental health. This study was published in 2008.

Mental health promotion and preventive efforts requires collaboration with individual employers and industry groups to minimise workplace risks to health. This project was in development stages throughout 2008 and has culminated in a successful Australian Research Council (ARC) Linkage project which will begin in 2009.

This study will rigorously evaluate a novel, multimedia-based intervention designed to enhance the psychological wellbeing of managers' and their employees and reduce their depression risk. The study will directly inform research partners' objectives (Beyond Blue, Workcover Tasmania, Tasmanian Chamber of Commerce and Industry) to increase mental health program access for regional small businesses.



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Bayer HealthCare

High Blood Pressure Research
Council of Australia

National Health and
Medical Research Council

National Heart Foundation

Royal Australian College
of General Practitioners

Aspirin Reducing Events in the Elderly (ASPREE) (in Partnership with Monash University)

ASPREE is a study designed to detect a 15 per cent difference in major adverse events between placebo and aspirin in participants aged 70 years and above. 18,000 participants will be required to provide 90 per cent power of a true relative risk benefit of 0.85 for major cardiovascular endpoints in an intention-to-treat analysis with an average follow-up of five years.

The trial is supported by the Heart Foundation, the National Stroke Foundation, Alzheimer's Australia, and the Australian Divisions of General Practice. It has received financial and in kind support from the National Health and Medical Research Council of Australia (NHMRC), the National Heart Foundation of Australia, and Bayer HealthCare. We have enrolled about 250 participants in Tasmania. In addition to the NHMRC project grant of \$3.5 million, we have received an educational grant from Bayer HealthCare US for \$350,000.

The study has attracted \$3 million from CSIRO for genetics and biomarker sub study, and a further \$1.2 million from the NHMRC for a vision sub study. We have secured pre-approval for US\$50 million from the National Institute of Aging (NIA) subject to review from the National Institute of Health (NIH).

Spirometry and Asthma Management in Children and Adults in General Practice (in Partnership with The University of Adelaide)

This study aims to critically examine the impact of the measurement of airflow obstruction, using spirometry, on the management of asthma



Sharon Kelly and Professor Mark Nelson

in adults and children. The study will provide evidence for the costs and benefits of spirometry use in the monitoring of asthma. Analysis and publication should commence shortly after completion in South Australia March/April 2008.

Secondary Prevention in Acute Coronary Syndromes: Identifying the Smoking Related Beliefs of People who Continue to Smoke after an Acute Coronary Event

Quitting smoking is one of the most effective actions a person can take after having a heart attack or angina (an acute coronary event often termed an ACE) in order to prevent having a second and more serious event. This project addresses the question 'Why do some smokers successfully quit after an ACE while others continue to smoke?' A corollary study is also being conducted for the former.

REduction of Atherothrombosis for Continued Health (REACH) (with Monash University)

This is an international registry of individuals with established cardiovascular disease (CVD) or at high risk of developing said (three CVD risk factors present). The project was completed in 2007.

Yoga for Depression in Adults

A Cochrane systematic literature review titled *Yoga for depression in adults*.

A Cluster Randomised Controlled Trial of an Automated Versus Manual Device for Blood Pressure Management (CRAB)

Automated devices are replacing mercury sphygmomanometers. This may affect blood pressure (BP) measurement and management of hypertension. This study aimed to determine the effect of automated oscillometric sphygmomanometers on digit preference, BP measurement and antihypertensive drug prescribing in primary care.

Researching Practice Nurses Communication Needs in Tasmania 2006

This census located 239 practice nurses (PNs) in the state, the majority working in a clinical capacity. The response rate was for the self-completed questionnaire was 71 per cent (n=140).

The Primary Health Care Research, Evaluation and Development (PHCRED) Study

Research capacity building program funded by Department of Health and Ageing.

Post Hoc Analyses in the ANBP2 (Second Australian National Blood Pressure Study) Dataset

ANBP2 was the largest clinical trial ever conducted in Australian general practice. We continue to produce papers from the rich database of the GP management of 6083 hypertensive elderly Australians.

Barriers to Initiating Treatment in Hypertension and Treating to Target Levels

This research project aims to explore the barriers to general practitioners' initiating treatment and treating hypertension to target goals, in the Australian setting.

A Cross-Sectional Survey of the Management of Cardiovascular Disease Risk in Southern Tasmanian General Practice

A survey of GPs in Southern Tasmania to determine their understanding of Absolute Cardiovascular Risk and how they determine cardiovascular risk in general practice. In particular, assessing use of cardiovascular risk calculators and how they influence patient management.

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Research Council

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Research Foundation

Clifford Craig Medical
Research Trust

Department of Health and Ageing

Australian Lung Foundation

Asthma Foundation Tasmania

Asthma Foundation Victoria

Astro Zeneca

Norvartis

Sypkes Family Research Fund

Active Research Areas

- 1) Respiratory Immuno-pathology – current NHMRC project grant
- 2) Epidemiology – three current NHMRC project grants
- 3) Respiratory Physiology – support to three current NHMRC grants
- 4) Cystic Fibrosis – three current NHMRC project grants
- 5) Health Services Research – NHMRC current project grant

Flow-Dependence of Anatomical Dead Space: A Test of Abnormal Airway Emptying

We have previously shown that the effective volume of the lung airways (anatomical dead space) varies with expired flow, particularly in the presence of lung disease. We refer to this relationship as 'flow-dependence of anatomical dead space'.

In 2008 we continued to investigate its clinical utility as a sensitive method and potential screening test for detecting and quantifying early lung disease.

This year, our two applied physiology research students (Rhea Longley and Annabel Short) completed a study that shows that the method is reproducible (within and between testing sessions) and the data has been accepted for presentation at

the Annual Scientific Meeting of the Australian and New Zealand Society of Respiratory Science.

We have also simplified the methodology so it can now be more easily applied as a screening test of early lung disease and plan to incorporate it into a large National Health Committee funded epidemiological study of respiratory health that will commence in 2009.

Discovering the Patterns of Lung Function from Medical Datasets Using a Custom Expert Knowledge Acquisition System

This study is being conducted by Tristan Ling as part of his PhD studies. The major aim of this study is to develop and apply a web-based expert knowledge acquisition system (MCRDR) to provide automatic classification and analysis of lung function data. An interrogative tool will be built into the expert system to assist lung experts to explore large datasets of patient cases to discover and evaluate new knowledge and to discover and test research hypotheses.

The web-based expert system is now fully developed and lung function datasets from two major laboratory hospitals in Australia have been uploaded. The expert system is also being used to analyse full lung function data obtained in a large long-term epidemiological study of respiratory health (Tasmanian Longitudinal Health Study) to determine whether childhood diseases (e.g. asthma) and respiratory symptoms (cough, wheeze, asthma, chest infections, etc) are determinants of lung function in middle-age.

In 2008, the expert system we developed was presented as a full paper at the International Conference on Information Technology: New Generations, USA.

National Spirometry Training Course for General Practitioners

Spirometry is an important and reliable test of lung function for

screening and monitoring lung diseases (e.g. asthma and chronic obstructive lung disease) and practice guidelines all over the world strongly recommend its routine use in general practice. However, in Australia, relatively few General Practitioners (GPs) incorporate spirometry as part of their routine clinical practice even when assessing patients at risk of lung disease (e.g. smokers).

We have found that whilst there are a number of reasons why most GPs are reluctant to use spirometry, a key factor is that they lack confidence about its measurement and interpretation. What is needed is GP access to a spirometry course that is relevant to the needs of general practice, low cost and offered at multiple urban and rural areas throughout Australia.

We have worked closely with the National Asthma Council of Australia and the Australian and New Zealand Society of Respiratory Science to develop Australia's first national and fully funded (Department of Health and Ageing) endorsed spirometry training course specifically designed for GPs. Between May-December 2008, sixty-three (63) courses were run (52 per cent in urban areas) throughout Australia.

The course has been independently evaluated and results show that 97 per cent of GPs who attended the course are able to confidently perform and interpret spirometry, and at six-month follow-up interview, 72 per cent claim to use spirometry more often in diagnosis and management.

Burden of Obstructive Lung Disease (BOLD) in Australia

Chronic obstructive pulmonary disease (COPD) is a major lung disease most commonly associated with smoking. COPD as a cause of mortality is increasing and globally is expected to rank fifth in burden of disease by 2020.

BOLD in Australia (National Health Committee (NHC) funded) is the Australian arm of an international collaborative project to describe the



Dr David Reid, Professor Haydn Walters and Associate Professor Richard Wood-Baker

prevalence, burden, severity, risk factors and management of COPD.

Our study targets people aged ≥ 40 years from populations located at a number of diverse regions in Australia including Busselton (WA), Kimberley (NT), Melbourne (Vic), Launceston and Hobart (Tas). We have now complete lung function data collection on more than 1,400 people located in Busselton (WA), Melbourne (Vic), Launceston and Hobart (Tas) and Kimberley (NT).

The study is due to be completed toward the end of 2009 and data analysis will commence shortly.

Prediction Equations for Single Breath Diffusing Capacity in a Middle-Aged Caucasian Population

The diffusing capacity of the lung (DLCO) is a lung function test that measures the gas exchanging capacity of the lung and its measurement is routinely performed in almost all lung function laboratories worldwide.

In this study we developed a set of prediction equations for DLCO based on a large middle-aged population

of healthy subjects using modern computerised equipment and testing methods that meet international standards. Because existing prediction equations for DLCO are based on studies of predominantly younger subjects, our new prediction equations are more clinically relevant to the older population in which DLCO is most commonly abnormal due to lung disease such as chronic obstructive lung disease.

In 2008, the study was presented at the Annual Scientific Meeting of the Thoracic Society of Australia and New Zealand Melbourne and published in the international journal, *Thorax*.

Cystic Fibrosis: Pathogenesis of *Pseudomonas aeruginosa* Infection; Microbe – Host Interactions

We are collecting serial monthly sputum samples and comprehensive clinical data from 50 adult and 50 child CF patients, to relate disease activity to airway environment (pH, iron, cyanide, nitrite, and ammonium levels), to specific quantitative bacterial content and host inflammatory responses (sputum cells and cytokines). We have developed

novel molecular techniques to quantify *P.aeruginosa* quorum sensing and virulence factors in “raw” sputum samples. Assessing host and bacterial events in “real time” and relating these to clinical status, might allow earlier and better interventions. We are developing new therapeutic strategies based on our observations of excess iron in CF airways e.g. iron-chelation therapy which disrupts *P. aeruginosa* biofilms, and have leveraged long-term partner funding from Novartis. We are investigating a novel causal link between *P.aeruginosa* QS molecules and CF diabetes. We have initiated a national collaborative study of bacterial genetic variations and CF severity. We wish to leverage our CF experience in novel molecular tools to investigate H.influenzae infection/host response in COPD.

Respiratory Physiology: Detecting Early and Subtle Airway Dysfunction

The focus is further development with a commercial partner (nnd, Switzerland), of a high-tech but simple, quick to perform physiological measurement of airway stiffness and non-uniform

lung emptying in early, sub-clinical disease or lung ageing. Our method depends on accurate, rapid, on line measurement of airway volume at different lung volumes and expiratory flows using the ultrasonic spirometer (Easyone). We are applying this methodology to asthma and COPD and will relate findings to airway wall remodelling. We have assessed GP use of the Easyone, and shown that it does not need calibrating and is remarkably robust. Utilising the equipment's new capacities could transform screening for early COPD in general practices, and a feasibility trial is required.

RCT of Timing and Dose of Oral Corticosteroid (OCS) in COPD Exacerbations (AECOPD)

We know from a systematic review we published that OCS regimens in AECOPD are effective but vary widely in practice, and can have significant adverse effects. A pilot study conducted at the RHH has demonstrated that airway inflammation resolved, and anti-protease defenses improved, within 48 hours of OCS treatment in patients admitted with AECOPD.

We have instituted a follow-on RCT of short-course (three days) versus more conventional long course (ten days) OCS therapy, with the primary objective being shorter length-of-stay (LOS), fewer side effects but equivalent efficacy. After 12 months and with 480 COPD admissions screened, we have recruited just 50 individuals, because the majority of AECOPD are excluded because of co-morbidities. We are gaining huge insights into "hospital-COPD" by documenting these in relation to LOS and outcomes. This rate of recruitment means we need to be patient and continue recruitment for another two years to get numbers for adequate power, but with such an important clinical issue it will be worthwhile.

Clinical Health Informatics Research in COPD – Pathways Home Program

COPD has a profound impact on health-related quality of life (HRQOL), is a major contributor to the burden of disease in Australia and is ranked among the top causes of hospitalisation. We have recently developed a new model for

COPD clinical care in collaboration with the Tasmanian Department of Health, involving community health nurse mentoring to facilitate self-efficacy for self-management among people with COPD living in the community, and use of ITS to provide rapid feedback on clinical and HRQOL. We have shown this to be feasible in a pilot RCT of 110 people with COPD recruited during hospitalisation in which active self-management support was compared to control 'usual care'. We worked in partnership with 25 community health nurses trained in methods to facilitate self-efficacy, to achieve behavioural change through a cycle of goal setting and action planning. Intervention subjects completed a web-based diary, enabling them to closely monitor their disease and start early treatment of acute exacerbations. Despite the major impact of COPD on dyspnoea, depression and anxiety experienced by participants, mean Stanford self-efficacy scores (0-10) improved significantly (0.84 in the active arm, 0.05 in control) and this was associated with decreased depression and Emergency Department visits.



In 2008, we commenced an NHMRC-funded RCT building on this work, but in a community setting. The aims focus on early intervention in COPD in participants recruited in general practices, comparing community nurse mentoring delivered by telephone against usual care and control phone calls. We aim for early COPD recognition, reducing risk-behaviour, and improving HRQOL in COPD, while reducing healthcare costs. To date, we have recruited 182 patients in 31 practices around Tasmania and trained over 40 community nurses. To maintain sustainability and long-term follow-up, more administrative support staff will be required.

EBM – Cochrane Systematic Reviews

We are the hub/HQ for the Australian Cochrane Airway Group network, with three other groups around Australia and receive some financial support from DoHA in Canberra. We are supported technically by the international group (St George's University of London). Our centre has published 29 full systematic reviews in the past six years, which have actively informed international clinical guidelines. There are several reviews on therapeutics and allied-health interventions in airway diseases in preparation, which need more support.

Respiratory Aged Care: Developing an Evidence-Based Approach

We have strong links through Menzies to the Wicking Dementia Research Centre. We are leveraging this to develop research into evidence-based approaches to the multi-disciplinary respiratory management of the elderly, including the frail and dementing, and those living in aged care homes. Preliminary work shows that COPD and Asthma are highly prevalent in these settings and occur frequently on death certifications. Management plans, which optimise respiratory function while dealing with the inherent progressive respiratory and cognitive co-declines of

ageing, need to be central to a truly palliative approach. Our first phase is observational, but CRE funding will allow trials (with cluster randomisation) of such interventions.

Community Pharmacy Interventional RCTs

Non-optimal medicine use in the community is a significant public health burden, which is rapidly increasing with an ageing population. The respiratory group has incorporated a highly successful collaboration with UTAS School of Pharmacy to use its computing software capability for interrogating community prescribing information throughout Tasmania that is developing new, exciting, and highly pertinent clinical studies. In the first such trial we performed an intervention study where pharmacists detecting poorly-controlled asthma sent patients an advisory letter. This improved inhaler adherence, and hence DRQOL in the intervention group. This effect may still be present at 12 months, but a current qualitative survey of patients and GPs suggests that further improvements could be possible with better involvement of GPs in the process e.g. by pharmacist initiating GP patient recall; a randomised control trial will test this in the CRE.

We are currently undertaking a study to investigate adherence to long-acting anticholinergics in COPD, and preliminary results suggest the main block to adherence beyond three months is poor interaction with the GP and lack of understanding and confidence in the drug. Again, this emphasises that studies directed at GP-patient interactions on prescribing (monitored by community prescribing adherence) are urgently needed but quite feasible. We plan to interface these operational studies with our expertise in physiological and pathological outcome assessments.

Clinical Epidemiology: Clinical Management and Outcomes in Current Long-Term Cohorts – TAHS

The centerpiece of our clinical epidemiology research is this

Tasmanian Longitudinal Health Study (TAHS), one of the world's largest and longest running population-based longitudinal studies. The TAHS includes all 8583 school children born in Tasmania in 1961, with surveys also administered to parents and siblings. Subsequently, three follow-up surveys have been carried out at ages 13, 20 and 31 years (1992) on either the total cohort or sub-samples. Since 2001, (the 40-year follow-up of TAHS), we continue to identify risk factors for asthma and COPD in middle age, investigate their biological pathways and influence of clinical care on physiological outcomes. Because 25 per cent of the original participants have migrated to other states, TAHS has now become a national collaboration.

The first phase of the 37-year follow-up of the participants (90 per cent traced, 80 per cent response) has led to many publications. A sample of 1500 respondents, enriched for childhood asthma, recently participated in lab phase tests (weight/height, waist and hip circumferences, skin allergen prick testing and full lung function). Physiological outcomes are being analysed and will be a rich source of data on respiratory health in middle age and risk factors for lung dysfunction. Blood samples have been collected for biomarkers and analysis begun: we have shown that early onset persistent and early onset resolved asthma at age 44 can be differentiated by levels of the immuno-inhibitory cytokine IL-10, suggesting this could be a therapeutic target; adult onset asthma has markedly less circulating IL-4, suggesting it is a different immunological entity (also suggested by clinical and risk factors); allergic individuals with mould allergies have different cytokine profiles than those with HDM and grass allergies, again suggesting different immunology and the need for different therapeutic strategies. TAHS gives us unique opportunities to address important clinical research questions within different phenotypes of chronic respiratory disease.

WICKING DEMENTIA RESEARCH AND EDUCATION CENTRE

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Cellular Degeneration in Alzheimer's Disease and Related Dementias

Alzheimer's disease is a neurodegenerative disease that progresses over the course of many years and has several pathological hallmarks, namely, β -amyloid plaques, neurofibrillary tangles and neuropil threads. Although much is now known about Alzheimer's disease there is still considerable controversy over which of the pathological hallmarks causes the disease, why only certain populations of nerves cells die and

how these nerve cells degenerate in this condition. The aim of this project is to study the pathological hallmarks of Alzheimer's disease in human brains and to utilise *in vivo* and *in vitro* models to investigate the crucial cellular changes underlying neurodegeneration in this condition, as well as related conditions such as Dementia with Lewy bodies.

Our studies utilising human brain tissue and transgenic mouse models have identified the earliest neuronal changes associated with dementing disorders. These investigations provide new insights into potential

therapeutic interventions that target the early brain changes of the disease, before substantial nerve cell degeneration has occurred. We also determined the particular characteristics of the pathological changes that occur in strongly inherited forms of Alzheimer's linked to mutations in the 'presenilin' genes.

Study of Carers of People with Dementia Living in the Community

This study investigated carers' stress levels and experience of dementia services, as well as



the cognitive abilities of people with dementia (PWD). The data collection utilised a mixed methods approach and involved 20 carers of PWD in Tasmania. Data collection is complete and data analysis is underway with a number of publications forthcoming.

A Strategic Intervention Tool for Dementia (the SIT Project)

Work has begun on this important project which involves researchers and aged care allied health, nursing and medical staff from the Royal Hobart Hospital. The overall aim of the SIT Project is to improve the sharing of dementia care data in Tasmania and thereby assist dementia research and better management of dementia care services. A prototype of a data collection tool has been developed and will be trialed in two wards of the RHH.

CarersCARE Project

This project builds on findings of baseline data on the well-being and service usage of a small HACC sample population which demonstrated that carers of people with dementia (PWD) have high levels of stress and are caring for a very cognitively impaired group. In addition there was evidence that carers welcomed information and support which they were not accessing in a consistent way. This exciting research project involves a pilot randomised control trial of a new model of carer self help- CarersCARE - involving a DVD and a guidebook.

An investigation into aged care staff and family caregivers' communication about and participation in care provision for people living with moderate and severe dementia in residential aged care facilities (RACFs).

This study will investigate issues associated with Registered Nurses (RNs), Enrolled Nurses (ENs), Extended Care Assistants (ECAs) and relatives' communication about and participation in care provision

for people living with moderate and severe dementia in residential aged care facilities (RACFs). The project will use a two stage mixed method approach. The first stage will involve surveying RACF staff and family carers/PR about their knowledge of and attitudes towards dementia. The second stage will include the conduct of interviews with various staff and family carers/PR to investigate their experiences of care provision for people with dementia in the facility. The study results will provide a baseline which will inform a subsequent intervention study aimed at improving RACF staff-family collaboration in dementia-related care processes.

Rural Dementia

A growing body of research in recent years has highlighted the particular issues around health and health services in rural and regional areas where poorer health status and outcomes, compared with those living in urban environments, are exacerbated by poorer access to health services. It is therefore likely that the rural/regional experience of dementia, both from the perspective of dementia sufferers and their carers, will be at least different to, if not worse than, the experience of those living in the city. This project explores the particularities of the rural experience of dementia across all dimensions: diagnosis, services and supports, carers and outcomes. The study has commenced with a systematic wider review of the literature with a view to identifying some of the major issues for a future research program.

Gold Book Project

This study will introduce a Decision Aid, called the GOLD Book (an abbreviation of Getting on Living with Dementia) for the person with dementia and their carer. Many different community care services are provided to people with dementia and their carers to enable them to continue to live within the community. One of the difficulties is ensuring

that the services provided meet the needs of the client.

Our GOLD Book will help people with dementia and their carers to make better decisions about the help they need, containing current medical and social information about the person with dementia and decision tools.

Diagnosing Dementia in Primary Care

An established body of research and the experiences of PWD and their carers all show that dementia often goes undiagnosed or is not diagnosed until the condition is considerably advanced. Our research will investigate several aspects of the diagnostic process for dementia in primary care in series of linked projects. (1) The attitudes and knowledge of GPs, practice nurses, PWD and their carers towards diagnosing dementia. (2) Identifying and recording how a diagnosis occurs. (3) The impact of a diagnosis on PWD and carers particularly in terms of access to services. (4) Developing and evaluating new approaches to diagnosis such as increasing the role of practice nurses in identifying dementia. Our work in this area includes collaboration with Professor Dimity Pond at the University of Newcastle.

Environmental Design for People with Dementia: Charting the Gap between Theory and Practice in the Design of Residential Facilities

The purpose of the study is to (i) investigate the design of Residential Aged Care (RAC) settings, which accommodate people with dementia with reference to evidence-based dementia design principles and, (ii) to explore barriers and facilitators to implementing evidence based design within the residential aged care setting. We anticipate recruiting five Tasmanian Residential Aged Care Facilities (RACFs) that accommodate people with dementia, in addition to ten sites which will be recruited in Victoria and New South Wales.

ACRF TASMANIAN INHERITED CANCER CENTRE

RESEARCH TEAM

Professor Simon Foote, Director

Professor Ray Lowenthal,
Honorary Fellow and Member

Dr Jo Dickinson, Senior Member

Dr Brendan McMorran,
Senior Member

Dr Briony Patterson,
Research Fellow

Australian
Cancer Research
Foundation



Menzies Research Institute was awarded \$1.1 million in funding from the Australian Cancer Research Foundation to form the ACRF Tasmanian Inherited Cancer Centre (ACRF Centre) in 2007.

A Collaborative Approach

The ACRF Centre provides researchers with significant resources needed to unlock the causes of inherited cancers like prostate cancer and leukaemia.

The ACRF Centre brings together a number of groups in Tasmania that are working on different aspects of cancer research. The ACRF Centre draws together geneticists, biologists, clinicians and ethicists to enhance cooperation and build a world-class cancer genetics program.

Using this collaborative approach, Menzies will enhance and expand its genealogical resources, and link them with cutting edge biomedical and genetic research.

Cancer Research

Many cancers, including some forms of prostate cancer and leukaemia, are caused by an inherited, or genetic, tendency that interacts with



other factors to result in the onset of the cancer. The identification of the genes underlying many diseases has led to both a greater understanding of the disease and, in some cases, significant advances in treatment therapies.

Some cancers are due to a combination of genetic factors

and environmental events.

The ACRF grant enables Menzies to put all systems in place to allow researchers to identify not only disease genes but also the environmental triggers to disease.

Please go to pages 12 and 13 to view related cancer research projects.

TASMANIAN CANCER REGISTRY

RESEARCH – Director:

Associate Professor Alison Venn

STAFF:

Marita Dalton, Manager

Krystyna Jackman,
Administration Officer

Jackie Luck,
Medical Coder

Pam Whelan,
Data Entry

Petr Otahal,
Statistical Officer

FUNDING BODY:

Department of Health and Human
Services, Tasmanian Government

Cancer in Tasmania

The Tasmanian Cancer Registry is responsible for collecting, collating and reporting all new cases of cancer and deaths from cancer of Tasmanian residents. By law, cancer registration is required in all Australian states and territories to assist state and national efforts to understand the causes of cancer, to plan health services and to assist prevention efforts.

The Tasmanian Cancer Registry is operated by the Menzies Research Institute under a service agreement with the State Department of Health and Human Services.

In 2008, the registry released its report Cancer Incidence and Mortality 2005. There were 2737 new cases of cancer (excluding non-melanoma skin cancers) in Tasmanian residents in 2005 (1508 males, 1229 females). The overall age-standardised incidence was 376.4 per 100,000 for males and 292.2 per 100,000 for females. There were 1051 cancer-related deaths (568 males, 483 females) giving age-standardised mortality rates of 128.4 per 100,000 males and 94.0 per 100,000 females.

The most commonly diagnosed cancers were colorectal cancer, cancers of the breast, prostate and lung, and melanoma of the skin.



Tasmanian Cancer Registry team

TASMANIAN CEREBRAL PALSY REGISTRY



Julie Bunyard is the project officer for the Tasmanian Cerebral Palsy Registry

RESEARCH – Director:

Associate Professor Alison Venn

STAFF:

Julie Bunyard, Project Officer

EXTERNAL COLLABORATORS:

Associate Professor Peter Flett,
Statewide Paediatric
Rehabilitation Services

Kevin Kreiner,
Cerebral Palsy Tasmania

Staff of the Australian Cerebral
Palsy Register

FUNDING BODY:

Tasmanian Community Fund

Cerebral Palsy in Tasmania

Cerebral palsy (CP) is the most common motor disability affecting Australian children, with a rate of 2.0-2.5 per 1000 live births. Despite improvements in obstetric and neonatal care, the incidence of CP has remained largely unchanged and in many cases the cause of CP remains unknown.

The Tasmanian Cerebral Palsy Register relies on the voluntary registration of affected children and adults.

By collecting information about people with CP, the register aims to improve understanding of the

prevalence and severity of the condition in Tasmania and the needs of people affected. Registers from all Australian states and territories contribute information to the Australian CP Register making it the largest CP register in the world and a rich resource for research into the causes, prevention and treatment of CP.

In 2008, the Tasmanian CP register was newly established and policies and procedures were put in place to enable our first registrants to participate.

GRANTS

Commenced in 2008

Arthritis Australia. Grant-Project.

Zochling, JM*. Tasmanian ankylosing spondylitis study. \$10,000

Australian Cystic Fibrosis Research Trust. Grant.

Reid, DW*; Lamont, IJ; O'May, C*. Unravelling P. aeruginosa iron acquisition mechanisms in vivo: novel insights and potential therapies. \$87,879

Australian Research Council. Grant-Discovery Projects.

Keske, MAV*; Rattigan, S*. Blood Flow Routes in Muscle. \$390,000

Cancer Council Tasmania. Grant-Cancer Research.

Dickinson, JL*; Holloway, AF*; Patterson, B*; McMorran, BJ*; Stankovich, J*. Elucidation of the role of a novel susceptibility gene in prostate cancer. \$25,000

Cancer Council Tasmania. Grant-Cancer Research.

Woods, GM*; Muller, HK (Medicine (Discipline)). The effect of UV radiation and vitamin D deficiency on the development of the skin immune system. \$50,000

Clifford Craig Medical Research Trust. Grant.

Woods, GM*; Holloway, AF*; Casey, NP*. Silencing the AML1/ETO fusion gene as a treatment strategy for acute myeloid leukaemia. \$7,704

David Collins Leukaemia Foundation. Grant.

Dickinson, JL*; Foote, SJ*; Stankovich, J*; Lowenthal, RM*; Marsden, KA*; Bahlo, M*. Investigating the genetics of familial haematological cancers in Tasmania. \$25,000

David Collins Leukaemia Foundation. Grant.

Holloway, AF*. Characterising aberrant RUNX1 transcriptional complexes. \$20,000

Department of Health and Human Services. Funding Agreement.

Vickers, JC*; Robinson, AL* (Nursing and Midwifery). The Wicking Dementia Research and Education Centre (WDREC). \$250,000

Department of Health and Human Services – Home and Community Care. Project Grant.

Scott, JL (Psychology); Croft, T; Robinson, AL (Nursing and Midwifery); Vickers, JC*; Sanderson, K*. Development and evaluation of an innovative self help coping program for dementia care givers (CarersCARE). \$78,000

Heart Foundation. Grant-In-Aid.

Rattigan, S*; Richards, SM*. Interaction between adiponectin and insulin in

vascular control of glucose uptake in muscle. \$119,574

Heart Foundation. Grant-Travel.

Gall, SL*. Childhood Determinants of Adult Health Study: Associations between childhood negative affect, adult depression and the PDAY atherosclerosis risk score in a cohort of young Australian adults. \$2,000

Heart Foundation. Grant-Travel.

Magnussen, CG*. Potentially modifiable risk factors in adolescence and high carotid artery intima-media thickness in young adults: population attributable risks from three prospective cohort studies. \$2,000

Masonic Centenary Medical Research Foundation. Fellowship-Research.

Staal, JA*. The Masonic Medical Research Foundation Fellow. \$300,000

Motor Accident Insurance Board, Injury Prevention and Management Foundation. Grant.

Chung, RS*; West, AK*; Chuah, MI*. Developing metallothionein as a therapeutic agent for the treatment of traumatic brain injury. \$231,666

Motor Neurone Disease Research Institute of Australia Inc. Fellowship-Bill Gole MND Research.

King, AE*. Investigating the causes and consequences of axonal pathology in amyotrophic lateral sclerosis. \$217,500

Multiple Sclerosis Research Australia. Grant-Seeding.

Perera, DI*. Funding to support the ANZgene Project as negotiated with the MS Society of Tasmania. \$40,000

National Health and Medical Research Council. Award-Career Development.

Blizzard, CL*. Goodness-of-fit testing and extensions of relative risk models. \$370,000

National Health and Medical Research Council. Award-Career Development.

Dickson, TC*. Cellular mechanisms underlying neurodegenerative disease and responses to trauma. \$362,000

National Health and Medical Research Council. Award-Career Development.

Ding, C*. Longitudinal studies of knee osteoarthritic changes using magnetic resonance imaging. \$409,000

National Health and Medical Research Council. Fellowship-Australian Based Biomedical.

Vincent, AJ*. The role of SPARC in regeneration and

neurogenesis in the central nervous system (Australia). \$279,000

National Health and Medical Research Council. Fellowship-Australian Health Professional (Part-time).

Johnston, F*. Understanding the health effects of biomass smoke in Australian towns and cities. \$167,400

National Health and Medical Research Council. Fellowship-Research.

Rattigan, S*. NHMRC Research Fellowship (SRFA). \$537,500

National Health and Medical Research Council. Grant-Equipment.

Bennett, MA*. NHMRC Standard Equipment Grant – 2008. \$72,611

National Health and Medical Research Council. Grant-General Practice Clinical Research Program.

Nelson, MR*; Reid, C; Ryan, P; Tonkin, AM; Wing, LM. Absolute risk prediction of subsequent cardiovascular events in a large cohort of elderly Australians with hypertension. \$192,000

National Health and Medical Research Council. Grant-Program.

Foote, SJ*; Speed, TP*; Smyth, G; Bahlo, M*; Chalmers, DRC (Law); Amor, D. Genetic and bioinformatic analysis of complex human diseases. \$8,134,805

National Health and Medical Research Council. Grant-Project.

Blizzard, CL*; Hosmer, D*; Quinn, SJ*. Goodness-of-fit testing of log-link models for categorical outcome data. \$252,025

National Health and Medical Research Council. Grant-Project.

Ding, C*; Jones, G*; Venn, A*; Cicuttini, FM; Dwyer, T*. Does childhood physical activity, fitness and fatness impact on knee structural change 20 years later? \$292,926

National Health and Medical Research Council. Grant-Project.

Holloway, AF*; Shannon, MF. How does basal chromatin structure predict cytokine gene responses? \$501,000

National Health and Medical Research Council. Grant-Project.

Sanderson, K*; Oldenburg, B; Graves, N; Nicholson, J. Depression and anxiety in working adults: the costs and outcomes of working while ill. \$133,438

National Health and Medical Research Council. Grant-Project.

Small, DH*; Vickers, JC*; West, AK*. Regulation of the beta-secretase (BACE1) by glycosaminoglycans. \$539,250

*Denotes Menzies' researcher or honorary researcher associated with Menzies.



National Health and Medical Research Council. Grant-Project. van der Mei, IAF*; Ponsonby, AL*; Taylor, BVM*; Dwyer, D; Dwyer, T*; Blizzard, CL*. Effect of EBV and HHV-6 latent infection or reactivation on MS activity: a prospective clinical cohort study. \$258,500

National Health and Medical Research Council. Grant-Project. Walters, EH*; Wood-Baker, R*; Reid, DW*; Muller, HK (Medicine (Discipline)); Holloway, AF*. Scarring and angiogenesis in the airway wall in smoking and COPD: links between inflammation and remodelling. \$347,125

National Health and Medical Research Council. Grant-Project. West, AK*; Chung, RS*; Vickers, JC*; Chuah, MI*. Interactions between injured neurons, astrocytes and metallothionein. \$458,750

National Health and Medical Research Council. Grant-Project. Wood-Baker, R*; Walters, EH*; Robinson, AL (Nursing and Midwifery); Nelson, MR*; Turner, P (Computing); Scott, JL (Psychology). A comprehensive self-management programme for chronic obstructive pulmonary disease in the community. \$375,375

Physiotherapy Research Foundation. Grant-Seeding. Jose, KA*; Hansen, EC*. Physical activity and young adults: what factors help to explain participation in physical activity during the transition from dependent adolescent to independent adult? \$4,704

Royal Australasian College of Physicians. Fellowship-Jacquot Research Establishment Award. Jose, MD*. Chronic kidney disease in Tasmania. \$90,000

Royal Australian College of General Practitioners. Grant-Cardiovascular Research. Howes, FS*; Nelson, MR*; Hansen, EC*. Barriers to initiating treatment in hypertension and treating to target levels. \$11,920

Royal Hobart Hospital Research Foundation. Fellowship-Clinical Research. Reid, DW*. Clinical Research Fellowship – Respiratory Medicine. \$200,000

Royal Hobart Hospital Research Foundation. Fellowship-Research. Tegg, EM*. The Tasmanian familial haematological malignancies study. \$300,000

Royal Hobart Hospital Research Foundation. Grant-Equipment. Walters, EH*; Woods, GM*. Flow cytometer and ancillary assay kits. \$150,000

Royal Hobart Hospital Research Foundation. Grant-NHMRC Recommended. Reid, DW*. For support of 2008 NHMRC recommended projects at the researcher's discretion. \$27,273

Royal Hobart Hospital Research Foundation. Grant-Research. Amor, D; Burke, J; Thomson, R*; Fitzpatrick, E; Drini, M; Bahlo, M*; Stankovich, J*. Colorectal medicine and genetics: linkage studies in hyperplastic polyposis syndrome. \$14,960

Royal Hobart Hospital Research Foundation. Grant-Research. Dickinson, JL*; Holloway, AF*; Patterson, B*; McMorran, BJ*; Stankovich, J*. Elucidation of the role of a novel susceptibility gene in prostate cancer. \$25,000

Royal Hobart Hospital Research Foundation. Grant-Research. Walters, EH*; Dharmage, S*; Abramson, M; Erbas, B; Matheson, MC*. Epidemiology of middle-age BHR: prospective study from childhood to middle-age. \$22,727

Royal Hobart Hospital Research Foundation. Grant-Research. Winzenberg, TM*; Jones, G*; Nelson, MR*. The effects of vitamin D supplementation bone density in vitamin D insufficient teenagers: randomised controlled trial. \$22,727

Royal Hobart Hospital Research Foundation. Grant-Starter. Stewart, NJ*; Bettiol, SS (Medicine (Discipline)); Reid, DW*. Do mediators produced by the bacterium *Pseudomonas aeruginosa* prevent the immune system from 'switching off' in cystic fibrosis sufferers? \$8,164

Royal Society of Tasmania. Grant-Award Postdoctoral. Haas, MA*. Royal Society of Tasmania, Doctoral Award (PhD). \$1,000

Tasmanian Community Fund. Grant. Dickinson, JL*. Development of the Tasmanian Familial Prostate Cancer Genetic Resource. \$76,588

Tasmanian Community Fund. Grant. Reid, DW*; Busch, JK (Medicine (Discipline)); Turner, P (Computing); Cummings, EA (Computing); Cameron-Tucker, HL (Computing); Beggs, S (Medicine (Discipline)); Walters, EH*; Foote, SJ*. Tasmanian community network of mentors and smart information technology solutions (SITS) for families affected by cystic fibrosis. \$130,000

University of Tasmania. Grant-Institutional Research Scheme. Walters, JAE*. Health-mentoring by Community Health Nurses to enhance self-efficacy for people with moderate Chronic Obstructive Pulmonary Disease in the community. \$10,000

University of Tasmania. Grant-Pre Seed. Foote, SJ*; Smith, Jason (Chemistry); McMorran, BJ*. Development of novel, host-directed antimalarial compounds. \$75,000

University of Tasmania Foundation. Donation-Dr Eric Guiler Tasmanian Devil Research. Woods, GM*; Kreiss, A*. Immunohistochemistry as a tool to search for evidence of immunity against Devil Facial Tumour Disease (DFTD). \$16,657

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Presentations

Menzies' researchers attended a number of national and international medical research conferences throughout the year. In 2008, 141 oral and 65 poster presentations were delivered.

*Denotes Menzies' researcher or honorary researcher associated with Menzies.

EDUCATION AND TRAINING

TEAM:

Associate Professor Leigh Blizzard,
Graduate Research Coordinator
(City campuses)

Dr Sue Pearson, Honours and
UROP Coordinator

Dr Stephen Richards, Graduate
Research Coordinator (Sandy Bay)

Our Graduate Research Environment

One of the key goals of the Menzies Research Institute is to attract quality research students and early career postdoctoral researchers, and train them to become future research leaders.

Graduate research life continued to be vibrant at Menzies in 2008 with 51 students enrolled as candidates for postgraduate degrees. Another six students completed an honours degree during the year, and five undergraduate students were placed in the Undergraduate Research Opportunities Program (UROP) that was first introduced in 2005.

Providing a stimulating and rewarding learning environment that is responsive to student needs has become an important focus of Menzies. One initiative taken in 2008 was to provide a five-day course in, "Logistic regression and Survival Analysis" presented by Professor David W Hosmer, Emeritus Professor of Biostatistics at the University of Massachusetts. This was supplemented by a weekly program of teaching in statistics by Menzies' staff.

Monthly journal club meetings were conducted at each of the Macquarie Street and Bathurst Street sites to train students in the critical appraisal of scientific literature.



The Childhood Determinants of Adult Health (CDAH) team continued their monthly journal club and planning meetings at which students and postdoctoral fellows are given opportunities to critically appraise published papers, discuss issues in questionnaire design, present preliminary data, plan analyses and paper writing, discuss reviewers' comments on submitted papers, and address common data management and data analysis problems.

The Neuroscience group made use of international conferences and collaborations to expand their range of scientific capacities. In November, Catherine Blizzard spent time with Dr Jyoti Chuckowree at the University of Lausanne, Switzerland, learning a technique that allows in vivo imaging in the mouse brain. This capability has been passed on to others in her group.

PhD Completions

There were six PhD completions in 2008. They are listed below with their topics:

| | |
|--------------------------------|--|
| Samantha Fung | Interactions between metallathionein and neurons of the CNS |
| Robert Gasperini | Homer, TRP channels and calcium: the signalling triad of growth cone motility |
| Mohammad Rassem Irhimeh | Clinical haemopoietic implications of fucoidan treatment |
| Anna King | Unravelling the cellular pathology leading to neurodegeneration in motor neurone disease |
| Phillippa Oakford | Regulation of gene expression by the RUNX1 transcription factor |
| Adele Woodhouse | Pathological changes leading to neuronal degeneration in Alzheimer's disease |

Samantha Fung completed her PhD with the Neuroscience group supervised by Associate Professor Adrian West and Dr Roger Chung.

She is now a Postdoctoral Research Fellow at the Prince of Wales Medical Research Institute, Sydney.

Robert Gasperini completed his PhD with the Neuroscience group co-supervised by Associate Professor Inn Chuah. He is now a Research Fellow at Menzies, employed in the laboratory of Professor David Small.

Mohammad Rassem Irhimeh completed his PhD with Associate Professor Greg Woods. He has taken up a teaching/research position in Saudi Arabia.

Anna King completed her PhD with the Neuroscience group supervised by Professor James Vickers and Dr Tracey Dickson. She is now a Research Fellow at Menzies, and the recipient of a nationally competitive fellowship from the Motor Neurone Disease Research Institute of Australia.

Phillippa Oakford completed her PhD with the Cancer and Immunology group supervised by Dr Adele Holloway. She is now at the Norris Comprehensive Cancer Center at the University of Southern California.

Adele Woodhouse completed her PhD with the Neuroscience group supervised by Professor James Vickers and Dr Tracey Dickson. After a brief stint as a Postdoctoral Junior Research Fellow with the Wicking Dementia Research and Education Centre at Menzies, she was awarded an NHMRC CJ Martin Fellowship to undertake postdoctoral studies at the Institute Jean Roche in Marseille and plans to return to Menzies in 2011 for the final two years of this fellowship.

Published Papers

Our graduate research students make a significant contribution to the research output of Menzies. Their research topics focus on some of the most important health-related conditions and diseases affecting the human and animal populations of Australia and the world.

Students who were first author on a paper published in 2008 include **Richard Bradbury, Michele Callisaya, Dawn Dore, Stella Foley** (two papers), **Samantha Fung**, and **Jacqueline Leung**. Honours student **Meriam Shabbar** was co-author on a paper accepted for publication in the prestigious journal *Science* (it will be published in 2009). Among our 2007 graduates, **Kate Brettingham-Moore, Verity Cleland** (three papers), **Liesel Fitzgerald** (two papers), **Renee Ross** and **Julia Walters** continued to have publications in 2008 from work completed during their candidature.

Prizes, Awards and Honours

Judged on the scientific quality of her submitted abstract, a student bursary was awarded to **Dr Au Bich Thuy** at the Population Health Congress in Brisbane in July. This was the inaugural combined meeting of the Australasian Epidemiological Association, the Australian Health Professionals Association, the Australasian Faculty of Public Health Medicine and the Public Health Association of Australia – a meeting that attracted 896 abstracts and 1307 delegates.

Catherine Blizzard was the winner of the Australian Society for Medical Research Medical Research (ASMR) Student Award for Tasmania awarded during Medical Science Week in May 2008.

Helen Cameron-Tucker was a finalist in the ASMR Student Award for 2008.

Belinda Cochrane was an invited speaker at the Airways 2008 Scientific Meeting, which is a biennial national meeting with a theme of Chronic Obstructive Pulmonary Disease (COPD). Dr Cochrane presented her research on heart disease in the COPD patient.

Amanda Genders was awarded a National Heart Foundation Travel Award and a Student Travel Award from the European Association for the Study of Diabetes to attend

a major international diabetes conference in Rome during September 2008. This was the 44th Annual Meeting of the European Association for the Study of Diabetes. Amanda submitted an abstract entitled "Zaprinast acutely augments insulin-mediated capillary recruitment and glucose disposal in rats in vivo." The work reports on the insulin sensitising action of a phosphodiesterase inhibitor in muscle. The work was done jointly by Amanda and Eloise Bradley of the Muscle Research Group.

Heather McGee was awarded a prize for the best student presentation at the Mutagenesis and Experimental Pathology section of the Australian Health and Medical Research Congress in Brisbane in November 2008. Her presentation was titled "Early changes in the skin immune system following neonatal exposure to ssUVR".

Costan Magnussen was awarded the 2008 Menzies Student Prize for excellence in research achievement during the previous 12 months, as indicated by journal articles published or accepted for publication, grants awarded, conference presentations and honours and awards. Costan's research publications (4) and international conference presentation in 2008 were of the highest international standard as judged by independent peer review. He was the first author of a paper published in *Circulation*, a journal that has an impact factor of 12.75 and a ranking of 1/74 among journals in the field of cardiac and cardiovascular systems. Publication of his paper was accompanied by an editorial attesting to the importance of the paper. Costan also had a paper accepted by the *Journal of the American College of Cardiology*, a journal that has an impact factor of 11 and a ranking of 2/74 in the field of cardiac and cardiovascular systems. In addition, Costan was a finalist in the ASMR Student Award for 2008 and in the TEMCO Science



and Technology Award, an award under the Southern Cross Young Achiever Awards.

Clare Smith won a GlaxoSmithKline Australia Postgraduate Student Research Support Grant of \$25000 to provide travel support and research expenses. She was the Tasmanian winner of the AusBiotech–GSK Student Excellence Awards. This is a national event that encourages students to think about the potential commercial outcomes of their research. Additionally, Clare won a prize for best poster at University of Tasmania Postgraduate Student Association Research Day 2008. Clare is researching a new anti-malarial therapy and is supervised by Professor Simon Foote.

Liz Tegg was awarded a three-year Royal Hobart Hospital Research Foundation Clinical Fellowship,

and a Haematology and Oncology Targeted Therapies (HOTT) Award by Roche Oncology & Haematology in conjunction with the Clinical Oncological Society of Australia. The HOTT Award is provided to support a clinician in their research.

Adele Woodhouse was a finalist for the TEMCO Science and Technology Award, an award under the Southern Cross Young Achiever Awards. The purpose of these awards is to acknowledge, encourage and promote the positive achievements of young Tasmanians aged between 14 and 27 years of age.

Retrospective

Alison West was awarded a NHMRC Post-graduate research scholarship in 2008 and is undertaking a PhD at the Peter McCallum Institute in Victoria. Alison is a former UROP student and Cancer Council Tasmania Honours Scholarship

holder. She was supervised by Dr Jo Dickinson and Dr Adele Holloway during her honours year in 2007 and as a research assistant in 2008.

Honours Students

With the guidance of academic staff at Menzies, eight students successfully completed an honours degree in 2008.

They were **Gabriella Brown** and **Shirley (Flora) Cheong** under the supervision of Associate Professor Greg Woods, **Christopher Butler** under the supervision of Dr Roger Chung, **Emma Cazaly** and **Stanislaw Mitew** under the supervision of Dr Tracey Dickson, **Angela Lanzlinger** under the supervision of Dr Louise Roddam, **Moses Otto** under the supervision of Dr Seana Gall, and **Soo Yee Khor** under the supervision of Dr Stephen Richards.

Three of those have gone on to postgraduate work at Menzies.

Gabriella Brown is assessing chemotherapy and radiation in the treatment of the devil facial tumour disease under the supervision of Associate Professor Greg Woods. During her honours year she was the recipient of a Qantas Tasmanian Devil Honours Scholarship.

Angela Lanzlinger is pursuing her PhD studies exploring mechanisms of inhibition of pseudomonas aeruginosa biofilm under the supervision of Dr Louise Roddam and Dr David Reid.

Stan Mitew is undertaking his PhD studies in the area of axon pathology in neurodegenerative disease under the supervision of Dr Tracey Dickson and Professor James Vickers.

A fourth honours student,

Chris Butler, is working as a Graduate Research Assistant in the Neuroscience group with Dr Roger Chung.

Menzies' UROPs

Each year Menzies offers a number of Undergraduate Research Opportunity Program (UROP) scholarships to undergraduate students attending the University of Tasmania. They receive \$5000 to work closely with a supervisor at the MRI to undertake a small research project that provides research experience they may not otherwise receive during their undergraduate years. In 2008 the following students were successful in being awarded a scholarship to work at the Institute over the summer of 2008–09 and part-time during the 2009 academic year:

Nicholas Blackburn: Development of Metallothionein-IIA alpha and beta subunit constructs and exploration of their individual neuroprotective and neuroregenerative roles in comparison with the entire MT-IIA protein. Supervisors: Associate Professor Adrian West and Dr Roger Chung. This was a second UROP scholarship for Nicholas, who was rewarded for his previous efforts as a UROP scholarship holder. Nicholas will continue his work into the development of metallothionein-

IIA alpha and beta subunit constructs. This scholarship was funded by his supervisors.

Felicity Graham: Topics in applied biostatistics. Supervisor: Associate Professor Leigh Blizzard. Felicity investigated the association between the measured lung function of long-term tobacco smokers classified by the tar content of the cigarettes they had smoked, and analysed data from a randomized controlled trial of the use of mentoring and information technology in the management of adolescents with cystic fibrosis.

Ben Hunn: Neurobiology project. Supervisor: Professor David Small. Ben is working on a developmental neurobiology project to gain experience in the use of microscopy, dissection, making up solutions, preparing plates for experiments and running assays.

Carla Morley: Correlating ambulatory blood pressure measurements with clinic blood pressure measurements. Supervisor: Professor Mark Nelson. Carla searched existing databases for blood pressure measurements that had been collected in outpatient and primary care clinics. She provided Tasmanian data for a national initiative of the High Blood Pressure Research Council of Australia to correlate ambulatory BP measurements with clinic blood pressure measurements. This data was presented at the European Society for Hypertension conference.

Oliver Sargent: Genes that increase risk of multiple sclerosis. Supervisor: Dr Brendan McMorran. Previous work by Dr Jim Stankovich using genetic linkage-based approaches identified a number of genetic loci associated with the complex autoimmune disease multiple sclerosis (MS). The hypothesis is that one or more genes located within these loci contain rare mutations that increase risk of MS. Oliver selected a candidate gene in one of these loci following extensive literature searches, and sequenced the coding region of this gene in a selection of DNA samples from people with

MS looking for mutations that may alter gene function and thus provide partial explanation for the observed genetic susceptibility to MS.

Among students awarded UROP scholarships in 2007 to work at Menzies during 2007–08, two have since been employed at Menzies as part-time research assistants as they continue their undergraduate degree. They are **Kathryn Bowditch** (nee Hampton) who is working with Dr Adele Holloway, and **Ella Hoban** who is working with Dr Brendan McMorran.

Other support for Undergraduate Students

Several members of academic staff led by Professor Simon Foote provided lectures in genetics and statistical genetics as part of an undergraduate curriculum at the University of Tasmania, but with an open invitation to attend extended to Menzies' staff and research students.

Another important contribution to the undergraduate curriculum in 2008 was the third year undergraduate unit "Research Projects in Medical Sciences". In this unit, students spent one day each week of a semester undertaking a research project with a research group from Menzies or from the School of Medicine at the University of Tasmania. This unit provides students with an insight into laboratory research.

Research staff, postgraduate students and honorary members or associates of Menzies who participated in 2008 were Eloise Bradley, Carol Bussey, Dr Roger Chung, Dr Margaret Cooley, Dr Jo Dickinson, Professor Simon Foote, Dr Adele Holloway, Associate Professor Inn Chuah, Julie Harris, Dr Michelle Keske, Roger Latham, Dr Brendan McMorran, Dr John Newman, Dr Fiona Poke, Associate Professor Steve Rattigan, Dr David Reid, Dr Steve Richards, Dr Louise Roddam, Philippe St Pierre and Associate Professor Adrian West.

Of the 24 undergraduate students who enrolled in this unit in 2008, 18 subsequently enrolled in an honours degree in 2009.

ANIMAL SERVICES

STAFF:

Fleur Rodda,
Manager Animal Services

Peta Lawrie,
Animal Technician

Shelley Lampkin,
Animal Technician

Jacqueline Noonan,
Animal Technician

Stephen Mackintosh,
Animal Technician support

Keri Playford,
Animal Technician support

Angela Maher,
Animal Technician support

Jeff Eager,
Animal Technician support

Murray Plaister,
Animal Technician

Marcus Pollard,
Animal Technician

Animal Services provides animal resources and technical services, advice and support to researchers upon request. In addition, they provide advice for ethics applications, including help with which techniques are best suited.

Menzies' Animal Services complies in strict adherence with the Australian Code of Practice.

Animal Services currently have two facilities, one conventional and one micro isolator PC2 facility.

In 2008, Animal Services commenced set up for embryo transfers and is now able to provide pronuclear and blastocyst microinjection, as well as cryopreservation services.

Importation is another service provided, including coordination of the import and housing of animals from a variety of sources throughout the world.



Daily care and maintenance of the University's range of strains, is the largest part of Animal Services work, as well as the running of a health status program to continue providing animals with a defined health report.

The new co-location building will provide a small holding facility, which will be staffed, stocked and run by Animal Services.

ADMINISTRATION TEAM

STAFF:

Tim Albion, IT Systems Manager
Mark Bennett, General Manager
Alistair Chilcott, IT Systems Administrator
Jenny Cochrane, Data Manager
Ben Duan, Computer Support Officer (from 26 May)
Ceri Flowers, Executive Assistant to Director
Julia Garry, Administrative Officer – Research Management

Felicity Gates, Administrative Assistant – Receptionist (from 14 January)
Melita Griffin, Development Manager (to 29 September)
Fiona Horwood, Communications and Events Manager (from 21 January)
Furley Johnston, Receptionist (on maternity leave)
Dr Lisa Koutoulis, Research Manager
Dixie Prenter, Secretary to the Director (to 9 April)
Karena Richards, Finance Manager (from 8 December)

Emma Stubbs, Administrative Assistant
Susan Sussems, Development Officer
Kathryn Thomson, Administration Manager
Felicity Tracy, Administrative Assistant - Development (from 3 September)
Imogen Tyson, Administrative Assistant – Research Management (from 13 November)
Stewart Wells, Administration Officer – Finance
Barbara Zimmerman, Development Coordinator (from April 23)

The Administration Team aims to provide efficient and effective support to the Director, Board and staff at Menzies. The Team supports Menzies' research activities across a number of areas, including administration and reception, human resource management, finance, grants management, information technology, development and communications.

Administration, Reception and Human Resources

Administration, reception and human resources staff played a significant role supporting the achievement of Menzies' core goal areas and its strategic direction during 2008. Menzies continued to grow in this time with staff and student numbers increasing by 21 per cent from 229 to 277. To accommodate our growth and to make room for our new building, our operations are now spread across six sites in Hobart.

The new building is being constructed on the old Menzies' site in Liverpool Street to accommodate all of our operations. The building is scheduled for completion in late 2009. While the building will have space to house 290 Menzies staff and students, we anticipate that we will continue to grow to reach our

optimum size of 500 people in 2013. This means that we are working hard to obtain additional funds to add an additional stage to the building to accommodate our future growth.

The Administration Team has played a key role in the new building process, including managing the consultation process to ensure that the building is suitable and adequately equipped to carry out our work.

Research Management

The Research Management Team supports researchers in the submission and maintenance of their grants. This includes assistance in the writing, checking and editing, interpretation of eligibility requirements, formatting, formulation of budgets, as well as the coordination and compilation of large research initiatives. Once a grant is successful, the Research Management Team ensures compliance with research agreements including progress and financial reporting, and liaising between the funding bodies and the researchers to ensure the needs of both parties are met. The Research Management Team is also responsible for ensuring the accurate and timely reporting of

research income and publications to the University of Tasmania for the allocation of federal government funding to the institute.

The funding highlight for 2008 was the awarding of \$12 million in federal government funding from the National Health and Medical Research Council (NHMRC). This included a prestigious Program Grant looking at the genetics of complex diseases (the first time a Program Grant has been awarded in Tasmania), a record nine Project Grants in health related areas ranging from the effect of the herpes virus in multiple sclerosis to the impact of physical activity in childhood on the progression of knee arthritis in later life. Additionally we received five NHMRC fellowships to support researchers, from those straight out of their PhD studies through to Senior Members of the Institute.

Finance

In 2008, Menzies received income of \$17.6 million from a variety of funding sources, including \$6.3 million from nationally competitive grants via the NHMRC and the Australian Research Council.

Menzies also received \$4.1 million from the University of Tasmania



The Administration Team

(UTAS). The majority of these funds are performance based and are received in recognition of the level of research income obtained by Menzies, the number of journal publications and the number of completing and enrolled research higher degree students.

The Tasmanian Government continued to provide support in a number of areas including recognition of Menzies' status, achievements and place in the Tasmanian community by awarding funding under the Tasmanian Icons Program through the Department of Economic Development and Tourism. The Department of Health and Human Services also provided funds, including the Tasmanian Cancer Registry which is managed by Menzies on behalf of the Tasmanian Government, to support our epidemiological research, and a postdoctoral fellowship – the Dick Butfield Fellowship.

The Menzies Foundation was largely responsible for the formation of

Menzies and has supported the Institute since its inception. The Foundation continued this support in 2008, providing \$150,000 towards the activities of the Institute.

Menzies continued its strong relationship with international philanthropic organisation The Atlantic Philanthropies. In addition to the \$7.5 million received to support the construction and basic fit-out of the new building in 2005 and 2006, The Atlantic Philanthropies provided \$354,000 during 2008 as part of a \$US2,000,000 project over the period 2006 to 2010 that will see Menzies' researchers oversee the development of a national non-communicable disease surveillance system for Vietnam.

Menzies has developed excellent working relationships with a number of local and interstate organisations with common goals. During 2008 we were fortunate to receive significant funding from these organisations, including:

- Australian Cancer Research Foundation – \$550,000;
- Royal Hobart Hospital Research Foundation – \$487,000;
- ANZ Trustees Ltd (Wicking Trust) – \$300,000;
- The Cancer Council Tasmania – \$183,000;
- Tasmanian Community Fund – \$155,000;
- National Heart Foundation – \$150,000;
- Royal Australasian College of Physicians – \$130,000;
- Motor Accident Insurance Board – \$116,000;
- Multiple Sclerosis Society of Tasmania – \$100,000;
- Alzheimer's Australia – \$82,000;
- Australian Cystic Fibrosis Research Trust – \$81,000;
- Motor Neurone Disease Research Institute of Australia – \$77,500;
- Masonic Centenary Medical Research Foundation – \$70,000;
- Australian Lung Foundation – \$60,000;

- General Practice Training Tasmania – \$54,000;
- David Collins Leukaemia Foundation – \$50,000; and
- Cerebral Palsy Tasmania – \$49,500.

Menzies obtained a significant surplus in 2008 with an operating surplus of \$2.9 million. A majority of the surplus relates to research project funding that has not been expensed, but will be expensed on those projects in future periods. The Income Statement and Balance Sheet for the year ended 31 December 2008 are included in this report on pages 73 and 74.



Information Technology

Staff from Information Technology (IT) aim to provide reliable, effective, secure and innovative IT solutions to assist Menzies in pursuing its aspiration.

Menzies' IT systems are continually being maintained and improved to ensure the secure and confidential storage of data and the reliable and effective use of computers and software in the day to day running of Menzies.

The IT Team is also responsible for the in-house development of

software applications which improve work efficiencies for Menzies' staff. In 2008 we saw the development of systems for scanning the vast amounts of paper based data that Menzies has collected over the last two decades.

Converting this data to an electronic format not only makes it more accessible to our researchers and better protected against catastrophic destruction, but also reduces the storage space required in our new building.

Development

Menzies was the beneficiary of the dedicated work of a record number of volunteers and supporters in 2008.

Over 1600 donations resulted in \$255,230 raised. In addition, Menzies was privileged to receive two bequests totalling \$650,000. Menzies is grateful for every gift of every amount. All supporters are listed on pages 69 to 72.

Over 750 donors continued their loyal annual support of Menzies through four direct mail appeals that focused on one area of research per appeal. We thank Menzies' researchers and their patients who work with development staff on the appeals as well as Red Jelly and Southern Cross Television for their continued support. The Every Day Angel program, consisting of donors who support Menzies on a monthly basis, continues to build a stream of reliable income for our research and we wish to thank each and every Angel. We also express our gratitude for the gifts we receive in honour and in memory of loved ones.

We wish to pay tribute to the many community and service groups that arranged fundraisers in towns and suburbs throughout Tasmania, and all the individual members of the groups who took time out of



Art of Christmas event 2008

their busy schedules to coordinate the logistics. We want to thank the members of clubs, associations, schools, churches, nonprofits, corporations and government agencies who made donations or attended a Menzies' talk to learn more about our research.

Under the continuing voluntary leadership of Ian Matterson, Chairman of major gifts, Menzies invited supporters to join the bequest *Society for the Future* and 21 individuals did so by informing Menzies of a gift in their Wills. Thank you to the families of our bequest supporters and to the solicitors and trust companies who are a part of Menzies' bequest program.

In 2009, Menzies will launch the *Healthy Community Fund*, a fundraising initiative for

scholarships, equipment and seed funding for new research. Five honours scholarships were funded in 2008 and will be awarded to student researchers in 2009. We wish to acknowledge and thank Ian Matterson for his role in helping launch new programs that diversify fundraising income for Menzies.

Collaboration with the Royal Hobart Research Foundation on the fourth Art of Christmas ensured this event enjoyed increased support. Artworks donated by local artists Patrick Grieve, Cathy McAuliffe, Louise Bloomfield, Leigh Oates, Georgina Pajak, Hilton Owen, Nigel Lazenby, Tony Flowers, Rebecca Murdoch and Michael Weitnauer were auctioned at a gala cocktail evening at the Key Australia, with eleven of the works being featured on Christmas greeting

cards. The greeting card collection has been the most popular to date, and thanks to support from Print Applied Technology, Spicers Paper and Red Jelly, profit from sales has been very encouraging. More than \$32,000 was raised from artwork and card sales.

Our annual Thank You Day was held on November 26 at the Royal Tasmanian Botanical Gardens. Director, Professor Simon Foote thanked Menzies' volunteers, philanthropic partners and *Society for the Future* members who came from throughout the state to attend.

We want to express our sincere gratitude to everyone who took part in development programs in 2008, for helping grow research funding at Menzies.



VOLUNTEERS

Volunteers are vital to Menzies' research effort and successes. They allow us to carry out work that would not otherwise be achievable across a broad range of research projects and administration areas. The significant contributions made by volunteers are deeply appreciated by researchers and administration staff at Menzies.

Volunteers are introduced to Menzies through a variety of sources, including participating in a study, learning about us from the talks program or from the many media releases that Menzies is featured in.

During 2008 there were approximately 60 active volunteers at Menzies, many providing valuable assistance to research projects. Many others helped with administration work, mail-outs and data entry, while those with medical skills worked in our clinics. Some volunteers become very involved in our special events and work alongside the development team.



Volunteers find the Menzies' volunteer program helps them to gain confidence and skills to return to the

workforce, many come and go, but still remain loyal and hard-working, and for this we say a big thank you.

Menzies would like to thank the following volunteers for their commitment and dedication in 2008:

Davys Baldwin
Irma Baumeler
Denis Black
Beverly Brown
Catherine Brown
Margaret Brown
Alexander Buckman
Audrey Button
Yang (Carol) Cao
Ray Carroll
Robyn Chapman
Joan Clough
Fay Cox
Ian Crouch
Wendy Davidson
Kate Dell
Kathryn Edwards
Pam Elwell

Sandy Fleming
Jeff Fung
Colleen Hay
Gary Hay
Barbara Hayes
Cheryl Hewitt
Keryl Houlgrave
Jean Keil
Lyn Kirkbride
Mary Leon
Barbara Long
Barbara Maccana
Sylvia Macleod
Marie Magill
John Mathewson
Dorothy Melross
Elise Millington
Leon Morrell

Susan Morrell
Elizabeth Neal
Pauline Payne
Judy Pennicott
Dale Pitt
Rhona Puclin
Kate Rutherford
Margaret Stewart
Mary Stuart
Samantha Twigg
Marylyn U'Ren
Robert U'Ren
Gerald Veldhuis
Fay Wheeler
Jenny Wiggins
Janice Williams
Helen Wood
Simone Yemm

THANK YOU TO OUR VALUED SUPPORTERS

Community

Donations – Community and Business Groups

Anonymous (14)
A Giving Circle Inc
Aurora Energy
Bothwell Masonic Lodge
Bride of the Year
Brighton & Broadmarsh Branch CWA
Brighton Block Pty Ltd
Broadmarsh Branch – CWA
Burnie Bridge Club
Burnie Handweavers, Spinners and Dyers Guild
CAF Australia
Calvary Operating Theatre Staff
CDC Management Pty Ltd
City Of Hobart Preceptory
Clarence Pensioner's Association Inc
Clarence RSL War Memorial Trust
Community Rehab Clinic
Corporate Express Office Equipment
Country Womens Association – Magra
CWA Sandy Bay Branch
Derwent Tavern Social Club
Derwent Valley Lodge
Hotel Grand Chancellor – Hobart
Jackson Tremayne & Fay Lawyers
Launceston Church Grammar School
LGAT Assist
Lindisfarne RSL
Lindisfarne School for Seniors
Lions Club Of (Launceston)
Windmill Hill Inc
Lions Club of Bridport Inc
Lions Club of Burnie Emu Bay Inc
Lions Club of Deloraine Inc
Lions Club of Devonport Mersey Inc
Lions Club of Hadspen South Esk Inc
Lions Club of Huon Inc
Lions Club of Kentish Inc
Lions Club of King Island Inc
Lions Club of Perth Tasmania Inc
Lions Club of Port Cygnet Inc
Lions Club of Queenstown Inc
Lions Club of Sorell Inc
Lions Club of Wynyard Inc
Mansfield Builders
Members Equity Bank
Mount Lyell Lodge No 24 TC
Newstead Heights School
North Bruny Island Country Women's Association

RACT Insurance Fun Committee
Ranelagh Branch Country Women's Association In Tasmania Inc
Rotary Club of Smithton
Rotary Club of Ulverstone
Rowella Health Auxiliary
Sandford Morning Tea Group
Sheffield RSL Women's Auxiliary
Soroptimist International – Circular Head
Tasmanian Alkaloids Pty Ltd
Thirlstane Golf Club Associates
UTAS Sport & Recreation
Veolia Environmental Services
Westpac Huon Contact Centre

Art of Christmas 2008

4Lunch
AW Photography
Art Poster
Bartercard
Christopher Lawrence
Corporate Express
Eye Spy Signs
Foster's Group
Highly Strung
Neville Moane
Print Applied Technology
Pure Tasmania
Red Jelly
Spicers Paper
The Henry Jones Art Hotel
The Key Australia
The Mercury

Artists:

Louise Bloomfield
Tony Flowers
Patrick Grieve
Nigel Lazenby
Cathy McAuliffe
Rebecca Murdoch
Leigh Oates
Hilton Owen
Georgina Pajak
Michael Weitnauer

Everyday Angels

Anonymous (6)
Mr Tim Albion
Mr Bill Avery
Mr Stephen Bender
Dr David Boadle
Mrs Anita Clarkson
Mr & Mrs Don & Lillian Cornish AO
Mrs Elizabeth Darvell
Mr Brendon Davidson

Miss Matty June Doering
Mr & Mrs Josh & Felicity Ey
Ms Kerry Forrest
Mr Geoffrey and Miss Julia Goss
Mr & Mrs Paul & Melita Griffin
Mr & Mrs Garth & Brenda Haas
Mr John Hudson
Mrs Doreen Elaine Ireland
Miss Emma Jackson
Mrs Margaret Keogh
Mrs Margaret Knight
Mr Ian McConnelly
Mr Sam Mollard
Mrs Wendy Noye
Ms Felicity Oakford
Kim Paterson
Mrs Glenda Paton
Mr & Mrs Bob & Frances Russon
Mrs June Scott
Mrs Gwynneth Sperring
Mr & Mrs Richard & Susan Sussems
Ms Carmel Taylor
Mrs Cynthia Tennant
Mrs Pat Vallance
Mr & Mrs Walter & Robin Verth
Mrs Margaret Williams
Ms Barbara Zimmerman
and Prof John Dickey
Menzies Research Institute's
Healthy Community Fund
Gifts for Scholarships, Medical
Equipment and Research Support
Veolia Environmental Services
Corporate Express
Mansfield Builders
The Helene Matterson Medical
Research Scholarship

Donations – Individuals

A

Anonymous (256)
Miss Maureen Absolom
Mrs Barbara Adams
Mrs Christine Adams
The Hon. Dick Adams MP
Mr & Mrs Pat and Dorothea Albion
Mrs Sheila Allwright
Mrs Carole Andrews
Mrs Ila Andrews
Ald Elise Archer
Mr David Arnold

B

Mr & Mrs Brian and Beverley Baker
Mr & Mrs James and Justine Bamford

Alison Milsana and Roger Banfield
 Mrs S Bardenhagen
 Mrs Jessie Barker
 Mrs M Barnden
 Ms Jan Barren
 Mr Joseph Barta
 Mrs Beryl Bates
 Mr Douglas Beath
 Mr Jon Belkner
 Mrs Nancy Bell
 Ms Ursula Bennett
 Mr & Mrs Nigel and Barbara Bentley
 Mr David Besanvalle
 Ms Felicity Bever
 Mr & Mrs Reginald Bingham
 Mrs Mary Birtwistle
 Mr & Mrs Gustav and Doreen Bjorklund
 Mr & Mrs R Bluemmel
 Mrs WC Blyth
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 Mrs R Bradfield
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 Mrs Rosemary Breen
 Mrs Ann Bridley
 Mrs Gwen Briscoe
 Mr & Mrs Charles & Gwenneth Brown
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 Dr Catherine Bulman
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 Mr Russell Burgess
 Mrs Lola Burk
 Mrs Dot Burleigh
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 Mr Kenrick Burrows
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C

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 Mr Geoff Cavanagh
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 Mr Ian Chapman
 Mr Peter Charlesworth
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 Ms Patricia Colegrave
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 Mrs Erica Conway
 Mrs Gillian Cooley
 Mrs Cynthia Coombe
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 Mr DC Copping
 Ms Margaret Cormack
 Ms Georgina Cornelius
 Mrs Joan Cornwall
 Mrs Joy Coton
 Ms Sylvia Cowan
 Mrs Fay Cox
 Mrs Johanna Coy
 Mrs Andrea Cranny
 Dr Colin Crawford
 Mrs Nancy Crew
 Mrs Jill Critchlow
 Mr Graeme Crole
 Mrs Norah Crowther
 Mrs Elizabeth Curtis
 Mrs Suzanna Curtiss
 Mr Max Cute

D

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 Mr Richard Darcey
 Ms Dorothy Davies
 Mrs Doreen Dawes
 Mrs Cora Dean
 Mrs S Dean
 Ms Adrienne Denholm
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 Mr & Mrs R & K Dilger
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 Mrs Susan Folder
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 Mr Henry Foster
 Mrs Noeline Foster
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 Mrs MJ Geeves
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 Mr Thomas Goodwin
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 Mrs Marcia Gourlay
 Mrs Judy Grant
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 Mrs Beverley Leitch
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 Mr Blair Richards
 Mr Brian Richardson
 Mrs J Richardson
 Mrs Rita Richter
 Mr Warwick Risby
 Mr & Mrs Paul K & Coral G Roberts
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 Mrs Anne Rood
 Drs Thomas & Antonia Ross
 Mr Matthew Ryan

S

Mr Gregor Salmon
 Mr Rodney Saunders
 Ms Alison Savage
 Mr Charles F Saville
 Mr Paul Sayer
 Mrs Robin Scharaschkin
 Mr & Mrs Geoffrey & Joyce Seymour
 Mr Stan Sheppard

Mrs Lynda Sherriff
 Ms Tania Sierink
 Mrs A Sims
 Mrs Kaye Skinner
 Mrs Tryntje Smit
 Miss Joy Smith
 Miss Maureen Smith
 Mr & Mrs Ross & Necia Smith
 Mr G Smith
 Ms Wendy Spencer
 Mr & Mrs Ralph & Robeeta Spinks
 Mr Colin Sproule
 Mrs Joanne Staite
 Ms Margareta Stanojevic
 Mrs Valerie Stanton
 Mrs Roxanne Steenbergen
 Mrs Pauline Stolp
 Mrs J Stringer
 Ms Mary Stuart
 Mr James Swan
 Mrs Gwen Sweet
 Mr Terry Sykes

T

Mrs Phillipa Tatchell
 Ms Jenny Tayler
 Mrs Gina Taylor
 Mrs Clara Tegg
 Mrs K Thiessen
 Ms A Thom
 Mrs J Thompson
 Ms Kaye Tidey
 Mrs A Todd
 Mrs Shirley Topfer
 Mrs Helen Torenus
 Mr Peter Toubert
 Mrs Elaine Tracey
 Ms Geraldine Trainor
 Mrs Helen Travers Hawker
 Mr Lloyd Trenham
 Mr Eugene Triffett
 Mr Amastasios Tom Tsiakis
 Mrs Jennifer Turnbull
 Ms Marie Ann Turnbull
 Ms Fiona Tustian
 Dr A Tymms
 Ms Annabel Tyson

V

Mrs Voula Vafakos
 Ms Ree Van Galen
 Mr Jaap Wim Vermaas
 Mr & Mrs Brian & Julie Von Bibra
 Mr & Mrs Robert & Katharine Von Bibra

W

Mrs Margaret Wade
 Ms Helen Walch
 Drs Alan & Hilary Wallace
 Mrs Judith Wallace
 Mrs Molly Walsh
 Mrs Valmay Walsh
 Mrs R Ward

Mr Phillip Warrener
 Mrs Kathryn Washusen
 Mr Peter Wass
 Mr & Mrs James & Freda Watson
 Mrs Beverley Watson
 Mrs Bessie Webb
 Ms Belinda Webster
 Mr John Wedd
 Mrs J Weldon
 Mr Stewart Wells
 Mrs Valma Wells
 Mrs Tessie West
 Mr Jim Wharton
 Mrs Joan Whelan
 Mrs Pamela Whelan
 Mr Rob Whitehouse
 Mrs Marion Whittle
 Mrs L Williams
 Mrs Joan Williamson
 Mr Graham Willing
 Mr Neil Wilson
 Mr Robert Wilson
 Mrs Hilary Wiltshire
 Mrs Rosalie Winduss
 Dr Tania Winzenberg
 Mr & Mrs Ron & Pam Wisbey
 The Hon. R C Wood
 Mr Graham Woodward
 Mrs Joan Woolley
 Mr Dave Wootton
 Mr K G Worsley
 Mrs Margaret Woudwyk
 Mrs Caroline Wright
 Mrs Annamarie Wyatt

Y

Dr Rosemary Young
 Mr Leslie Young
 Mrs Diana Young

Bequests and Trusts

Anonymous (8)
 M & WHC Boys Donation
 Max Bruce Trust administered by Peter Worrall Lawyers
 Estate of the late Ronald Buss
 Estate of the late Patricia Crabtree
 Estate of the late Joyce Winifred Doherty
 Estate of the late Rosina Gostling
 Estate of the late Christopher Warren Hallam
 Estate of the late Gerald Harvey
 Estate of the late Rita Hughes
 Bessie Kable Trust
 Estate of the late Margaret Annette Rose Mack
 Estate of the late Brian Marks
 Matterson Family Trust on Behalf of the late Helene Elizabeth Matterson
 Estate of the late Ruby Josephine Menzies
 Estate of the late Arthur and Mary Paton
 Estate of the late Dulcie Stewart

Estate of the late Elise Patricia Hilda Trevor
 Estate of the late Ethel Marion Young

Society for the Future Members

Anonymous (27)
 Mrs Susan Butterworth
 BW Flassman
 Catherine Jean Halley Garvie
 Mr & Mrs Garth and Brenda Haas
 Jill Marie Hallam
 Kim Paterson
 Mavis Purcell and Carol Davenport
 Mr & Mrs Ken and Jeanette Wills

In Memorium

Mr Willi Eugen Andree
 Mrs Iris Banner
 Mr Paul Belderson
 Mr Barry Bennett
 Mr Lindsay Chadwick
 Mr Max Cherry
 Mr Brian Coe
 Mrs Audrey Dale
 Mrs Lenna Downham
 Mrs Jennifer Dunn
 Mr Gary Eastley
 Dr Arthur Geoffrey Fenton
 Mr Keith (Peter) Fenton
 Mr Clifford Garwood
 Mr Harry Gill
 Mr William Logan Glachan
 Mr Reginald Robert Gregg
 Mrs Ruth Jean Gregg
 Mr Arthur Hansch
 Mrs Eleanor Heaton
 Mrs Anita Higginson
 Mr David Hill
 Mrs Edna Hirst
 Mr William (Bill) Jackman
 Mrs Anne Jager
 Ms Marie Jasinkski
 Mrs Elaine John
 Mr Graham Kean
 Mr Clifford Kingston
 Mrs Eileen Lewis
 Mr Harry Lietzau
 Mrs Gwendolene Lucas
 Mrs Valerie Marsh
 Mr David Vincent McCann
 Mr Peter McKenzie
 Mr Ron Mee
 Mrs Marjorie Isobel Moores
 Mr Peter Selwyn Ryan
 Mrs Patricia Scarafiotti
 Mr & Mrs Albert Thodey
 Mr Leslie Watson
 Mr Colin Samuel Weeding
 Mr Ronald Westcott

INCOME STATEMENT

for the year ended 31 December 2008

| | 31 Dec 08 | 31 Dec 07 |
|--|--------------------|-------------------|
| | \$ | \$ |
| REVENUE | | |
| Commonwealth Government grants | 6,904,950 | 3,890,239 |
| Tasmanian Government grants | 1,067,182 | 958,969 |
| University of Tasmania | 4,113,684 | 2,757,612 |
| Menzies Foundation | 150,000 | 150,000 |
| Atlantic Philanthropies (New building project) | — | — |
| Other contracts and agreements | 3,969,033 | 3,432,102 |
| Donations | 226,306 | 216,474 |
| Bequest and donation transfers from UTAS and UTAS Foundation | — | — |
| Bequests | 653,971 | 67,556 |
| Interest from trust investments | 0 | 65,845 |
| Other interest | 28,298 | — |
| Interest from research accounts | 72,842 | 61,542 |
| Other income | 392,631 | 471,031 |
| Total Revenue | 17,578, 897 | 12,071,370 |
| EXPENSES | | |
| Salaries and on-costs | 8,885,963 | 7,114,004 |
| New building project contribution | — | — |
| General consultancy services | 2,392,154 | 1,170,196 |
| Scholarships | 419,109 | 361,149 |
| New appointment expenses | 56,511 | 50,150 |
| Staff development | 227,857 | 99,729 |
| Public relations and marketing | 119,554 | 75,403 |
| Administration and operating costs | 1,662,494 | 1,145,512 |
| General travel | 331,947 | 350,670 |
| Infrastructure charges and recoveries to University | 130,323 | 9,966 |
| Equipment purchases | 138,625 | 91,851 |
| Hire of facilities and equipment | 20,182 | 74,967 |
| Repairs and maintenance | 56,099 | 74,319 |
| Electricity | 2,668 | 4,710 |
| Depreciation plant and equipment | 240,418 | 102,819 |
| Total Expenses | 14,683,904 | 10,725,445 |
| Operating Result | 2,894,993 | 1,345,925 |

BALANCE SHEET

as at 31 December 2008

| | 31 Dec 08 \$ | 31 Dec 07 \$ |
|--|------------------|------------------|
| CURRENT ASSETS | | |
| Funds held by University of Tasmania | 8,070,160 | 4,763,070 |
| Receivables | – | 359,427 |
| Prepayments | – | 3,680 |
| Total Current Assets | 8,070,160 | 5,126,177 |
| NON-CURRENT ASSETS | | |
| Plant and Equipment | 2,099,951 | 1,381,146 |
| Less Accumulated Depreciation | (682,268) | (441,849) |
| Total Non-Current Assets | 1,417,683 | 939,297 |
| Total Assets | 9,487,843 | 6,065,474 |
| CURRENT LIABILITIES | | |
| Creditors and accruals | 484,352 | 86,870 |
| Income Received In Advance | 86,216 | – |
| Provision for Annual Leave | 136,541 | 92,863 |
| Total Current Liabilities | 707,109 | 179,733 |
| Total Liabilities | 707,109 | 179,733 |
| Net Assets | 8,780,734 | 5,885,741 |
| EQUITY | | |
| Opening Retained Surplus | 5,885,741 | 3,698,576 |
| Items transferred to Menzies 1 January 2007: | | |
| Animal Services plant and equipment | – | 92,513 |
| Animal Services project balances | – | (14,301) |
| Health Sciences research projects | – | 763,028 |
| Add: Profit/(Loss) for the Period | 2,894,993 | 1,345,925 |
| Total Equity | 8,780,734 | 5,885,741 |

NOTES TO THE FINANCIAL STATEMENTS

for the year ended 31 December 2008

1. Summary of Significant Policies

The University of Tasmania prepares general purpose financial statements which are audited by the Tasmanian Auditor-General. A copy of the latest audited statements is available, upon request, from Financial Services.

These financial statements represent those transactions and balances specifically pertaining to the Menzies Research Institute. The statements do not include all disclosures required by Australian equivalents to International Financial Reporting Standards.

Relevant accounting policies which have been adopted in the preparation of the attached Income Statement and Balance Sheet of the Menzies Research Institute are:

a) Basis of Accounting

The financial statements have been prepared on the accrual basis of accounting using the historic cost convention unless otherwise stated.

b) Funds held by University of Tasmania

The funds held by the University of Tasmania comprise:

| | |
|--|--------------------|
| Research Projects | \$5,308,882 |
| Trust Funds | \$1,181,718 |
| Wicking Dementia Research and Education Centre | \$623,437 |
| Discretionary Funds | \$449,132 |
| Contingency Reserve | \$400,000 |
| Strategic Funds | \$67,127 |
| Animal Services | \$39,864 |
| Total | \$8,070,160 |

c) Trust Funds

The University of Tasmania holds a number of trust fund accounts on behalf of the Menzies Research Institute. Investment earnings in respect of these trust fund accounts are distributed to the Menzies Research Institute, however, the trust fund account balances, totalling \$879,870 at 31 December 2008, are not reflected in the attached Balance Sheet. During 2008, no amount from these trust fund accounts has been recognised as interest revenue to the Menzies Research Institute.

In addition, the Menzies Research Institute holds a number of trust accounts. The balance of the accounts, totalling \$1,181,718 at 31 December 2008, is reflected in the attached Balance Sheet.

d) Plant and Equipment

Plant and equipment is brought to account, and carried at cost, where the value is greater than ten thousand dollars.

Plant and equipment is depreciated on a straight line basis over its useful life commencing from the time the asset is held ready for use. Depreciation rates for plant and equipment applicable during 2008 are 10–33 per cent, and this is consistent with the prior year.

Gains and losses on disposals are determined by comparing proceeds with carrying amount. These are included in the income statement.

e) Creditors and accruals

These amounts represent liabilities for goods and services provided to the Menzies Research Institute prior to the end of the year which are unpaid. The amounts are unsecured and are normally settled within 30 days.

f) Employee entitlements

Wages and salaries, and sick leave

Liabilities for wages and salaries are recognised as payables in respect of employees' services up to the reporting date. Sick leave entitlements provided to the employees of the University are non-vesting and are based on a cumulative sick leave system. Liabilities for non-accumulating sick leave are recognised when the leave is taken.

Annual Leave

Liabilities for annual leave in respect to non-academic staff are recognised and measured as the amount unpaid at the reporting date at current pay rates in respect of employees' service up to that date. Related on-costs have been included in the provision. Annual leave for academic staff is deemed to be taken in the year in which it is accrued, hence, no provision is made in respect of these employees.

Long Service Leave

The University charges a levy on the salaries of certain staff and has assumed the liability for long service leave.

g) Equity

In October 2006 a number of research staff from the Faculty of Health Science at the University of Tasmania joined Menzies as part of a significant growth strategy. From 1 January 2007, the research grants associated with these researchers were transferred from the Faculty of Health Science to Menzies. The balance of these grants at 31 December 2006, \$763,028, was brought into the Menzies accounts in 2007. These are reflected in 2007 comparative figures.

From 1 January 2007, Menzies began to manage the University of Tasmania's Animal Services. The 31 December 2006 equity in Animal Services—\$14,301—was transferred to Menzies. These are reflected in the 2007 comparative figures.

Statement of Certification

We certify that the financial statements reflect an accurate record of income and expenditure recorded through the University of Tasmania's financial system, together with assets and liabilities specific to the Menzies Research Institute.

Mark Bennett

General Manager
Menzies Research Institute

Garry Hennessy

Director of Financial Services
University of Tasmania

DATE: 16 March 2009



University of Tasmania

The Menzies Research Institute is an institute of the University of Tasmania.



A Tasmanian Icon

The Tasmanian Government proudly supports the work of Menzies through the Icons Program. The Icons Program showcases the very best that Tasmania has to offer, nationally and internationally.



Menzies Foundation

The Menzies Foundation was largely responsible for the formation of the Menzies Research Institute and has generously supported Menzies since its inception.



Australian Cancer Research Foundation

Proudly supported by the Australian Cancer Research Foundation.



research|thanks to you