

## Biomed Benchmark

News from Biomedical Science at Monash – June 2006, Issue 1

### Introduction

Our knowledge of human biology has been accelerating for more than half a century. Medicine is being transformed through new therapeutic approaches and sophisticated preventative strategies.

However, there is still a long way to go in tackling the diseases that plague humankind around the world. At Monash, our goal is to bring together outstanding researchers in a collaborative environment, supported by state of the art equipment, to understand life, right down to the molecular level. By combining the talents of more than 800 scientists, supported by chemists, physicists, engineers, synchrotron scientists and e-research scientists in the Clayton precinct, we plan to bring an energy and ambition not previously seen in Australia to further accelerate medical research.

Our research encompasses a very wide range – from premature baby health, to cancer, the prevention of malaria, protein folding disease (CJD, Alzheimer's), tissue engineering and repair, high blood pressure and vascular disease, problems in development affecting the brain, Multiple Sclerosis, stem cells and organ regeneration, obesity and many others.

This is the first Biomed Benchmark publication to let you know what we are doing to reduce both the human and financial burdens of ill-health.

Professor Warwick Anderson AM  
Head, School of Biomedical Sciences



### New research labs

By December 2008, the first of two new buildings will be ready for occupation by Monash biomedical researchers.

Over the past five years the School of Biomedical Sciences (SOBS) has expanded its research capabilities significantly. The construction of the STRIP (Science Technology Research and Innovation Precinct) 2 and 3 buildings will provide the much needed space and new facilities to accommodate current and future growth.

When completed in December 2009, the new buildings and current buildings, designed solely for research, will provide the largest dedicated biomedical research complex in Australia. The design will encourage further collaborative research within Monash and act as a gateway through which industry and commercial interests can gain access to the vast expertise and technology available at Monash University.

The new buildings have been designed to accommodate a large majority of the current research groups within SOBS with the view of co-locating existing research groups who have similar research interests and share similar technologies.



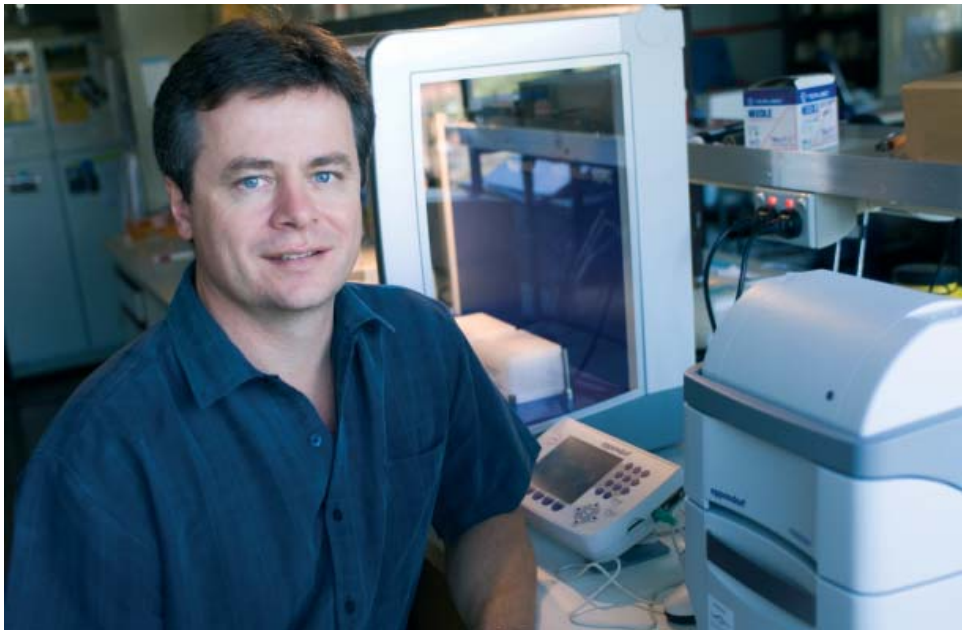
*STRIP 2 building commences in January 2007 and will be completed by December 2008.*

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The School of Biomedical Sciences has:

- 340 research staff (2005)
- 285 higher research degree students\*
- 942 undergraduates

*\*as of 27 April 2006*



Associate Professor Stuart Hooper

## Babies to breathe easier

Understanding lung development in preterm babies could be the key to helping them to breathe easier.

A team of Monash biomedical scientists, led by Associate Professor Stuart Hooper, is researching the factors that regulate normal lung development in humans and how they are altered by premature birth.

Approximately 2000-3000 premature babies are born each year in Australia with lungs that have not developed to an appropriate level. In most instances, these infants require the assistance of mechanical ventilators to breathe. However, this can damage their fragile lungs, leading to the development of chronic lung disease later in life.

“But by understanding lung growth during fetal development, and how the lung transforms from being a liquid-filled organ to an air-filled organ, scientists can identify the mechanisms by which artificial ventilation injures immature lungs,” Associate Professor Hooper says. “We can then develop better methods for ventilating premature infants without injuring their lungs or impeding their development.”

To study the transformation of the lung into a gas-exchange organ, researchers are using a unique X-ray beam produced by a synchrotron to determine how the lung fills with air after birth. It has enabled them to image the pattern of lung aeration from birth in real-time.

A synchrotron is a large machine (about the size of a football field) that accelerates electrons to almost the speed of light. As the electrons are deflected through magnetic fields they create extremely bright light. The light is channelled down beamlines to experimental workstations where it is used for research.

“This technique is a major step forward in determining the factors that influence and enhance lung aeration so that premature infants are ventilated to produce an even distribution of air throughout the lungs”, Associate Professor Hooper says.

Researchers will use the new Australian Synchrotron when it opens at Monash University in 2007.

## Moving away from cancer

Understanding how cancer cells move around the body is crucial in preventing the disease from spreading.

Dr Martin Lackmann and his team are trying to understand and halt the development of cancer by investigating how cells move and position themselves in cancerous tumours.

Cancer is the leading cause of death in Australia, with one in three men and one in four women being affected before the age of 75.\*

Proteins called Eph receptors coordinate the movement and positioning of cells. They are active during embryonic development, but generally not later in life.

In cancers, Eph receptors re-emerge and are involved in the movement of cancerous cells, both in driving the formation of blood vessels necessary for tumour growth, and also in a process called metastasis. This is where cells from the primary tumour invade surrounding tissue and then move to other sites around the body, thus influencing the extent of the disease and causing secondary tumours.

The research group led by Dr Martin Lackmann is investigating the function of Eph-receptors to try and develop an agent that will target cancerous cells bearing these receptors.

“We are examining tumour cells expressing Eph receptors so that an Eph-specific anti-cancer agent can be developed for use

in treating a range of cancers, including kidney, brain, skin and colon cancers,” Dr Lackmann says.

In further investigations, the group recently discovered that they can halt the ability of the Eph receptors to cause cells to move away from each other by blocking association of the receptor with the enzyme ADAM10. Activation of this enzyme breaks cell-cell interactions caused by Eph receptors and has important implications for metastasis.

“If we can stop the activity of ADAM10 on Eph receptors, then we can potentially prevent tumour cells from repelling each other and travelling throughout the body to invade other areas”.

\* The Cancer Council Australia  
[www.cancer.org.au](http://www.cancer.org.au)

*Dr Peter Janes and Dr Martin Lackmann*



## Answer in the sting

Screening toxins from jellyfish venoms could help develop more effective antivenom and be the source of new drugs.

Associate Professor Wayne Hodgson, from the Monash Venom Group, is leading a team of researchers investigating the pharmacological properties of venoms to provide further information about the effectiveness of antivenoms and also to see if the toxins they contain can be used to develop new pharmaceutical products or highly selective biomedical research tools.

Considered to be some of the world's most venomous creatures, the box jellyfish, the brown snake and the funnel web spider, all reside in Australia. Due to the toxins their venom contains, these animals are capable of causing rapid death. Antivenoms are available, but some clinicians still question how effective some of them really are.

The major box jellyfish (*Chironex fleckeri*), considered to be the world's most venomous creature, is responsible for more deaths in Australia than snakes, sharks and salt water crocodiles. *Carukia barnesi*, more commonly known as the Irukandji jellyfish, is closely related to the major box jellyfish but is much smaller with



Associate Professor Wayne Hodgson

a body diameter of approximately 2.5 cm. Both jellyfish deliver their venoms into the blood stream causing profound effects on the victim's cardiovascular system, which may result in rapid death.

"Recent work by our marine biology colleagues at James Cook University have indicated that the Irukandji symptoms are now produced by more than one species of jellyfish," Associate Professor Hodgson says. "Our research has shown that the antivenom produced for the major box jellyfish is not as

effective as we once thought and appears to be ineffective against Irukandji jellyfish."

Associate Professor Hodgson's group is extracting toxins from the jellyfish venoms to see if they can inhibit or reverse their effects. They are testing to see if new treatment strategies, given in conjunction with antivenom, would be more effective, while also checking whether the toxins contain other useful compounds suitable for other pharmaceutical purposes.

"By screening these toxins we are attempting to optimise the use of the venoms", he says.

## Stem cell promise for kidneys

Stem cell therapy could save people from kidney transplants or on-going dialysis.

Dr Sharon Ricardo and her team from the Monash Immunology and Stem Cell Laboratories are investigating whether stem cells from bone marrow can be induced to replace specialised adult kidney cells and therefore repair damaged kidneys. They are hopeful that stem cells injected into the kidney will replace the diseased cells and reproduce to form a healthy kidney.

One in three Australians are at risk of kidney disease, and one in seven people show at least one indicator of kidney damage.\* Unfortunately, the demand for kidney transplants is so high that many people die waiting for a matched organ. On-going kidney dialysis is an alternative, but offers only marginally increased kidney function and requires long treatment times – often more than once a day. As the number of people with kidney failure grows by six per cent each

year\*, there is a real urgency to develop new therapies.

"Current long-term dialysis treatment results in a very poor quality of life," Dr Ricardo says. "As an alternative we are investigating the ability of stem cells to replace damaged kidney cells and restore function."

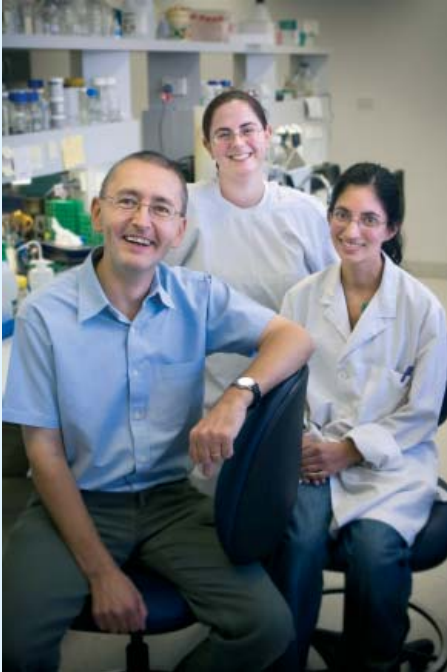
Dr Ricardo is using bone marrow transplantation techniques to sort stem cells from bone marrow and deliver them back to mice with kidney disease to determine if they have the ability to repair injured cells. She is using mouse models with renal disease and tracking the delivery of stem cells to the kidney to identify which cells are used in repair and how this process is controlled.

"We know that bone marrow cells can replenish damaged kidney cells, it is just a matter of working out how to control this process to promote tissue regrowth", she says. "The kidney has the ability to repair itself following acute damage. We are investigating the processes that regulate renal repair and cellular replacement in order to apply this to a chronic disease setting."



Dr Sharon Ricardo

\*Kidney Health Australia ([www.kidney.org.au](http://www.kidney.org.au))



Dr Brian Cooke and his lab team

## Knocking out malaria

Removing a single gene from the Malaria parasite could prevent the most severe forms of the disease and save millions of lives.

Dr Brian Cooke, and his team have found that by “knocking out” the SBP1 (skeleton binding protein-1) gene from the malaria parasite, red blood cells infected with malaria can no longer stick to the inside of blood vessels and block blood flow to vital organs; a process that can cause severe disease and, frequently, death.

The team is now trying to develop a drug that will target the SBP1 gene so they can stop Malaria from being such a severe and potentially fatal disease.

Between 300 to 500 million people worldwide suffer from Malaria. Each year, in more than 105 countries, more than two million people, mostly young children, die from the disease. There are four malaria parasites that infect humans but only one is deadly – *Plasmodium falciparum*. The

parasite is injected into the bloodstream when a mosquito bites, and enters and grows inside red blood cells.

Once inside the cells, the parasite sends proteins throughout the blood cells via membrane structures known as Maurer’s clefts. The clefts dock under the surface of a red blood cell’s outer membrane and deposit a parasitic protein called PfEMP1 onto the cell’s surface, enabling it to anchor to the inside of blood vessels.

The docking generally occurs in major organs such as the heart, lung, kidney, brain or the placenta of pregnant women. The infected cells eventually build up and block blood flow to these organs, frequently resulting in death.

“The SBP1 gene acts as a kind of ‘chauffeur’ which ferries PfEMP1 onto the red cell surface,” Dr Cooke says. “Without the chauffeur, PfEMP1 can not get out of the red blood cell and can not anchor to blood vessels so severe forms of the disease are unlikely to develop.”

## New centre – fighting infectious diseases

March 2006 marked the official opening of the Australian Research Council (ARC) Centre of Excellence in Structural and Functional Microbial Genomics.

The centre is equipped with state-of-the-art equipment, including the world’s largest parallel protein purification workstation and its staff will also have access to the Australian Synchrotron.

The centre has nine Chief Investigators, who work collaboratively from the following areas of biomedical sciences- microbiology, pharmacology, and biochemistry and molecular biology. It also has links with researchers from the University of Queensland, the University of Sydney, CSIRO Livestock Industries, the Victorian Bioinformatics Consortium, the Australian Genome Research Facility, Victorian Partnerships for Advanced Computing, Pfizer Animal Health and Intervet International.

Centre director Professor Ben Adler said the opening of the centre had great implications for the future research of infectious diseases affecting both people and livestock in Australia.



Professor Ben Adler

“The centre will enable us to further both fundamental and applied research with commercialisation potential”, he said.

The centre has been funded through Monash University, the Victorian Department of Innovation Industry and Regional Development and the ARC.

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Edited by Amanda Hamilton, Communication Office, School of Biomedical Sciences.

Phone: 9902 0024

Email: [Biomed.Communication@med.monash.edu.au](mailto:Biomed.Communication@med.monash.edu.au)