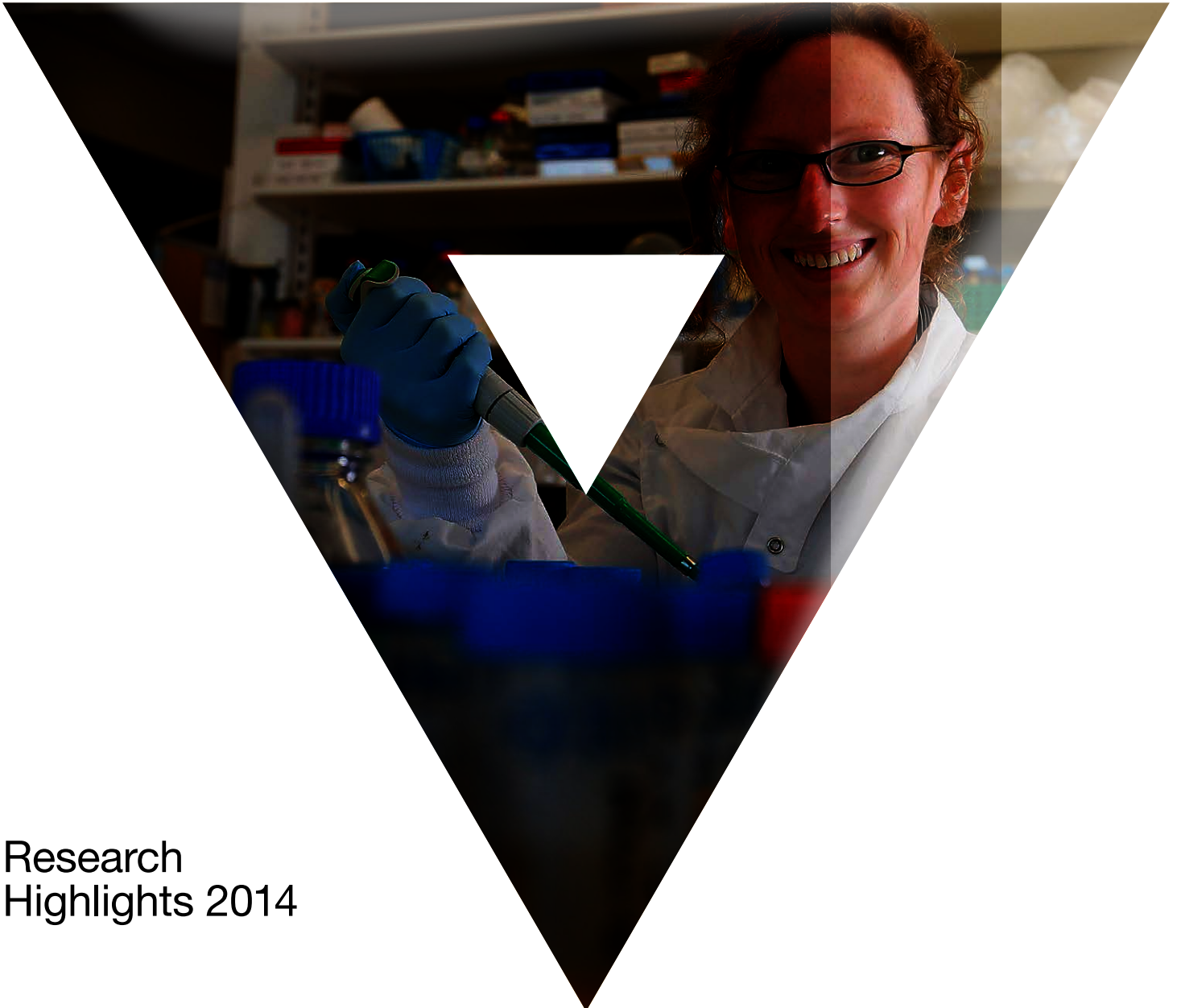




UNIVERSITY of
TASMANIA

MENZIES
Institute for Medical Research

Menzies Institute for Medical Research



Research
Highlights 2014



For more than a quarter of a century the **Menzies Institute for Medical Research** has been making discoveries to improve the health of our community. Every year researchers at Menzies investigate the biggest health issues facing us here in Tasmania and globally.

We continue to align our research structure within themes that address the burden of disease in our community. This year we have delivered remarkable results that will contribute to improving the health and wellbeing of our community and save many lives. Among our research highlights for 2014 were:

Dr Seana Gall's research provided important new evidence to support the protection of children from passive smoke exposure.

Public Health and Primary Care

PHPC is the largest theme of the Institute, bringing together researchers with expertise in environmental, psychiatric and chronic disease epidemiology, biostatistics, health economics, health services and primary care. We aim to better understand risk factors and prevention of disease and to improve population health approaches to disease management.

The long-term effects on vascular health of childhood exposure to parental smoking. This study pooled data from the Menzies' Childhood Determinants of Adult Health study and a similar cohort in Finland, the Cardiovascular Risk in Young Finns Study. Follow-up of 3,776 children for up to 25 years showed that children exposed to their parents' smoking had poorer vascular health in adulthood than their peers whose parents did not smoke. The study looked at whether parents' smoking behaviour was associated with the structure of carotid artery in adulthood, measured using non-invasive ultrasound. While a number of adverse effects on children of parental smoking have been established previously, this study provided important new evidence to support the protection of children from passive smoke exposure for the sake of their blood vessel health in later life. The paper, led by Dr Seana Gall, was published in the *European Heart Journal*, one of the leading cardiovascular journals worldwide.

Is workplace health promotion a good investment? There has been considerable interest internationally in investigating whether investment in workplace health promotion programs give a good return to employers. Workplace health promotion

takes advantage of the fact that adults in the workplace are a captive audience and that employers might gain from a more productive and engaged workforce. Menzies is coming to the end of a five-year NHMRC-funded research program in partnership with the Tasmanian Government to evaluate the effectiveness of a workplace health promotion program for State service employees. Siyan Baxter conducted a review of the world's literature on return on investment of workplace health programs which showed that the better the quality of the study, the lower the return on investment. Published by the *American Journal of Health Promotion* the paper was accompanied by an editorial describing it as "the most extensive and well-conceived review conducted to date".

Blood lipids can predict the progression of disability in people with multiple sclerosis. Growing evidence suggests that some 'bad' fats – that are usually associated with poor cardiovascular health – are linked to the progression of MS. This particular study examined the fat profiles from blood samples of 141 people with relapsing remitting MS. The samples were collected at six-monthly intervals over two-and-a-half years as part of the NHMRC-funded Tasmanian MS Longitudinal Study. The results showed the amounts of a number of different fats in the blood, including total cholesterol, were closely associated with disability level. This association remained strong even when factors such as smoking, exercise, age and sex were taken into account. The research was led by Prudence Tettey and published in the *Multiple Sclerosis* journal.

Musculoskeletal Health and Diseases

Because of the burden of arthritis in an ageing community, this disease theme is an extremely important one to Menzies. The theme leader, Professor Graeme Jones, received the University of Tasmania Research Medal in 2014.

Knee fat and osteoarthritis. The infrapatellar fat pad is located close to the cartilage and bone surface under the kneepad. In studies published in 2014 we reported that the area of the infrapatellar fat pad was associated with reduced radiographic arthritis and pain, decreased knee cartilage defects and bone marrow lesions, and increased cartilage volume in older adults. In a follow-up study, we reported that infrapatellar fat pad area in women was associated with reduced risks of cartilage defects and pain, and reduced risk of cartilage loss over 2.6 years. Our results suggest that infrapatellar fat pad size appears to have a protective role for knee symptoms and structural damage in older adults.

Vitamin D and joint pain. Vitamin D is important for bone, cartilage and muscle function. Bone and muscle pain are common in persons with severe vitamin D deficiency, but the relationship to joint pain is uncertain. This study demonstrated that moderate vitamin D deficiency was associated with new or worsening knee pain (and possibly hip pain) over five years in a group of older Tasmanian adults. This suggests that ensuring normal vitamin D levels may prevent or reduce worsening of knee or hip pain in elderly people. However, giving vitamin D supplements to people who have normal vitamin D levels or only mild vitamin D deficiency is unlikely to have any effect on pain.

Obesity and arthritis. A Menzies report described the associations between overweight measures in childhood and knee pain, stiffness and dysfunction among adults 25 years later. We found that childhood overweight was associated with adulthood knee mechanical joint pain, stiffness and dysfunction among males. Most importantly, these associations were independent of adult overweight measures. The change in weight status from childhood to adulthood was also associated with knee pain, with subjects who were overweight in both childhood and adult life having the greatest prevalence and risk of knee pain. Subjects who were overweight in childhood and then of normal weight in adulthood also had an increased amount of knee pain compared to people without weight problems.

Dr Dawn Aitken is an NHMRC Postdoctoral Research Fellow in the Musculoskeletal Health and Diseases theme. Her work focuses on identifying the risk factors for the onset and progression of osteoarthritis.

Cardio-Metabolic Health and Diseases

Cardiovascular disease – still the primary cause of premature death and disability among Tasmanians – has its roots in disturbances in the body's chemistry that long precede the development of disease. The cardio-metabolic theme at Menzies is multidisciplinary in nature, ranging from the laboratory bench to the patient's bedside and to population health.

Blood pressure: deepening understanding of human physiology. For many decades it has been believed that pressure wave travel within the large arteries plays a major role in driving abnormal blood pressure. However, work by Dr Martin Schultz (in collaboration with the Royal Hobart Hospital Cardiology Department) debunked this theory and showed for the first time in humans that the dynamic function of the arterial system (rather than wave travel) was more important in determining an individual's underlying blood pressure. This finding supports a shift in fundamental understanding of blood pressure physiology. The study comprised part of Dr Schultz's PhD thesis that was awarded the Royal Society of Tasmania Doctoral Award for the most outstanding PhD across all science disciplines in Tasmania.

Another advance from the cardio-metabolic group in 2014 was the successful launch of the Menzies' clinic for difficult-to-manage blood pressure. Our statewide randomised trial (Tas-ELF) to identify the benefit of early diagnosis of heart failure recruited more than 400 patients. We have had excellent progress with our major studies aimed at reducing re-admission for heart failure, as well our trial to identify whether targeted lowering of central blood pressure will improve clinical outcomes. A very exciting development at the end of 2014 was the award of a \$2.6 million grant to identify the value of coronary CT (a form of imaging) in family members of patients with premature coronary disease.



Cancer, Genetics and Immunology

Tasmania has a history of contributions to the understanding of genetics in disease, including Huntington's chorea, multiple endocrine neoplasia, eye disease, multiple sclerosis and cancer. Significant advantages of genetic research in Tasmania include the depth of genealogical information and a relatively stable, historically isolated population, in addition to logistical considerations such as small geographic distances and few health care service providers.

Biobanking. We remain committed to engaging the public in consultation in the way in which genetic research is conducted. A deliberative democracy consultation was undertaken in 2013 by a team comprising Associate Professor Jo Dickinson and Dr Bek McWhirter of the Menzies Institute for Medical Research and Professors Chalmers, Otlowski and Nicol of the Centre for Law and Genetics, University of Tasmania, in conjunction with national and international collaborators. The outcomes of this research were published in 2014 and are informing the development of frameworks for conducting future genetic research.

Cancer. Menzies' work in the field of human genetics research is conducted in collaboration with world-wide international experts in the field. Last year we reported on our work in prostate cancer which has identified common genetic variants associated with increased risk. In total more than 70 genetic variants have now been identified which explain approximately 40% of the heritability of this condition. In 2014, the Menzies School of Population Health, Northern Territory and the Menzies Institute for Medical Research were awarded \$1 million of nationally competitive funding from the NHMRC to investigate the genetic contributors to vulvar cancer. We have recently undertaken whole genome analysis to identify how the genetic makeup of a population may increase risk of this cancer.

Eye Disease. Associate Professor Kathryn Burdon is working to understand the genetic contributors to eye diseases, such as glaucoma. This work is conducted in collaboration with national and international experts in the field. Our team has identified a number of new genes which contribute to the development of glaucoma.

Devil Facial Tumour Disease. Professor Greg Woods' group has made significant in-roads into our understanding of the Devil Facial Tumour Disease. We are now much closer to understanding how we may be able to combat this disease by gaining a better understanding of the immune response to the tumour cells. This work has revealed that the immune response can be manipulated to increase normal defence processes against tumour cells.

Immune Function. Our understanding of how the immune system contributes to disease development and progression is closely linked to our understanding of human disease. Professor Heinrich Korner has been working towards understanding the intricacies of how inflammation contributes to skin lesions during parasitic infection.



Associate Professor James Sharman and Dr Martin Schultz are developing our understanding of the physiology and clinical applications of central (aortic) blood pressure.

A new measure of cardiac function. The Menzies' Director, Professor Tom Marwick, is a leader in international efforts to introduce a new measure of cardiac function called global longitudinal strain (GLS) into routine clinical practice. This is a robust, well validated and reproducible technique for the measurement of heart muscle deformation. In this study, the Menzies team sought to assemble evidence that GLS is an accurate marker in predicting cardiovascular outcomes, compared to the current standard measurement, ejection fraction (LVEF). All of the published evidence comparing GLS against LVEF was reviewed and 16 articles (involving more than 5700 patients with heart failure, heart attack, heart valve disease and other conditions) were identified. GLS was found to be a stronger predictor of death than LVEF. This important study was published in the international cardiac journal *Heart*.

Another danger from dietary salt. Excess dietary salt has historically been associated with development of high blood pressure. The Menzies' diabetes research group has found that too much salt in the diet can also cause insulin resistance, the condition that precedes the development of type 2 diabetes. A diet high in salt can cause insulin resistance by reducing the ability of small blood vessels in skeletal muscle to function properly in response to the hormone insulin. This work was published in the journal *Diabetologia*.



Lab work on a vaccine against Devil Facial Tumour Disease is progressing with the development of our understanding of the immune response to the tumour cells.

Neurodegenerative Diseases/Brain Injury

Tasmania has an ageing population, with many at risk of neurodegenerative diseases including Alzheimer's disease, other dementias, Parkinson's disease and other movement disorders such as motor neurone disease. We also have an increased prevalence of multiple sclerosis. There are no cures and only limited treatments available for these diseases. At Menzies our neuroscientists are performing cutting edge laboratory research into the causes and mechanisms underlying these diseases.

Making new brain cells and new connections. We are working to harness and encourage the brain's innate capacity to respond to disease and injury through the generation of new brain cells or the development of new connections. Within this field, Dr Kaylene Young was awarded of the inaugural Metcalf Prize from the National Stem Cell Foundation of Australia in 2014 in recognition of leadership in stem cell research. Dr Young has been studying three distinct types of brain stem cells, which generate new nerve cells for different brain regions. She has also discovered an immature cell population which can feed, protect and assist nerve cells in the cortex, the outer part of the brain most prone to damage.

Young Investigator. Dr Catherine Blizzard was one of only two Australians selected for the internationally competitive 2014 Young Investigator Training Fellowship from the Federation of European Neuroscience Society. The fellowship included a fully supported placement at the University of Bologna in the lab of internationally renowned stem cell researcher Professor Laura Claza for two months and an invited presentation at the 8th FENs International Symposium of Neuroscience in Milan. Dr Blizzard is now applying these techniques to her work with Associate Professor Tracey Dickson in understanding frontotemporal dementia and motor neurone disease.

Understanding the cause of Alzheimer's disease. Work led by Professor David Small has revealed further insight into the mechanisms underlying Alzheimer's – particularly the amyloid precursor protein (APP), which is central to the disease's development. Professor Small and his team have shown that the normal role of the APP protein is to stimulate neurogenesis or the creation of new brain stem cells. We are hoping that by understanding more about this process ongoing studies will be able to harness this property in the fight against Alzheimer's and acquired brain injury.

Dr Michelle Keske's research within the Cardio-Metabolic Health and Diseases theme has found that too much salt in the diet can cause insulin resistance, the condition that precedes the development of type 2 diabetes.



Would you like to know more?

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about our current research projects:

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If you would like information on how you can support Menzies
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*Cover image: In 2014 Menzies neuroscientist Dr Kaylene Young
was one of two Australians to win the inaugural Metcalf Prize
for leadership in stem cell research from the National Stem Cell
Foundation of Australia.*



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