

WE ARE 10 YEARS OLD!

Since 2000 the ANZAC Research Institute has grown steadily in both size and reputation, until today we are home to almost 140 medical scientists publishing around 170 research papers each year in prominent journals worldwide.

And to mark the occasion and celebrate our many achievements, the ANZAC Health and Medical Research Foundation will hold a commemorative dinner on **Friday 22 October**.

Guests will include members of Parliament, supporters in the business community and veterans' representatives.

The celebratory dinner will be held at Angelo's on the Bay at Prince Edward Park in Cabarita, and will be accompanied by high quality Tintilla wines from the Hunter Valley

We invite friends of the ANZAC Research Institute, the University of Sydney and Concord Hospital to join us at our 10th anniversary dinner. The cost is **\$150 per person. Tickets are available by telephoning 9767 9100.**

Celebrate our achievements – help us continue vital medical research.

Newest team aims to help organ transplants

The ANZAC Research Institute has this year welcomed a new group – the 10th – to the campus and it's a team that promises exciting developments in the fields of organ transplants and fighting diseases such as cancer and diabetes.



Professor Derek Hart (right) and Prof Ken Bradstock

Professor Derek Hart has arrived from Brisbane to take up his appointment as Professor of Transplantation and Immunotherapy at the University of Sydney, a task that includes establishing the Dendritic Cell Biology and Therapeutics research program at the Institute.

Dendritic Cells are unique subsets of white blood cells, found throughout the body, for example in the lymph nodes and the spleen, which are responsible for initiating and directing immune responses.

Prof Hart is an academic haematologist, recognized as a world leader in his field. He also played a significant role in establishing

the Cooperative Research Centre for Biomarker Translation. His appointment adds considerable national and international impact to both the University and the ANZAC Research Institute.

"This move allows me to focus on taking our DC research into clinical practice with the assistance of very motivated clinical colleagues," he says.

"The contemporary working environment and the ANZAC and Concord Hospital's collaborative culture, combined with the opportunity to be in the same city as other top colleagues convinced me that the prospects in Sydney were superior to

Avoiding the side effects of glucocorticoid steroids

Anyone who's had glucocorticoid drugs prescribed, for problems like asthma, arthritis and autoimmune diseases, will have received a warning that prolonged use can lead to severe side-effects.

Although these extremely valuable drugs have been used for more than 60 years to treat inflammatory conditions of for immunosuppression with organ transplants, they cause or increase osteoporosis, hyperglycaemia, excessive fat accumulation and muscle wasting.



Assoc. Prof Hong Zhou and Prof Markus Seibel are leading a team at the ANZAC Research Institute examining the role glucocorticoids such as

prednisone and dexamethasone play in the loss of bone and our reduced ability to replace bone.

"If you continue taking even a low dose for 3 months you have side effects, in particular in the bone," says Dr Zhou.

"The bone loss starts straight away. If we look at the bone markers, they drop as soon as you take the drug so that side-effect has really limited this very powerful and useful medicine."

Using a special strain of genetically modified mice created to study the interruption of steroid effects on bone, the researchers have discovered that the bone-making cells are the first to be affected by synthetic steroids.

"The bone cells themselves stimulate their own stem cells, and when glucocorticoid steroids stop that signal, the stem cells switch into developing fat cells instead," says Dr Zhou. "We are the first to discover this important fact."

The team has discovered that the body's own natural glucocorticoid, through the bone forming cells (osteoblasts) regulate stem cell commitment away from fat toward bone formation, and in mice, play an important role in developing and maintaining normal bone.

Dr Zhou says that in the case of rheumatoid arthritis the genetically modified mice have less inflammation than normal mice. This suggests that in addition to a high dose of the glucocorticoid steroid suppressing the arthritis, the inflammation is also reduced by blocking the body's own manufacture of natural glucocorticoid.

"This cycle is part of the explanation why rheumatoid arthritis goes in waves of flaring up, sometimes better, sometimes worse. It becomes a vicious cycle," she explains.

The project involves collaboration with researchers in the USA, Germany and UK, and in Australia is funded by ongoing grants from the NHMRC.

"It's all very exciting," says Dr Zhou. "But there's a long way to go."

Copper - and its significance to our health

Studies at the ANZAC Research Institute show that copper may play an important part in the cause of a number of diseases including Alzheimers and Parkinsons.



Dr Marina Kennerson (pictured left) has earned international recognition for her work at the Northcott Neuroscience Laboratory, looking at genetic mutations which lead to the degeneration of nerves and motor neurons.

One of her projects has now identified a gene that is important for the balance of copper in our bodies, and which may have significant implications for research into a variety of diseases.

"The disease I work on is a non-fatal type of Motor Neuron Disease. What we see is that the patients can't walk properly

neurons are different from other cells because they have to go long distances, up to metres. So if you have a signal from your spinal cord that has to get down to the end of your toe you have to move things like copper all that distance," she says.

Her studies have shown mutation in the protein, so the protein doesn't move around the cell correctly. When the cell is exposed to copper the protein becomes stuck and doesn't move to where it should be going. Copper is the third most common trace element in our bodies after iron and zinc, and it's fairly easy to supplement copper or mop up excess amounts.

"There's a theory that copper may play a role in the cause of a number of diseases including Alzheimers and Parkinsons," says Dr Kennerson. "The common feature is this dying back of the nerves, so we feel that if we can find a treatment for this particular disorder it may have relevance to other neurodegenerative disorders."

Dr Kennerson's introduction to this disease came about four years ago from American collaborators referring a particular family to her, and her subsequent identification of mutant genes in that family. She later found the same mutation in a Brazilian family, and brought in people with expertise in copper – Prof Julian Mercer at Deakin University in Melbourne and Dr Stephen Kaler at the National Institute of Health in the USA.

The research has shown there is a clear genetic basis to the nerve wasting disease.

"Males are almost exclusively affected while their mothers are carriers of the disease," says Dr Kennerson.

"There will be ways of treating these people if we can just understand the mechanism involved."

We have to remember that motor neurons are different from other cells because they have to go long distances, up to metres.

and they have muscle wasting," Dr Kennerson explains.

"It happens at the ends of their feet and their hands. We believe the nerves are dying at the ends of their extremities. About one in every 2500 people has it, so at any time in Australia there are about 8000 people affected."

Dr Kennerson's theory is that the protein involved is not trafficking copper properly in the neurons.

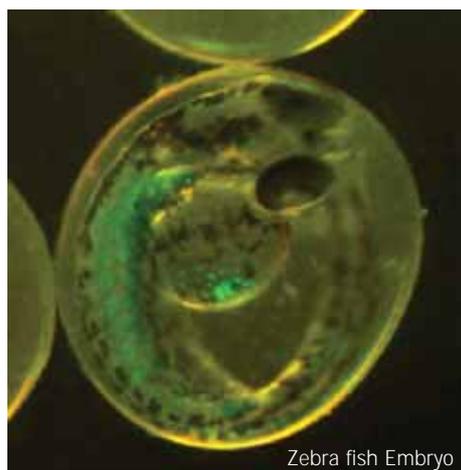
"We have to remember that motor

Zebrafish help investigate MND

The humble zebrafish, a small tropical freshwater species, may be on the verge of a significant contribution to understanding **Motor Neurone Disease (MND)**.

The zebrafish has a fairly simple genome which is fully sequenced and remarkably similar to the human genome. Dr Ian Blair, who heads the team at the ANZAC Research Institute's Northcott Neuroscience Laboratory investigating MND, says the fish are proving to be extremely useful in studies of the central nervous system.

"The zebrafish produce large numbers of eggs to reproduce rapidly and they are largely transparent," he explains.

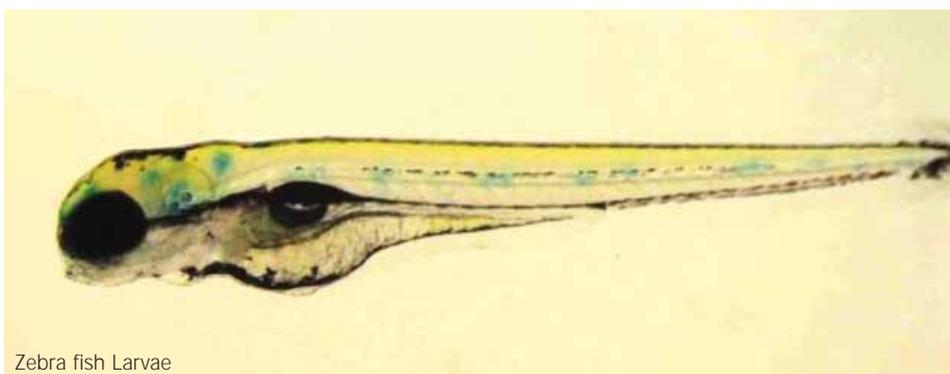


Zebra fish Embryo

"They lay eggs and the embryos develop externally, so we can actually see changes taking place, observing them in live fish in real time. If there are any defects during development we can track the progression of disease using time-lapse microscopy."

As reported in an earlier issue of "Discovery" the research team has identified two specific genes which, when they suffer a mutation, cause MND. MND affects around 1 Australian in every 5000 with about 1300 currently suffering from it.

MND is a devastating illness which typically appears in patients between 50 and 70, destroys the motor neurons that extend from the brain to the muscles, and causes paralysis and eventually death within 5 years.



Zebra fish Larvae

Dr Blair says traditionally mice have been used in this type of research but the zebrafish are particularly useful because of their genome, large population and transparency.

"The modification of the fish genes or the introduction of human disease genes allows us to investigate the nerves and to visualise nerve populations that are affected by neurological disease," he says.

"Through time lapse microscopy we are looking for the death of nerves, and then we are able to test drugs, possible therapeutic compounds, on the fish.

"If we see a defect in an embryo we can test to find those drugs that make it worse or those that make it better, and we can experiment with as many drugs as we like.



Zebra fish Larvae

MND affects around 1 Australian in every 5000...

So it's a case of working to find the defect, then working to identify a drug that will correct it."



Zebra fish Larvae

The project was initiated by Prof Garth Nicholson, Director of Neuroscience at the ANZAC Research Institute, with funding from the Snow Foundation. Work started about a year ago and Dr Blair expects its progress to accelerate in the next 6 months, working in conjunction with teams headed by Dr Nicholas Cole and Prof Thomas Becker at Sydney University's Brain and Mind Research Institute. A similar zebrafish project will also commence soon on another neurological disorder, Machado Joseph Disease (MJD), funded by the MJD Foundation.

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A new anti DC antibody developed by Prof Hart's program has been recognized as pioneering a different approach...

moving overseas for the next phase of our research”

Prof Hart developed his original description of these Dendritic Cells in the tissues by defining the human subsets, identifying DC membrane molecules, and producing antibodies to them which are now undergoing diagnostic and clinical trials. His research is significant in understanding the impact of the immune system on several organ systems and disease areas – cancer, infectious diseases, cardiovascular, and chronic inflammatory

diseases such as diabetes, arthritis and psoriasis.

A new anti DC antibody developed by Prof Hart's program has been recognized as pioneering a different approach to transplant immunosuppression, which preserves the patient's ability to fight infections and cancer. The first trial of this therapeutic antibody will involve Prof Hart's NHMRC Program Grant co-investigator, Prof Ken Bradstock in treating patients undergoing bone marrow transplants. Trials in organ transplantation and autoimmune or inflammatory disease are likely to follow.

A major step forward will be the trial of a new human antibody to purify DC for therapeutic vaccinations against prostate cancer, which will be followed by using this and other immunotherapy treatment for myeloma, leukaemia, lymphoma and other

cancers. Importantly, these will be free of side effects and will be cost effective.

Prof Hart is a New Zealand born Rhodes Scholar who is devoted to translating 25 years of pioneering discoveries about Dendritic Cells into clinical practice. His arrival is a coup for the ANZAC Research Institute and University of Sydney, enhancing its already high reputation and opening more opportunities for philanthropic support.

“Seeing the clinical problems makes you very motivated as a clinical scientist to try to get better therapies into action quickly” said Professor Hart. Clinical trials of truly novel therapies often require significant philanthropic funding and Prof Hart is seeking support to progress the Group's clinical trials as fast as possible.

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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