MONASH University
Medicine, Nursing and Health Sciences

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Spotlight: medical research at Monash

Volume 2, Winter 2007

Welcome to the Winter 2007 edition of *Spotlight*, a publication that highlights areas of research within Monash University's Faculty of Medicine, Nursing and Health Sciences. This edition focuses on the opportunities to use the new Australian Synchrotron and takes a more detailed look at prominent research into structural biology.

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What is the Australian Synchrotron?

The Australian 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. It may take a number of forms across the electromagnetic spectrum including radio waves, microwaves, infrared light, visible light, ultraviolet light, x-rays and gamma rays. Aside from the terrific intensity of the radiation, the great advantage is that any one, or subsets of these types of radiation, may be used.

The Monash Centre for Synchrotron Sciences will facilitate use of the facility to advance research across the university including that from the Faculty of Medicine, Nursing and Health Science. The proximity of this new national facility to Monash is expected to enhance national and international collaboration with the university and augment an already thriving medical research culture.

Scientists around the world use synchrotrons to investigate a broad range of science and technology questions including drug and vaccine development, medical imaging, computer chip development and testing, food technology, soil analysis and environmental science. The identification of the tastiest chocolate, the causes of death for both Beethoven and Phar Lap and the creation of more absorbent nappies were all discovered through the use of synchrotron technology.

Source: Australian Synchrotron website: *www.synchrotron.vic.gov.au.*

Investigating proteins to understand disease

Structural biologists study the shape of molecules, including proteins, and how this relates to their function. Knowledge about the precise shape of a protein provides an understanding, at the molecular level, of how proteins function normally and how abnormal function can lead to disease.

Protein crystallography is a major tool for discovering the shape of proteins and, as such, provides a wealth of information in understanding complex biological systems and the design of therapeutics at the molecular level. The Protein Crystallography Unit within Monash's Department of Biochemistry and Molecular Biology will use the Australian Synchrotron for x-ray crystallography to learn about the three-dimensional shape of proteins. The team, headed by award-winning life scientist Professor Jamie Rossjohn, is researching three broad but interrelated areas of immunity, infection and rational drug design.


Professor Jamie Rossjohn

In 2004, Professor Rossjohn won the Prime Minister's Life Scientist of the Year Award and he was awarded a Federation Fellowship in 2006. This year, he won the Commonwealth Health Minister's Award for Excellence in Health and Medical Research and the Gottscalk Medal from the Australian Academy of Science.

Professor Peter Rogers

Improvement in radiotherapy treatment for cancer patients

A collaborative project aims to develop radiotherapy treatment for cancer patients that can be delivered in much higher doses but with fewer side effects.

Approximately 50 per cent of cancer patients undergo radiotherapy. Current treatment has major limitations and involves targeting the tumour with one broad x-ray that also affects normal tissue nearby. The dose is administered over a series of days to allow the tissue time to recover.

A multidisciplinary team at Monash is devising a way to administer enough radiation to kill the tumour without destroying the surrounding, healthy tissue.

The team will generate x-ray beams up to 10 billion times stronger than current doses of radiotherapy using the Australian Synchrotron.

Synchrotron technology allows this process – called Microbeam Radiation Therapy (MRT) – to split the broad x-ray beam into many narrow, intense beams. For reasons scientists still don't understand, these microbeams kill the tumour, but cause less damage to the healthy tissue, even though a much higher dose of radiation is used.

Using animal models, the research team is now investigating why this phenomenon occurs. Armed with this knowledge, the team will design MRT treatment, that optimise the benefits of radiotherapy for certain cancer patients.

The collaboration includes Professor Peter Rogers, Director of the Centre for Women's Health Research at the Monash Institute of Medical Research (MIMR), Professor Bryan Williams, Director of MIMR, together with Professor Rob Lewis from the Monash Centre for Synchrotron Science, Dr Imants Svalbe from the School of Physics, and the Peter MacCallum Cancer Centre.

Australian Synchrotron collaboration creates firsts for Monash

Monash University's location adjacent to the Australian Synchrotron will create greater collaboration and more opportunities for all scientists using the new facility, according to the Chair of the Monash Centre for Synchrotron Science Advisory Board, Ms Sue Renkin.

"The Australian Synchrotron's location makes it one of the few facilities in the world to have university facilities nearby," Ms Renkin said. "Visiting scientists will have access to Monash libraries, laboratories and facilities through collaborative arrangements."

Monash University is one of a number of Australian and New Zealand organisations and consortia participating in the establishment of the synchrotron's technology and beamlines.

"Collaboration between scientists from throughout Australia and around the world will be fostered and new opportunities will grow from having the facility adjacent to a university."

Ms Renkin said another first was the proposed neighbouring medical imaging facility which will access the beamlines and produce high quality images of cells, tissue and bone.

"The Australian Synchrotron has the potential to be one of the first in the world that will be able to clinically treat patients," she said.

She said another advantage for Monash was that Professor Rob Lewis from the Faculty of Science was a world expert in the use of synchrotrons in research.

The Monash Centre for Synchrotron Science was established to support synchrotron-related research across the university, foster relevant collaborative and cross-disciplinary research programs and enable researchers to engage effectively with the Australian Synchrotron and other overseas light sources where appropriate.

"MCSS supports synchrotron researchers at Monash in a variety of ways," Professor Lewis said. "We fund a number of research fellowships and student scholarships and provide assistance to others who are interested in using synchrotron radiation as part of their research.

"We also act as a centralised, first point of contact between Monash and the Australian Synchrotron and other overseas light sources. "

The first experiments commenced at the Australian Synchrotron in April 2007.

Helping babies to breathe

At birth babies fill their lungs with air and take their first breaths. Understanding how this takes place could be the key to helping preterm babies breathe easier and reduce the debilitating lung diseases that many of them suffer.

The research team of Associate Professor Stuart Hooper and Dr Megan Wallace from the School of Biomedical Sciences and Professor Rob Lewis and Dr Marcus Kitchen from the School of Physics are researching the factors that regulate the onset of air breathing at birth in humans and how these are altered by premature birth.

To study the transformation of the lung into a gas-exchange organ, the researchers are using a unique x-ray beam produced by a synchrotron to image the lung as it fills with air after birth. They can image the pattern of lung aeration from birth in real-time and identify factors that injure the immature lung of preterm infants. This technique can also be used to image and study adult lung diseases.

The research team have been using the Spring-8 Synchrotron in Japan but will use the Australian Synchrotron from 2008.

Dr Megan Wallace, Dr Stuart Hooper and Dr Marcus Kitchen.

New facility produces antibodies for research and industry

The new Monash Antibody Technologies Facility (MATF) will meet the burgeoning international demand for antibodies from life scientists and industry.

Director of the MATF, Alan Sawyer said that the establishment of the new facility was important for the development of medical research in Australia and around the world, as monoclonal antibodies are being used in large quantities to formulate new diagnostic tests as well as treatments for autoimmune disease, cancer and other pathologies.

"The Monash facility is Australia's only high-throughput facility and one of two in the world," Mr Sawyer said.

"Crucial to the establishment of MATF at Monash is the new Australian Synchrotron, opening adjacent to the university's Clayton campus.

"The use of antibodies in helping to solve protein structure is a well-established technology, so positioning the MATF next to the biggest and best synchrotron in the southern hemisphere was an obvious choice."

Mr Sawyer is a world-leader in monoclonal antibody production and immunology, having worked in the area for more than 18 years. This includes 12

Alan Sawyer

years at the European Molecular Laboratory (EMBL) in Heidelberg and Rome where the world's first, much smaller facility was established to develop the high-throughput technologies.

As the driving force behind the transformation of the EMBL core facility, Mr Sawyer changed it from a classical, in-house low-throughput facility to a world and industry-renowned, high-throughput platform.

"The EMBL facility did much of the pioneering work developing the technology but remains a smaller unit than the one we are setting up at Monash. There is nothing in this part of the world that can make antibodies on this scale," Mr Sawyer said.

Synchrotron boosts cardiovascular research

Dr James Pearson, Monash Synchrotron Fellow, conducts fundamental cardiovascular research to discover new perspectives on the interactions between the lungs, brain, heart and kidney and to better understand mechanisms at the cellular level that are involved in heart malfunction.

He has been involved in synchrotron research for seven years, since working as a researcher at Japan's National Cardiovascular Centre in Osaka. His work included the use of the world's largest synchrotron at Spring-8 (Hyogo Prefecture in Southern Japan).

In 2005, Dr Pearson moved to Monash's Department of Physiology to lead a new research group in the area of synchrotron applications for physiological and medical sciences.

His work includes collaborations with other research scientists and postgraduate students, both locally and internationally, across the disciplines of engineering, physics and physiology.

Dr James Pearson

New breakthroughs in movement disorders and mental illness

A Monash research team co-led by Professor James Whisstock and Associate Professor Merrill Rowley has discovered the structure of two key proteins that function to control human movement and neural transmission.

Insufficient levels of the neural enzyme glutamic acid decarboxylase (GAD) and the neurotransmitter it synthesises (called GABA) may contribute to mental illnesses such as schizophrenia and movement disorders such as cerebral palsy. Increasing levels of GAD have also been successfully used in animal models to alleviate the symptoms of degenerative diseases such as Parkinson's disease.

The research, funded primarily by the NHMRC, is the result of 20 years of GAD-related research at Monash.

"This is an important medical breakthrough. We hope to now harness our knowledge of how GAD works to drive the design of new therapeutics," Professor Whisstock said.

Synchrotron radiation, together with high performance computing, was key to the project's success, and members of the team had to travel several times to the USA to use the Chicago synchrotron.

"Monash University recently invested $5 million to allow a major upgrade to our structural biology facilities. These new facilities will really be world-leading and will dramatically accelerate the pace of our research," Deputy Vice-Chancellor and Vice-President (Research) Professor Edwina Cornish said.

Professor Whisstock was named the 2006 Science Minister's Life Scientist of the Year for his work on proteases (enzymes that degrade protein molecules) and their inhibitors.

More Monash medical synchrotron research

- A team of structural biologists and microbiologists will use synchrotron radiation to investigate mycobacterium tuberculosis, a renewed cause of devastation in the developing world.
- The Australian Research Council Centre of Excellence in Structural and Functional Microbial Genomics is located within Monash's School of Biomedical Sciences and has nationwide collaboration with other research facilities and industry. It will use the synchrotron for research into infectious diseases affecting both people and livestock in Australia.
- Physicists at Monash are investigating improved methods of medical imaging using synchrotron technology. This, in turn, will provide improved systems for both medical researchers and clinicians. Work has already been carried out on the imaging of lungs and mammography.

Understanding more about molecules

- Associate Professor Matthew Wilce, his team and collaborators will use the Australian Synchrotron for x-ray crystallography to investigate certain enzymes, develop new antibiotics and understand protein behaviour. Projects explore the molecular basis of various aspects of immunity such as barriers to infection including the skin's oil, tears, stomach acid and the cough reflex.
- Working with both local and international collaborators, Dr Jackie Wilce is investigating how cells become inflamed and cancer cells move around the body. She aims to develop a molecule that will stop the proliferation of cancer cells.
- Dr Craig Clements is an Australian Research Council QEII Fellow. Working in the Protein Crystallography Unit, he is investigating the fundamental roles of MHC Class 1b molecules involved in innate and adaptive immunity.
- Dr Ashley Buckle and his team work in the area of structural biology and bioinformatics. His research is split between structural studies of a variety of interesting biological systems and bioinformatics. Dr Buckle's structural biology research focuses on proteases and their inhibitors, with an emphasis on those implicated in human disease. His bioinformatics interests include understanding how proteins fold, the prediction of protein-protein interactions, development of methods for protein structure determination, and the application of high-performance grid computing in protein crystallography.

The synchrotron display at the Monash Science Centre

Monash Science Centre

Learn more about the Australian Synchrotron

All the family can enjoy learning about the Australian Synchrotron at the Monash Science Centre.

The display is located at the Monash Science Centre, Building 74 on Monash University's Clayton campus and is open to the public each weekday from 10am to 4pm. Entry to the display is free. A free presentation is available for groups upon request and bookings are essential. For more information please call 9905 1370.

Related links

The Australian Synchrotron
www.synchrotron.vic.gov.au

Monash Centre for Synchrotron Science
www.sync.monash.edu.au

Monash Science Centre
www.science.monash.edu.au/msc/

Synchrotron fast facts

- The current stakeholders in the Australian Synchrotron are five state governments, 25 Australian universities, Australia's medical research institutes, Commonwealth Science and Industrial Research Organisation (CSIRO), Australian Nuclear Science and Technology Organisation and New Zealand who are collaborating to underpin innovation competitiveness and grow business.
- There are 76 non-portable synchrotrons proposed, under construction or operating world-wide.
- The Australian Synchrotron is designed to be operational with nine beamlines. Five beamlines are currently installed and the final four are expected to be operational by the end of 2008.

Source: Australian Synchrotron web site: *www.synchrotron.vic.gov.au.*

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 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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Next edition: vascular health

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