ANZAC Research Institute
discovery
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New research building named for asbestos campaigner Bernie Banton

On November 28th – just one day after he finally succumbed to mesothelioma – long-time anti-asbestos campaigner Bernie Banton was honoured by having the new building which will house both the new Asbestos Disease Research Institute as well as the extension of the ANZAC Research Institute named after him. Pictured are members of the Banton family, including Bernie's widow Karen and grandson Jack (with the spade) and NSW Premier Morris Iemma, as they prepared for the ceremony marking the start of construction. The $15m Bernie Banton Centre is being erected adjacent to the present ANZAC Research Institute. After its completion, scheduled for October this year, this will triple the research facilities on the Concord Hospital campus with the two research institutes operationally integrated.

ANZAC TEAM DISCOVERS MOTOR NEURON DISEASE GENE

There's new hope for sufferers of the fatal nerve-wasting Motor Neuron Disease worldwide, after scientists at the ANZAC Research Institute uncovered a genetic mutation which is one of the causes.

Professor Garth Nicholson says the gene, called TDP-43, produces a poison that destroys motor neurons.

"This is hugely exciting," said Prof. Nicholson, after the team's findings were published in the journal *Science*.

"We've been suspicious of this gene for a while. We knew there was smoke when high levels were found in people with MND, but now that we've found the mutation in some people, we've found the fire. The next step is to work out how to put the fire out."

Based at the Institute's Northcott Neuroscience Laboratory, and working as part of the Concord Clinical School, a teaching hospital of the University of Sydney's Faculty of Medicine, the team has been studying patients with MND for the past decade, analysing their genetic makeup. TDP-43 is only the second gene to be linked directly to the condition, opening the way for potential new therapies in an area where there has been almost no treatment at all.

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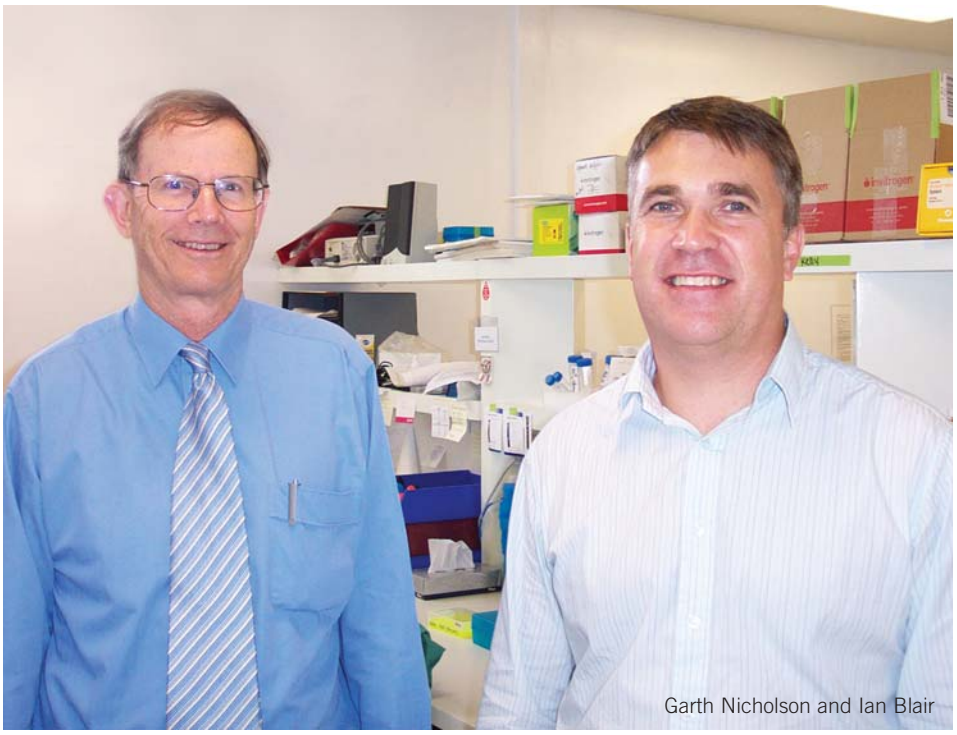

Garth Nicholson and Ian Blair

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MND is fatal and affects only people aged 50 and over. About one person in every 5000 suffers from the disease, which kills the nerves that go from the brain to the spinal cord and muscles. The first symptom is often the slurring of words, and within three years, patients lose the ability to move, eat, drink, and breathe.

"Many people have thought for some years that Motor Neuron Disease might be a poison of some sort in the environment," said Prof. Nicholson. "Here at the ANZAC Research Institute we have been able to show that it seems to be a poison in the body itself.

"The proof of it is that we found patients who have this abnormality where the disease runs in the family, and people who didn't get the disease didn't have this abnormality."

Hereditary factors are present in about 10 per cent of MND cases, but the other 90 per cent occur sporadically.

"Now we know this gene's involvement we, along with a lot of others, will be looking for drugs that can switch it off or regulate the levels of the protein it produces back to normal," said Prof. Nicholson.

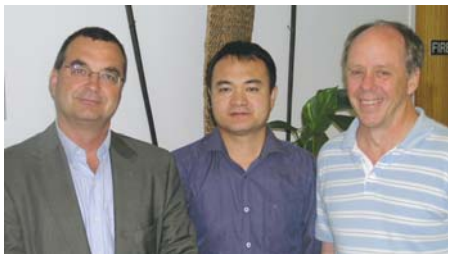
"This is obviously a long way off but there's hope that one day we will be able to slow or even stop the disease from developing."

Prof. Nicholson and Dr Ian Blair lead a team of 5 other researchers on this project at the Institute, working in collaboration with scientists at Kings College, London.

This work was supported by a bequest from a MND patient from New Zealand, Bill Gole Fellowship from MND Research Institute of Australia and the Pamela Churm Bequest.

Did you know MND affects about 1 in 5000 people over the age of 50.

Lack of Dietary Calcium Promotes Growth of Breast Cancer Bone Metastasis



L to R: Prof Markus Seibel, Dr Yu Zheng and A/Prof Colin Dunstan

Scientists at the ANZAC Research Institute's Bone Research Program have recently found that a diet low in calcium can greatly stimulate the growth of bone tumours in mice.

These findings, recently published as the cover story of the prestigious international journal "Cancer Research" may have clinical implications as breast cancer patients, much like the older population in general, frequently have a low dietary calcium intake.

Breast cancer is one of the most common malignancies in women and affects approximately one million women per year worldwide. About one in 12 women will suffer breast cancer during their lives. Approximately 70% of patients who develop advanced breast cancer will have secondary tumours in the bone, that is the breast cancer spreading to the bones. These "bone metastases" cause serious pain, fractures, immobility and spinal cord compression and are often the immediate cause of death.

In their study, the Institute's Dr Yu Zheng, Dr Colin Dunstan and Professor Markus Seibel fed laboratory mice a diet low or normal in calcium. After being exposed to cancer cells, mice on the low calcium diet developed bone tumours that grew much faster than those seen in animals on a normal calcium diet.

Also, bone turnover was accelerated in the "low calcium" mice.

Previous studies in cancer patients suggest that the level of bone turnover at the time of cancer diagnosis is a strong predictor of subsequent disease progression (e.g. bone metastases), survival and death. While these clinical data are intriguing, no-one knew why these associations existed in the first place. Why was bone turnover related to the progression of metastatic bone disease? Dr Zheng's study may provide the answer: a diet low in calcium results in accelerated bone turnover, which in turn strongly promotes cancer growth in bone.

Calcium deficiency is common, particularly in older people. Vitamin D deficiency is also widespread and promotes calcium deficiency as it results in impaired calcium absorption in the gut. Furthermore, when a women undergoes menopause, the fall in oestrogen levels leads not only to a significant increase in bone turnover but also to substantial decrease in intestinal calcium absorption. Hence, dietary calcium deficiency is particularly frequent in postmenopausal women. Unfortunately, most breast cancers are diagnosed after the menopause and their frequency continues to rise with advancing age, thus coinciding with a peak in calcium deficiency and bone turnover. In this sense, the experimental findings by Zheng, Dunstan and Seibel suggests that high bone turnover in postmenopausal women with breast cancer may increase their risk of disease progression to bone and that steps to overcome the high bone turnover may assist in the fight against breast cancer.

While human studies are required to directly test this new findings and ideas, these results do point to not only a connection between accelerated bone turnover and skeletal tumour growth but also towards possibly simple ways to fight the progression of breast cancer in bone.

Burns Research Group: our latest addition...

and how Sophie's ordeal prompts advances in burns techniques.

If you were asked to name a single hospital patient whose terrible injuries and courage have evoked an outpouring of sympathy and support, without doubt little Sophie Delezio would come to mind most readily.

Sophie's experience and her shocking burns have provided more than inspiration – they have also assisted medical scientists at the ANZAC Research Institute to understand more about what needs to be done to help patients like her.

"In my view the future will be regeneration and not reconstruction," says Dr Peter Maitz, medical director of the Burns Unit at Concord Hospital. "We must find out how we can enable the body to heal the wound and regenerate lost tissue."

Dr Maitz also heads the Burns and Reconstructive Surgery team, which has become the ninth research group at the Institute. For the first time those studying burns at Concord will be able to pool their knowledge by working in the one laboratory.

"We have three Masters students and three PhD students, enrolled at Sydney University, and one with the University of NSW. I have three fulltime research staff and they need to be integrated instead of working in isolation," says Dr Maitz. "I also need to get a senior scientist who will be the main person responsible for the research arm of the Burns Unit. In research people should not be isolated – not only can they share expensive equipment but also they can talk to each other, help each other, and create ideas."

The experiences of Sophie Delezio and victims from the Bali nightclub bombings and Canberra bushfires made Dr Maitz and other specialists more aware than ever of what limits there are to current knowledge and practice in treating burns. The main thrust of research at Concord now is to find a means by which not only skin can be replaced, but also the tissue beneath, which houses functions such as sweat glands and hair.

"We need to find a three-dimensional multi-layer construct," Peter Maitz explains. "We will succeed. It will take a while and it will take a lot of money but eventually we will be able to do it.

"What the media has dubbed as spray-on skin is entirely wrong. Skin is the human body's largest organ but it is one of the few organs that cannot be transplanted. You cannot live without skin. You will die, first, because of shock, secondly because of infection, and thirdly because you can't control your temperature. Spray-on skin has addressed one-hundredth of the problem by multiplying a specialised cell type that is the surface of the skin. But there is no integrity, no structure, and none of these other functions is addressed other than the physical barrier."

One of the limitations of current technology in skin culture is that it has no hardness. When used on wounds that go deep into muscle or fat, the wound will heal but will break open a month later.

Peter Maitz came to Sydney from his native Austria and quickly made a huge difference at Concord, establishing a world renowned Statewide Burns Service.

"We moved in here in 2004-05 and have been running since then on 100 percent occupancy," he says. "We have learned there are so many things we need to research about burns, because it is very frustrating when your intensive care unit colleagues can keep a patient alive, and you can't help the patient progress because the science is not there."

The treatment of burns is one of the most expensive procedures, and Dr Maitz is now leading a team in a world-first clinical trial and cost analysis to discover which types of treatment are most effective. The costs of most treatment in burns cases are borne by the public, through Medicare.

Rather than concentrate purely on treatment of burns, the research team is also investigating the causes. Australia led the way

Sophie Delezio at the 2007 Launch of Acceptance Day

in legislating for non-flammable children's nightwear, and Peter Maitz believes we need to take similar action to cut other types of burns. He points to domestic hot water systems being set to provide water at 65 or 70 degrees, simply because most people think that high temperature will kill bugs. It's all very well, says Dr Maitz, but it can also kill us.

"Household scalds are the number 2 injury in burns in old people. They go into the shower, turn on the hot water and slip. They let a bath run first with hot water only, they slip, and are scalded. People die because of something like this."

He argues that Australia must follow the European model and insist on thermostats being installed so no domestic hot water should come from a tap at more than 47 degrees.

Dr Maitz also expresses concern about the Australian habit of reusing metal drums that have contained flammable fluids like turpentine or oil. Angle grinders are frequently used to cut the tops from the drums – producing sparks, and all too often, explosions. The Concord Hospital Burns Unit had four such cases admitted in three weeks.

"Just fill the drum with water first, before you use the angle grinder," Dr Maitz pleads.

It's research like this – into the causes and prevention of burns, as well as the treatment – that will save lives. Working in the field of burns is not popular with plastic surgeons, who can make much more money from facelifts. But Dr Maitz points to one beneficial side effect of "tummy tucks" in particular: with the consent of patients, whole flaps of skin are preserved and used in further research in the skin culture laboratory!

"It's something quite unusual and I'm personally very proud that the work has been recognised by winning such highly competitive grants,"

Staff profile:

ASSOC. PROF PETER LIU

Peter Liu's outstanding work has been recognised by the National Health and Medical Research Council providing not only two grants for his projects, but also a Career Development Award.

"It's something quite unusual and I'm personally very proud that the work has been recognised by winning such highly competitive grants," says Peter. "$1.5m worth of NHMRC grant money has been awarded, and that's pretty significant for a new investigator."

Peter has been at the Institute since the start, funded through NHMRC awards and an American-Australian Association fellowship. His most recent work, which attracted media coverage worldwide last year after the Lancet published his findings, examined the effects of male hormonal contraception.

"We were looking at the recovery of fertility after men stopped using contraceptives, and addressing the safety of it in terms of reversibility," he explains. "What we showed was that every man who takes a male hormonal contraceptive, all of the wide variety of types tested so far, can expect to have full recovery of sperm output to levels consistent with normal fertility when they stop taking it."

Peter is medically trained as an endocrinologist/andrologist/clinical researcher. He completed his residency at Concord Hospital and advanced training at Royal Prince Alfred Hospital. His career has included a period at the renowned Mayo Clinic in the United States. A major project engaging his attention now is looking at the connection between testosterone and sleep apnea - where people repeatedly have long pauses in their breathing while asleep.

"It's a vicious cycle," says Peter. "As you develop sleep apnea you testosterone falls, and as this occurs there is possibly a worsening of sleep apnea. As you drop your testosterone you put on more fat, and as you put on more fat it pre-disposes you to develop more sleep apnea. So maybe the way to break that vicious cycle is to give men testosterone – that's really the basis of our study."

The NHMRC grants will enable Peter to continue his research into how androgen disorders lead to a host of common illnesses, including obesity, infertility and sleep apnea.

GIVING OPPORTUNITIES

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