



## Spotlight: vascular health

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Welcome to the Spring 2007 edition of Spotlight, a publication that highlights areas of research within Monash University's Faculty of Medicine, Nursing and Health Sciences. The edition provides examples of vascular health research underway.

Vascular health encompasses heart and blood vessel diseases. Coronary heart disease is predicted to become the world's leading public health problem by 2020. To tackle this important issue, Monash vascular health researchers are taking an approach that is broader than bench-to-bedside and encompasses discovery, development, clinical innovation and analysis of vascular health.



# Vascular health research at Monash

From laboratory to patient to community

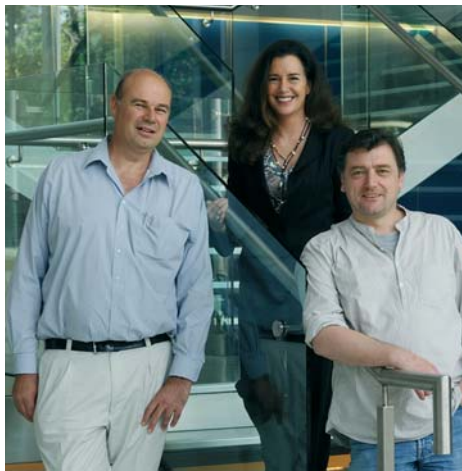
## Laboratory

### Enhancing cardiac regeneration with growth factors

Humans do not have the extraordinary regenerative capacities of our more distant relatives in the animal kingdom. Starfish, newts or fish can grow near perfect replacements for lost limbs, fins or tails. Human tissues do have an innate ability to repair themselves, but tissue that grows back after injury rarely looks as good, or works as well, as the one it replaced.

"Understanding such differences between species could lead to strategies to regrow lost or damaged human tissues and organs", explains Professor Nadia Rosenthal, an international leader in molecular biology and founding Director of Monash's new Australian Regenerative Medicine Institute (ARMI).

Regenerative medicine brings together several scientific fields including stem cell research, molecular biology and tissue engineering. Professor Rosenthal is internationally renowned for her work on the use of stem cells in muscle regeneration and heart repair.



Professor Ian Smith welcomes Professor Nadia Rosenthal and Mr Alan Sawyer

ARMI is a joint venture between Monash University and the Government of Victoria. It will be set up under stringent international standards to attract the world's best researchers, and to serve as a platform for increased collaboration with the European Molecular Biology Laboratory (EMBL). ARMI will adopt EMBL operating procedures and complementary programs to ensure exchange of scientists and collaborative research programs.

### Fast facts: Australians and coronary heart disease (CHD)

- Deaths each day due to CHD: 60
- Percentage of those who die within the first hour of their first-ever symptoms: approx. 25%
- Percentage of deaths in a private or home setting: 80%
- Estimated portion of the Australian population affected by CHD: 1.7% (355,600)

Source: Heart Foundation 2007 Fact Sheet (2004 results); Heart, stroke and vascular diseases, Australian facts 2004, Australian Institute of Health and Welfare.

**An estimated 61 percent of people who live through heart failure die within five years of the event. For those aged between 50 to 59 years around one person in 100 will develop the disease and the rate doubles for every decade thereon.**

Sources: National Heart Foundation and Institute of Health and Welfare; British Heart Foundation 2001.



Associate Professor Chris Sobey and Dr Grant Drummond

### Stroke: when oxygen can become toxic

Stroke is a serious condition brought about by a loss of blood supply to all or part of the brain resulting in damaged brain tissue.

After a stroke, levels of a short-lived highly reactive form of oxygen, oxygen-radicals, become excessive and toxic. Oxygen-radicals play an important role in a number of biological processes; however they damage cells if their levels become excessive. The body has a number of natural defences against this which include anti-oxidants such as vitamin C.

A team of vascular pharmacologists led by Associate Professor Chris Sobey and Dr Grant Drummond are probing the brain's blood vessels to understand how the dangerous increase in oxygen-radicals occurs following a stroke.

They have made the surprising finding that hormone replacement therapy (HRT) increases the risk of stroke and worsens its outcome in post-menopausal women.

## Clinical development

### New anti-clotting drugs discovered

A new class of drugs that prevent clot formation have been discovered and developed at Monash University's Australian Centre for Blood Diseases. These drugs appear to be more effective than aspirin at preventing disease-causing blood clots and have fewer side effects.

Researchers have identified the mechanisms that cause the formation of the type of clots leading to heart attack and stroke. They have also discovered how these differ from the mechanisms involved in normal blood clotting.

Another breakthrough for this team, led by Professor Shaun Jackson, is the development of high resolution imaging capabilities to visualise the formation of blood clots occurring in real time in small arterioles.

### Better blood pressure diagnosis

Studies to better define a person's true blood pressure are under way in Monash's Department of Vascular Sciences and Medicine, headed by Professor Barry McGrath.

Professor McGrath, who is also Clinical Director of the CVH, said that "although blood pressure taken in the clinic is currently the best marker of a person's risk of heart attack or stroke, there is now recognition that measuring blood pressure by itself is insufficient.

"Significant numbers of people can be misdiagnosed," Professor McGrath said. "Their blood pressure can be high in the clinic but not the rest of the time and those who are normal in the clinic may have high blood pressure the majority of the time.

"Approximately, ten percent of people are misclassified in this way, equating to two million individuals in Australia.

"By better identifying sub-clinical arterial disease, looking at arterial stiffness and other biomarkers, we seek to improve treatment and prevention of cardiovascular disease, thus improving an individual's chance of a longer disease-free life."

In addition, such improved diagnostic tests will assist in decreasing the costs to the community associated with preventable long-term illness such as heart attack and stroke.



An enzyme in Vampire bat saliva dissolves blood clots

### Vampire bats are the key to saving lives

Monash researchers are studying a clot-busting substance derived from vampire bats that may improve the treatment of patients with ischaemic stroke.

The substance, desmoteplase, targets and destroys fibrin, the structural scaffold of blood clots. It has the potential to be used up to three times longer than the current stroke treatment window, without increasing the risk for additional brain damage.

Lead scientist Associate Professor Robert Medcalf and his team at Monash's Australian Centre for Blood Diseases are also investigating the means by which the naturally occurring blood clot busting enzyme tissue-type plasminogen activator (t-PA) interacts with neurons and modulates brain function.

### High tech solution under way to predict vascular illness

The risk of heart disease and stroke will be easier to predict with the use of a state-of-the-art biochip developed in a collaboration between the Monash Antibody Technologies Facility and Monash's Centre for Vascular Health (CVH).

The biochip will be able to detect proteins and peptides contained in plasma and use them as biomarkers to predict the risk of heart diseases and stroke.

The CVH will also team with RMIT's accredited diagnostics facility to check and validate the technology before it is used in clinical trials to commence in 2008.

"With this jointly-developed technology, we hope to make a major step towards the identification of at risk patients with unprecedented precision," CVH Director Professor Harald Schmidt said.

"Currently too many patients are considered at risk when only a few of them actually will suffer from a cardiovascular event.

"Furthermore, monitoring of those at risk is poor, since there is no measure available to help assess whether a specific therapy is sufficient.

"This collaboration establishes the CVH diagnosis platform, one of three major platforms being developed by the centre." Professor Schmidt said.



Can a daily dose of aspirin help prevent cardiovascular disease?

### Aspirin as prevention?

Research into whether a daily dose of aspirin can help prevent cardiovascular disease and stroke, as well as dementia and some cancers, is underway in the Department of Epidemiology and Preventive Medicine at Monash University.

Called the ASPirin in Reducing Events in the Eldery (ASPREE) study, this research into aspirin is due to the drug's increased use as an alternative to non-steroidal anti-inflammatory drugs which have safety concerns.

"ASPREE will determine whether a daily low dose aspirin prolongs the healthy active life of people over 70 years," project leader and Head, Department of Epidemiology and Preventive Medicine, Professor John McNeil said.

The balance of risks and benefits are being carefully studied. In particular, possible negative side effects such as cerebral and gastrointestinal haemorrhage and anaemia need to be assessed.

It is planned that 20,500 healthy people over 70 years of age will take part in the study to either take 100mg of aspirin each day, or a placebo. Participants will be followed up for five years.

It is hoped that a Biobank will be established as part of the ASPREE trial. Blood samples and other information collected from participants annually will provide a resource for the evaluation of new disease predictors into the future. Funding for the Biobank is presently being sought.

## Clinical practice

### Can heart failure be detected earlier?

Heart failure is the inability of the heart to pump enough blood to meet the needs of the body, leading to a poor quality of life and early death for the sufferer. If detected early and treated, both quality of life and survival can be significantly improved. However, heart failure is often not diagnosed until late in the disorder.

A new community-based trial will test whether the hormone, BNP (brain-type natriuretic peptide), may be used as an early diagnostic marker or early indicator of pending heart failure.

SCREEN-HF (SCREening Evaluation of the Evolution of New Heart Failure) is a trial which will assess the heart function in 700 patients who have high levels of BNP to determine their risk of developing heart failure. The usefulness and cost effectiveness of BNP in this process will be assessed.

The study is to be completed in early 2008 and will provide information on the usefulness of BNP as part of an assessment tool for early diagnosis of heart failure.

The NHMRC Centre of Clinical Research Excellence in Therapeutics headed by Professor Henry Krum, at the Department of Epidemiology and Preventive Medicine, is working with BUPA Australia Health Pty Ltd on the project.

### Making headway with cardiovascular disease

The predominant cause of cardiovascular disease is the underlying inflammatory



Professor Ian Meredith



Professor John McNeil

process of atherosclerosis in which the arteries of the heart (and the rest of the body) stiffen and become blocked with fatty and fibrous plaques.

An international leader in research into the mechanisms and clinical manifestations of atherosclerosis is the Monash Cardiovascular Research Centre (the research unit of MonashHeart and the Department of Cardiothoracic surgery).

Using a very small high-frequency ultrasound receiver/transmitter mounted on the tip of a fine coronary artery catheter, clinicians and researchers can see the amount and type of plaque that is present in the walls of an individual's artery.

Director of MonashHeart and Monash Cardiovascular Research Centre, Professor Ian Meredith said that this technique provides exceptional insight into the presence and type of disease.

"Using this technology, much more information is available than from traditional dye and X-ray techniques. We participate in international studies to investigate new drugs and new coronary artery stents (expanding wire cages) that are used to keep arteries open," Professor Meredith said.

"In other studies we use very fine wires that record blood pressure and blood flow in the coronary arteries themselves to look at the way stiffening of the aorta affects blood flow to the heart muscle itself.

"This leading-edge concept of 'ventriculo-vascular' coupling is the basis of understanding of important and common medical conditions such as increased blood pressure, over-development of the heart muscle and in some cases, eventual failure of the heart to pump adequately," he said.

## Epidemiology of vascular disease

### Indigenous vascular health

Professors Brian Oldenburg and Andrew Tonkin and Dr Bronwyn Fredericks of the Department of Epidemiology and Preventive Medicine (DEPM) are working on a Queensland-based research program focusing on the prevention and management of circulatory and associated diseases in Aboriginal and Torres Strait Islander peoples living in urban areas.

The program is operating through the National Health and Medical Research Council funded Centre of Clinical Research Excellence.

It is a broad national partnership between the Queensland Aboriginal and Island Health Council, the DEPM at Monash University, University of Queensland, James Cook University, National Health Foundation and the University of Wollongong. The different research projects are aimed at developing new interventions and approaches to improve the cardiovascular health of Aboriginal and Torres Strait Islander peoples.

### Mediterranean diet prevents heart disease

Australia's largest study of eating habits has found that traditional mediterranean foods may prevent cardiovascular diseases such as heart attack and stroke.

"The mediterranean diet is a rich source of antioxidants, mono-unsaturated fats, omega-3 fatty acids and fibre, and relatively low in saturated fats. This combination is believed to have antioxidant, anti-inflammatory and anti-thrombotic properties that may help reduce cardiovascular disease," said Mr Linton Harriss a Monash PhD student involved in the study. Mr Harriss's research is focusing the effect of alcohol and diet on cardiovascular disease.

The 10 year study involves around 40,000 people, aged 40-69 years, who are participating in the Melbourne Collaborative Cohort Study (Health 2020), run by The Cancer Council Victoria. One quarter of the people on the study are migrants from Italy and Greece. Co-authors of the study include researchers from Monash University, The Cancer Council Victoria, The University of Melbourne, University of Cambridge and St Vincent's Hospital Melbourne.



Traditional Mediterranean foods may prevent cardiovascular disease.

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## The Centre for Vascular Health

### Prevention and improvement a priority

Since the treatment of diseased blood vessels is ineffective and expensive, researchers at CVH aim to preserve a healthier state of blood vessels, according to Centre Director, Professor Harald Schmidt.

"Organs like the heart and brain are affected in the very late stages of blood vessel disease, the origins of which started decades earlier during their twenties and thirties," Professor Harald Schmidt said. "Therefore, we need to identify and target blood vessel disorders in the earliest stages."

"We investigate the dysfunction of blood vessels in terms of their ability to dilate, regulate growth and wall thickness, to interact appropriately with blood constituents, and to control clot formation." Professor Harald Schmidt said.

CVH seeks to accomplish this through three major platforms: diagnostics, medical imaging and intelligent drugs.

### Innovation in diagnostic imaging

Scientists at the CVH are working on a molecular imaging platform for the early detection of vascular disease. Dr Stavros Selemidis is a key scientist in the imaging program.

CVH will establish the state-of-the-art facility in 2008 with the goal of creating medical imaging equipment to test the state of people's vascular health. "This highly innovative technology will enable researchers to image molecules that damage the blood vessel wall (free radicals), damage that leads to vascular disease," says Dr Selemidis.

The next stage of the development will occur in 2009, when technology will be established that has the potential of being directly applicable to human imaging. The technology is based on Magnetic Resonance Imaging (MRI) technology currently in clinical use and will form an important platform that will be further developed with scientists in the Faculty of Engineering and the Centre for Synchrotron Sciences.

## How to donate

Your donation to research conducted within the Faculty of Medicine, Nursing and Health Sciences at Monash University will be an important and much appreciated contribution. Donations over \$2 made to the Monash University Medical Foundation are tax deductible. Please send your cheque or money order to:

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## Spotlight

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