

Governor General to celebrate our 20 year milestone

The Institute's Patron, Governor General Sir Peter Cosgrove, will host a cocktail reception at Admiralty House, Kirribilli, on 21 November to celebrate 20 years since the Anzac Health and Medical Research Foundation was established as a charitable body.

The AHMRF was founded to coincide with the "Australia Remembers" campaign marking 50 years since the end of World War II and the transfer of Concord Repatriation General Hospital from Commonwealth to NSW Government administration. Commonwealth and State government funding of \$6 million led to the opening of the ANZAC Research Institute building in 2000.

In just 15 years the Institute has built an outstanding reputation for scientific excellence, providing a researcher-friendly environment for biomedical scientists to achieve important results across a wide spectrum of medical research. The Institute is now a scientific home for 150 research staff, including 60 graduate students, who collectively each year earn more than \$10 million of external research funding and publish more than 120 papers in top, peer-reviewed journals.

Each of its 11 research groups is headed by a clinician-scientist, all recognised leaders over a range of medical specialties including cardiovascular disease, neurological disease, immunology, psychiatry, osteoporosis and bone disease, burns, andrology, geriatrics and gastrointestinal disease.

So many significant achievements have been attained in the 20 years since the Institute was conceived. With the proven dedication and skills of our staff and with the support and cooperation of those who believe in what we do, so much more can, and will, be achieved.

Chance Favours the Prepared Mind



Dr Emma Verner, who treated the patient, with Prof David Le Couteur

A young Sydney woman has been cured of lymphoma and is once more leading a productive life after close cooperation between the ANZAC Research Institute and Concord Hospital, and in a quite unexpected result from an experiment deemed a "failure" eleven years earlier.

Professor David Le Couteur explains that in 2004 studies were carried out with rats in which a cancer drug, doxorubicin, was used inside a lipid or fatty bubble, called a liposome.

"We thought would be a useful way of assessing fenestrations or minute openings of the liver, he says.

"We used doxorubicin because it was fluorescent and easily measured. The experiments didn't work because we found the liposomes were too big to get through the holes in the blood vessels of the liver, and none of these particles got into the liver at all."

Professor Le Couteur published a paper on the subject, and no more was thought about it until earlier this year when he received a phone call from Dr Ilona Cunningham, head of Concord Hospital's haematology department. She told him they had a problematic patient and needed advice from him, as a clinical pharmacologist.

"The patient was a young woman, in her early 20s, who had a lymphoma and they'd given her a dose of chemotherapy, expecting to cure her, and she'd got severe liver failure. The chemotherapy included four drugs and they had advice that one of those was the likely culprit, so they gave her the next dose of chemotherapy without

Woman's life saved by "failed" experiment

that drug, and she got worse liver failure. So they were left with a real problem: do we continue giving this girl chemotherapy but risk her dying from liver failure, or do we change to a less effective type of chemotherapy and risk not curing her? "

Desperate to solve this problem, the woman's family and her doctors searched the world for an answer without success until Dr Cunningham's call to the ANZAC Research Institute, right there on the Concord campus.

"I had a look at the two lots of chemotherapy she'd been given and they both contained this drug, doxorubicin, not in liposomes but just in a free drug. So I said this drug is the most likely culprit to be causing the liver failure, and if they give it in the liposomes it won't get into the liver and will go to the cancer. So they should think about giving the same strong chemotherapy, but rather than give it in a soluble form, which will get into the liver and lead to her death, give it in this packaged form with liposomes which we know doesn't get into the liver. We were the only people in the world who would know this!

"They gave her some chemotherapy with a low dosage of doxorubicin and there were no problems. So they gave her the final therapy, a high dose, and again, no problems. So she's been cured of the cancer and she was protected from liver failure. All based on these funny experiments we'd done with rats some ten years ago."

In David Le Couteur's own words, "it was incredibly fortuitous."

Tackling age related obesity by blocking glucocorticoids



Mark Cooper

The NHMRC has granted \$820,000 over four years for an Adrenal Steroid Group project investigating the role of glucocorticoids in the development of obesity as we get older. The project headed by Professor Mark Cooper is developing ideas about how the body's production of certain adrenal steroids leads to changes in the appearance of the body as it ages.

Now, in collaboration with colleagues in the Bone Research Group, he has made the exciting discovery in mice that blocking the effects of adrenal steroids (known as glucocorticoids) in bone almost completely prevents the development of obesity.

"Ageing is associated with increased body weight, central fat accumulation and an increased risk of diabetes," he explains.

"Our research suggests that these changes may be the result of the actions of the body's own glucocorticoids on bone cell function. The idea that age related obesity might have its origins in the way glucocorticoids affect bone tissue was unexpected. Although these studies are based on research work with animals it potentially opens up new approaches to the treatment of human obesity."

Professor Cooper will head an international team bringing together world-leading experts for studying glucocorticoid effects on bone and fat. The Adrenal Steroid Group has strong ties with the Universities of Birmingham and Leeds in the UK.

Sydney Research Awards go to ANZAC Institute



Megan Brewer (centre) with cheque

The Minister for Medical Research, Pru Goward, and NSW Health Secretary, Dr Mary Foley, have presented inaugural Sydney Research awards to two scientists from the ANZAC Research Institute, recognising their efforts to improve our health system and the health and quality of life in our communities.

The Health Research Infrastructure Award, recognising a researcher with high basic science research potential, was presented to Dr Megan Brewer, who is using tiny transparent worms in her project to identify disease-causing genetic mutations found in patients with inherited peripheral neuropathy. These worms have a short life-cycle, well-characterised nervous system and transparent body (allowing for easy visualisation of their internal organs including neuronal cells), which makes them an ideal organism for modelling neurotoxic mutations found in our patients. The award provided a \$10,000 grant, which Dr Brewer is using to purchase two incubators to help maintain the worms.

"Worms like to be kept at around room temperature, or 22 degrees," she says.

"If they go above 27 degrees they become sterile. You can maintain them at a lower temperature, down to 15 degrees, which just slows their metabolism and it means they'll survive a bit longer. But when we run experiments, we need to know what developmental stage they're at, so having them regulated at an exact temperature is really important."

Dr Brewer has focused on the incurable Charcot-Marie-Tooth disorder, which affects about 9000 Australians, whose sensory and motor nerves degenerate, leading to weakness in arms and leg muscles, foot deformities and impaired sensation in hands and feet.

Dr Kirsty Walters, senior scientist in the Andrology department, received the Research Supervisor Award for outstanding effort as a postgraduate research supervisor. She has also been recognised for her work by receiving the 2015 Newcastle Reproduction Emerging Research Leader Award from the Society for Reproductive Biology.

Thank You
to Mr Ian Palmer of Ashfield in
Sydney who has very generously
made a donation of \$10,000

No expense spared for research mice and rats

There aren't too many people who'd look forward to spending their working hours in the company of thousands of mice and rats. Mamdouh Khalil does just that, and the job he loves is about to get even more attractive with the construction of a new translational research facility, for which he has had a major design input, and which is on target to open in early 2016.

"It consists of several carefully designed and juxtaposed animal breeding rooms and other experimental holding rooms. It houses mostly genetically modified mice bred specifically for research and some rats," he says.

"It will also feature a research imaging facility, so we can do X-rays and follow tracer chemicals in living animals, measure body composition and do detailed metabolic studies as well as preparing mice for bone marrow transplants. It will have a surgical laboratory operating under strict pathogen free guidelines, like surgical theatres, and NHMRC guidelines. All this allows for important experimental research which can't be done with humans."

The current facility is operating at capacity and space available to the scientists at the ANZAC Research Institute is becoming very tight. It has taken about five years to plan the new facility since government funding was announced.

This is the third and most advanced animal facility designed by Mamdouh, who has a BSc and a background in engineering as well as animal technology.

"It has to be a very clean environment. Every staff member who comes into the existing animal facility must go through a strict showering, gowning and sanitisation process. We'll avoid this in the new facility by having two entries, one for the animal housing staff so we can keep our breeding stock absolutely clean with no cross contamination, and the other entry for the research scientists who won't need to shower and gown to enter the experimental areas, so it will save them spending 15 or 20 minutes every time they come in, giving them more time to spend on animal work."

The mice and rats housed at the Institute are not readily available elsewhere as most are unique or specially bred research strains and their numbers have to be maintained through a breeding program.

"It's very technical," Mamdouh explains.

"When we build a facility like this we have to imitate springtime. So they will have spring temperatures, 20 degrees, very comfortable. The lighting is 12 hours day, 12 hours night. And there has to be a minimum of noise or other environmental disruption. Once these animals become stressed, if you even change the lighting cycle or temperature, they stop breeding and you finish up losing the population.

All work done with animals at the Institute is carried out within strict ethical guidelines approved by an animal ethics committee. The facility itself has to be approved and then will be inspected rigorously three times a year.



Researchers close to overcoming transplant rejection



Prof Derek Hart

For 20 years Professor Derek Hart, head of the Dendritic Cell Group at the ANZAC Research Institute, has been focused on finding ways to suppress dendritic

cells, which play a fundamental role in causing the human body to reject transplanted organs and bone marrow. An NHMRC grant of \$736,300 over three years will help bring that dream to reality.

"The grant gives us the opportunity to keep developing the concept with a therapeutic antibody which will remove the activated dendritic cells at the time of transplantation," says Prof Hart.

"We've done a lot of the pre-clinical work on human cells in mice and now we need to take it a bit further down the development path so we can potentially attract commercial support to develop it as a new drug, get it into clinical trials and out into patients, and out into the rest of the world."

Prof Hart's work and that of others has shown that dendritic cells, a unique subset of white cells, are responsible for initiating and directing immune responses.

"It is the dendritic cells that get activated that drives the transplant rejection response, or in the case of bone marrow transplant, it's the dendritic cells that activate the nasty and quite often lethal complications of graft versus host disease where the donor immune system attacks the recipient immune system.

"The current treatment to control graft rejection is non-specific immunosuppression, so you suppress all of the immune response. We reasoned that if you remove the dendritic cells you might be able to protect the transplant or prevent graft versus host disease, but leave the rest of the immune response intact to protect the patient against, for example, viruses or cancer."

The research team has engineered and patented a unique antibody named 3C12C, which has already proved to be very effective in suppressing graft versus host disease in mouse models. The NHMRC grant will enable this antibody to be developed and potentially commercialised as a new Australian therapeutic agent to help transplant patients worldwide.

Androgens assist in recovery from burns

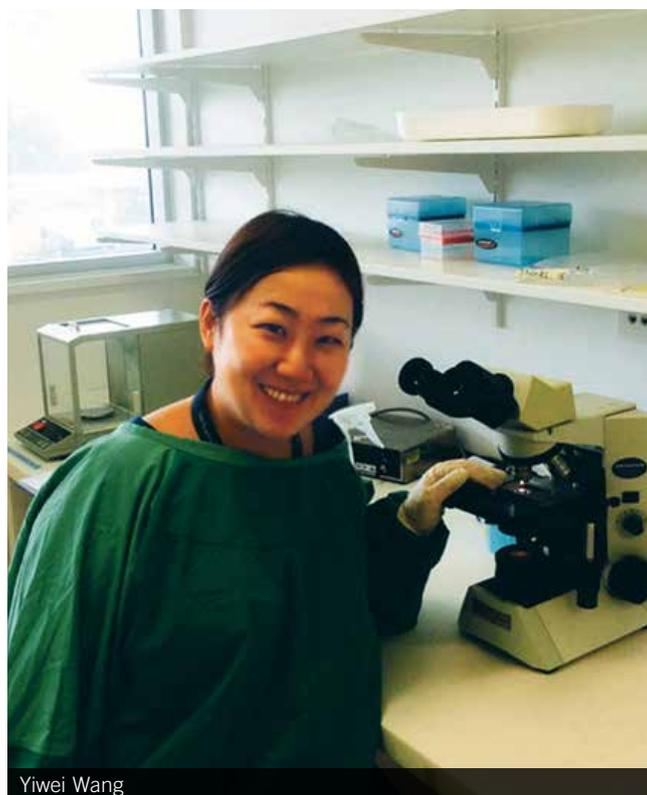
Three years ago we reported on a major project being undertaken in conjunction with the Burns Unit at Concord Hospital, in which Dr Yiwei Wang was developing a biodegradable and porous polymer skin scaffold, which could be constructed over severe burn wounds to regenerate the skin. Taking her successful research one step further, Dr Wang has now received a four-year NHMRC grant of \$439,480 to study the role of androgens (male hormones) in repairing such wounds.

More than 10,000 Australians are affected each year by severe burns, which are a major cause of morbidity and mortality because the patients' metabolism is changed.

"With severe burns, people lose 20 to 40 percent of their skin.

In addition to skin injury severe burn also induce a hypermetabolic or catabolic response, in which patients lose lots of lean muscle and weight and they are very sick. So we want to find out if androgens can help in treating this complex burn injury wound healing." Dr Wang explains.

"We found in the clinic that when burns injuries are treated with androgens, it accelerates wound healing but no-one knows the mechanism behind it. So this whole project is to find out what's the role of androgens in the healing process. So we'll be using animal models to mimic what happens in burns patients, starting with mice and then moving to pigs which are closer to the human model."



GIVING OPPORTUNITIES

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