ANZAC Research Institute
discovery
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PUTTING THE BRAKES ON BREAST CANCER

Researchers led by Associate Professor Andrew Burgess, Head of ANZAC's Cell Biology Research Group, have made a significant discovery in finding a way to stop breast cancers from growing, after identifying an oncogene called MASTL which is over-expressed in triple-negative breast cancers.

Associate Professor Andrew Burgess (centre) with Dr Kamila Manzec and PhD student Thomas Johnson

"When we put too much MASTL in to normal breast cells, it caused them to grow and move uncontrollably, which are hallmarks of aggressive tumours, like triple-negative breast cancer".

"More importantly, when we took MASTL out of triple negative breast cancer cells that had too much MASTL, it stopped those cancer cells from growing and spreading throughout the body.

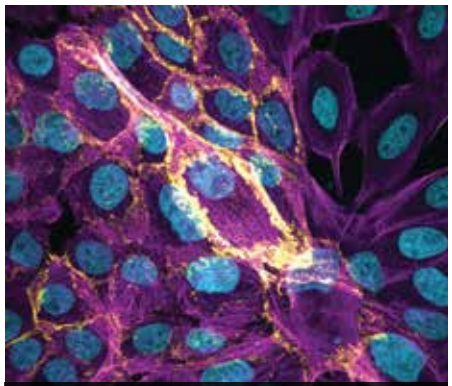
"This means we could put the brakes on breast cancer. It's preliminary work but potentially exciting if we could target MASTL and stop the cancer from growing."

Funded by a three-year grant from the National Breast Cancer Foundation, the team recently published the first part of this work in the international cancer research journal *Oncogene*, highlighting the importance of the research.

"MASTL is commonly over-expressed in up to 45% of triple-negative breast cancers," says Associate Professor Burgess.

"We know it can drive cancer and we know it can be targeted, but we don't really know what MASTL does in normal or cancer cells. So, we're now trying to figure out what MASTL does to drive cancer so that we can then use this information for future drug development.

"It's very much an evolutionary process. What we think is happening is that the cells get an initial hit which drives them to want to proliferate, but that in itself is very stressful for a cancer cell, to grow and make more copies of itself. So it needs to protect itself. We think MASTL is a protective gene that helps provide an evolutionary advantage for those cancer cells to survive."



An image of breast cancer cells that are over-expressing MASTL.

Andrew Burgess has also contributed to a major study published in Science Translational Medicine, which identified a new way of significantly improving treatment of lung cancer patients. That research, led by Professor Neil Watkins, Andrew's colleague at the Garvan Institute's Kinghorn Centre, has identified follistatin, a protein that is naturally produced within our bodies, which when given together with platinum based chemotherapy, dramatically increases the effectiveness of the treatment and also protect patients from kidney damage.

"We were able to identify a natural compound, follistatin, which your body naturally produces, and hence has no adverse effects by itself, but when you give it in combination with cisplatin, which is the current frontline therapy for lung cancer, you can protect the kidneys and dramatically increase sensitivity of cancer cells to cisplatin. So it's a terrific new discovery and opportunity for more effective cancer treatment."

"The survival rate for lung cancer is dismal, with only about 17% of patients surviving beyond 5 years; no treatment really works. Platinum-based chemotherapy is very effective in treating testicular and ovarian cancer but for some reason it just doesn't seem to work on lung cancer. So here we have an option where we can add an extra drug that does nothing by itself but now might give some patients hope, and extend and improve their quality of life, something which is not currently available."

PROFILE: PROFESSOR VICTORIA COGGER

Professor Victoria Cogger

Professor Victoria Cogger, who works alongside Professor David Le Couteur in the ANZAC Research Institute's Biogerontology group, has been appointed Associate Dean (Research Education) in the University of Sydney's Faculty of Medicine and Health. And in late 2018 she was promoted to full Professor by the University of Sydney.

This role involves overseeing and developing strategies to assist in the successful research training for over 1000 enrolled Higher Degree Research students within the Faculty.

Victoria was elected President of the International Society of Hepatic Sinusoidal Research (2017-2019) and will host the Society's International Symposium at the University of Sydney in September 2019. She is an Associate Editor of the *Journals of Gerontology: Biological Sciences.*

Victoria completed a BSc (Hons) in 1999 followed by a PhD on the Ultrastructure of the Ageing Liver, graduating from the University of Sydney in 2003. She was awarded a Healthy Ageing Postdoctoral Fellowship and travelled to the National Institutes of Health, Bethesda Maryland, USA to complete postdoctoral studies.

Victoria now leads research investigating the biology of ageing; with particular focus on the liver and targeted interventions for treating age related disease using nanomedicines.

"The diseases of ageing like cardiovascular disease and diabetes are significant social and medical burdens within our society," she says.

"By targeting the biology of ageing we are able to harness the underlying cause of these diseases to improve the quality of life for many people."

US SOCIETY RECOGNISES LIVER RESEARCH

The American Physiological Society has congratulated a team of researchers based at the ANZAC Research Institute for an outstanding paper published in its journal, detailing investigations into the effects drugs are having on blood vessels in the liver.

The study by Dr Nick Hunt, Glen Lockwood, Dr Alessandra Warren, and Professors David Le Couteur and Victoria Cogger was carried out in collaboration with Hong Mao and Peter McCourt, visiting researchers from the University of Tromsø in Norway.

"The work investigated commonly used medications and drugs and how they may be at least partly acting to treat disease via their effects on liver blood vessels," says Dr Hunt.

"The award from the American Journal of Physiology was the selection of our paper to be published in their flagship journal called *American Journal of Physiology Select*.

"The Society describes the award as intended to shine a bright light on the outstanding scientific discoveries published by our Society and be a timely, convenient, and concise "one-stop shopping" mechanism to broadly transmit our most exceptional work."

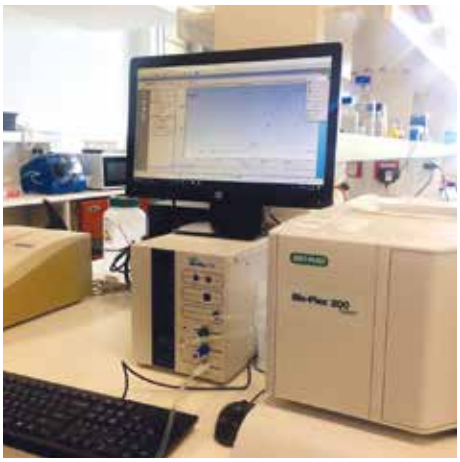
Dr Hunt is a Postdoctoral Research Fellow at the ANZAC Research Institute, working on the development of nanomedicines to improve the health of the liver in advanced ageing and obesity. He completed his BSc and PhD at the University of Sydney in 2016. His PhD focused on the changes in the neuropeptide orexin in the hypothalamus and pons of Sudden Infant Death Syndrome infants. These studies drew media attention both in Australia and abroad.

Nick has worked within the Bosch and Kolling Institutes in Sydney and was a pre-doctoral fellow at the European Molecular Biology Laboratory in Heidelberg, Germany.

A WONDERFUL BEQUEST

The ANZAC Research Institute was extremely grateful to be the beneficiary of a generous bequest from a World War II veteran who died in 2016 without family.

The Institute received an initial $732,000 in June last year, followed by another $180,000 in October – a total of $912,000.



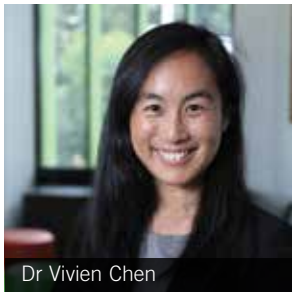
As a result the Institute has been able to purchase equipment vital in enabling researchers to pursue a number of projects. One significant purchase has been a Bio-Plex system, manufactured in California by Bio-Rad Laboratories.

The Bio-Plex 200 is a state-of-the-art device which allows for highly accurate measurement of tiny amounts of multiple substances in serum and other biological fluids. Up to 100 different molecules such as proteins, DNA and metabolic chemicals in a single sample can now be handled. In the past each chemical would have to be studied separately needing more samples and much greater effort. The Bio-Plex multiplex immunoassays use Luminex magnetic beads that allow measurement of over 450 biologically relevant target molecules for inflammation, diabetes, metabolic and hormone, cell signalling and growth, apoptosis, cancer, toxicity and more. This system has wide applications to generate insights into immunology, obesity, diabetes, cancer and cardiovascular disease.

The development and purchase of the most advanced technology is critical in medical science, allowing researchers to cross new frontiers in the campaign to overcome disease and generate better outcomes for patients.

A single bequest such as this will be instrumental in helping that campaign.

BLOOD RESEARCH COULD MEAN BETTER OUTCOMES FOR CARDIOVASCULAR PATIENTS


Dr Vivien Chen

Imagine that you could provide a blood sample, have it tested, then be told how likely you are to suffer a heart attack or stroke in the future, and if necessary to be prescribed medication to lessen the risk. Dr Vivien Chen dares to speculate that this could be the ultimate outcome of her studies into blood platelets.

These tiny blood cells are a critical component of our blood because they form clots to stop us bleeding when we suffer cuts.

"They need to be active, otherwise we would bleed to death. But when they're too active, or their activity is occurring in the wrong place, you get problems with heart attack or stroke," Dr Chen explains.

"Our research has shown that not all platelets act in the same way, that there are different subgroups within our platelets that have different roles. There's one particular sub-population that stimulates the coagulation proteins and clotting process. These "procoagulant platelets" seem to be in excess in patients who have a heart attack or stroke, but they're not as important in stopping bleeding.

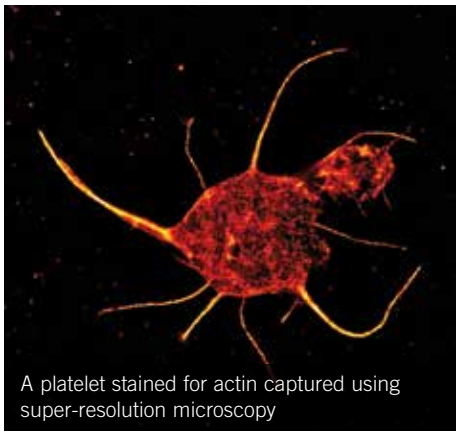
"Our hypothesis was that if you can interfere with the function of this sub-population of platelets, that drives the bad clots, you could decrease the incidence or frequency of heart attacks and strokes, without losing the good function of platelets which is to stop bleeding."

Dr Chen has shown that a patient who has coronary heart disease or who has suffered a stroke produces more of this form of platelet when the body is stimulated than a normal healthy person.

"We looked at a number of different drugs that might affect the interaction between the stimulant and the platelets. We came across a particular chemical substance that seems to specifically decrease the bad platelets without affecting the good platelets, bringing that hyperactivity back to normal. We don't want is to get rid of platelets entirely because then you'd have bleeding risks but we aim to modify their excessive clotting risk.

"If we can offer an anti-coagulant that affects only the bad platelets and doesn't affect the coagulation system, it would lead to less disability and a better outcome."

A grant from the University of Sydney Cardiovascular Initiative has allowed Dr Chen to have that same chemical synthesised by the CSIRO so she can confirm her results and take it further into animal studies. Her method of detecting procoagulant platelets has already been patented.


A platelet stained for actin captured using super-resolution microscopy

Cardiovascular disease on a global basis is responsible for 40% of deaths so the potential benefits of Dr Chen's research are vast. It's a development that could be applied in treating different diseases; although the research has concentrated on heart attack and stroke patients, highly active platelets have also been found in people with cancer and may be related to the increased risk of blood clots in cancer patients.

Dr Chen is a Staff Specialist Haematologist at Concord Hospital and Leader of the Platelet and Thrombosis Research Laboratory at the ANZAC Research Institute.

EARLY CAREER FELLOWSHIP AWARD


Dr Helena Liang

Dr Helena Liang has received a prestigious Early-Mid Career Fellowship awarded by the NSW Health Department.

"The fellowship has given me the valuable opportunity and resources to work alongside the very dedicated research and clinical teams at ANZAC Research Institute and Concord Hospital," Dr Liang said when she received the award.

"The fellowship will support me as I employ novel and state-of-the-art research tools to better understand the role of platelet subpopulations in coronary artery disease, in the hopes that we will be able to design new drugs that would provide more targeted therapeutic effects when treating patients, at the same time reducing their risk of abnormal bleeding."

The award is for three years and ensures Dr Liang will continue to play an important role in the ANZAC's Platelet and Thrombosis Research Laboratory alongside Dr Vivien Chen. Dr Liang says she is now developing skills in super resolution microscopy to study the minute blood cells known as platelets

"With standard microscopy it goes down to 200 nanometres. That's not a good enough resolution to look at the tiny structures on platelets, so we're hoping that with super resolution microscopy, which is a new technology, we'll be able to go down to about 20 nanometres. That's ten times the resolution, so we'll be able to see the structures we want to see.

"I'll be using a super resolution microscope here at the ANZAC Research Institute to look at fixed cells, and there's another at UTS that enables us to look at living cells so we can see the changes in real time. We're using mouse models but also human blood, by comparing samples from cardiovascular patients with blood from healthy people."

The research is being carried out with support from the cardiology and haematology departments at Concord Hospital.

Scientists and CMT Aussie Kids come together to learn about CMT Research

On a sunny Saturday in February, Associate Professor Marina Kennerson hosted a "Meet the people behind the microscope" day for 20 family and friends of CMT Aussie Kids to learn about the CMT research being done in the Northcott Neuroscience Laboratory at the ANZAC Research Institute.

Scientists here have led the world in discovering gene mutations causing Charcot-Marie-Tooth (CMT) neuropathy, a disease that affects both the motor and sensory nerves, weakening the muscles in the arms and feet leading to foot deformities and impaired sensation in the hands and feet. The research program led by Associate Professor Kennerson has now embarked on exciting projects working with patient nerve cells and *C. elegans* (worm) models for the development of therapies.

"After speaking with Jillian and Peter Critchley who are the co-organisers of CMT Aussie Kids, and learning of the different activities they have organised for the children and adolescents with CMT, I thought opening the doors of the Institute and inviting the families to look behind the scenes of a CMT research laboratory would be a great experience for them," Marina Kennerson explained.

To make the research accessible the team set up display stations in which members of CMT Aussie Kids (ranging from 6 to 20 years of age) could watch DNA being extracted from strawberries, look down microscopes at glowing worms and view patient motor neurons on the institute's powerful confocal microscope. In the words of Jillian Critchley, "we wanted CMT Aussie kids to **C**elebrate **M**icroscopes **T**ogether", a play on the acronym CMT Jillian used to promote the day and encourage participation.

The day was a resounding success and ended with a BBQ and informal conversation with Associate Professor Kennerson and her team of dedicated scientists and students. "Your team was engaging, informative and most importantly had the human touch," said Jillian Critchley. "We wanted the kids to realise and discover that there are real people working hard behind the scenes to find treatments and a cure for CMT."

"To see the smiles and enthusiasm of everyone on the day was wonderful," said Marina Kennerson. "This research would not be possible without the support of CMT patients and their families participating in our research programs. Today gave me and my team the opportunity to share our research and spend time with an inspirational group of young individuals and their families."

For more information on the research visit the ANZAC Research Institute website www.anzac.edu.au. For further information on CMT see the Charcot-Marie-Tooth Association website www.cmt.org.au

GIVING OPPORTUNITIES

All gifts over $2.00 are tax deductible

Please use this form if you wish to make a donation to help the ANZAC Institute in its exciting medical research, or if you would like to receive further information. We would love to hear from you, our supporters.

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