

Treasurer excited by ARI achievements



From left: Dr Zehra Elgundi, Dr Robin Gasiorowski, Prof. Derek Hart, Treasurer Joe Hockey, Craig Laundy MP

“It makes me proud to be an Australian!”

That was the reaction of Federal Treasurer Joe Hockey after receiving a briefing on some of the major research projects under way at the ANZAC Research Institute (ARI).

“This is exactly why we need the Medical Research Future Fund, so we can put a billion dollars a year into institutes like this which are at the forefront of global technology and development,” said Mr Hockey. “I want Australia to become the global hub for medical research.”

Accompanied by Craig Laundy, Federal MP for Reid, the Treasurer inspected the

ARI facilities on June 10th, talking to staff and expressing amazement and praise for their achievements.

After being welcomed by Professor David Handelsman, Director of the ARI, Mr Hockey was given an overview of the Concord Hospital research campus and a vision for future development by Dr Teresa Anderson, an ANZAC board member and CE of the Sydney Local Health District.

Professor Derek Hart, head of the Dendritic Cell Biology and Therapeutics Group of the ARI, explained his team’s world first research which could lead eventually to a cure or vaccination for some types of cancer, such as bone marrow and leukemia.

The Treasurer was clearly also impressed to hear from Professor Nico van Zandwijk, Director of the adjacent Asbestos Diseases Research Institute, that his unit’s work has reached the stage where clinical trials are now starting on a possible cure for mesothelioma. Prof. van Zandwijk said patients will be given what he described as “a magic bullet”, which could produce a radical improvement in their life expectancy.

The final presentation was from Professor David Le Couteur, head of Biogerontology research at ARI, who outlined the extensive research being carried out into ageing and cancer, and the effects of diet on both. He said trials

Back to the future for Megan



Megan Brewer

When Megan Brewer accepted a primary schools' citizenship award organized by Burwood Rotoract club back in 1996, she could hardly have dreamed that 17 years later she would return with a Ph.D and as a graduate of the Universities of New South Wales and Sydney to present the 2013 citizenship awards to 54 students from 28 schools.

Now a researcher at the Northcott Neuroscience Laboratory at the ANZAC Research Institute, Dr Brewer has joined the team studying the debilitating Charcot-Marie-Tooth disease. Dr Brewer was guest speaker at the citizenship awards, providing pupils, parents and teachers with an insight into the valuable work being carried out at ARI. The function raised \$1500 for charity – and that was donated to the institute.

Dr Brewer has also been an ambassador for the institute at Macquarie University's "Careers in Science" symposium, attended by 170 students, where she described her career in biomedical research.

Dr Brewer's first experience at the Concord research campus was as a second year undergraduate, when she took part in the summer scholarship scheme, working with the Neuro group, and enjoyed it so much she returned 12 months later and stayed for her honours and PhD degrees. An invitation followed from Dr Anthony Antonellis to undertake a postdoctoral research position in the Department of Human Genetics at the University of Michigan, where a team of researchers is collaborating with the team at the ANZAC Research Institute.

During 2 ½ years in the US, Dr Brewer was awarded a Sir Keith Murdoch Fellowship by the American Australian Association. Having studied new techniques in using cell and animal models, in particular zebrafish, Dr Brewer returned to Sydney to rejoin the Neurobiology Group, where she is now engaged in identifying new genetic causes of CMT in genetically-undiagnosed patients.

Those responsible for deciding which school pupils should receive the 1996 citizenship awards should be congratulated for choosing Megan Brewer, who's certainly repaying their confidence in her!

Treasurer excited by ARI achievements continued

based at the Institute with 900 mice had shown that a low protein/high carbohydrate diet had produced better blood pressure, reduced cholesterol and lower diabetes markers.

"By delaying ageing, we can delay age-related disease and disability," Prof. Le Couteur told the Treasurer.

It was Mr Hockey's first visit to a medical research institute since the Budget announcement of plans for a Medical Research Future Fund, which could by 2022 have \$20 billion invested, providing \$1 billion a year in additional



Assoc. Prof Georgina Clark explains dendritic cell research to Mr Hockey as local MP Craig Laundry listens

support for facilities such as the ANZAC Research Institute.

Teaching Next Generation Sequencing Strategies to identify Disease Genes



Dr Ahmad Annuar & A/Prof Kennerson



Course participants

Associate Professor Marina Kennerson was invited to the Faculty of Medicine, University of Malaya, in early June to run a 2 day workshop entitled "Find that Gene!"

The idea to run this workshop came about through her collaborative work with Dr Azlina Ahmad Annuar and Dr Nortina Shahrizaila to map genes for Charcot-Marie-Tooth (CMT) disease in Malaysian families. Next Generation Sequencing (NGS) is now an essential technology that we use to screen families for mutations in known CMT genes (80 genes are known to date) as well as discovering new CMT genes.

Dr Annuar, who heads the Neurogenetics Laboratory at the University Of Malaya, organised a program that included teaching lectures and a NGS computing practical by A/Prof Kennerson as well as company sessions and presentations by other research groups doing gene mapping in Malaysia. The overall goal was to bring together other researchers in Malaysia who had an interest in gene mapping and NGS and wanted to use these approaches in their research.

A/Prof Kennerson has worked in the gene mapping field for more than 20 years and has seen the evolution of modern genomic strategies to map new CMT genes. Through NHMRC funding she has been instrumental in implementing NGS technologies as part of the Inherited Peripheral Neuropathies Gene Discovery program at the ANZAC Research Institute.

Her recent discovery of two genes causing X-linked distal motor neuropathy (ATP7A) and X-linked CMT (PDK3) are a testament to her skills and wealth of experience in combining traditional gene mapping techniques with cutting edge genomic technologies. Over the years A/Prof Kennerson has given lectures and practical modules on linkage analysis at Cold Spring harbour Laboratories and the Sultan Qaboo University, Oman. The opportunity to share her knowledge and expertise with colleagues in Malaysia was a great experience and many participants gave positive feedback on the value of what they learnt and the appropriate timing to hold such a workshop in their country.

Regulating the steroids we produce



A relative newcomer to the ANZAC Research Institute is Professor Mark Cooper, Head of the Discipline of Medicine at Concord Hospital and Head of the Adrenal Steroid Lab at the ARI, who transferred from the University of Birmingham about 18 months ago.

“There’s nothing like a change of environment to stimulate you, and to reflect on where you’re going,” he says, explaining that while he has concentrated on laboratory work in Sydney, he still has his former colleagues in England co-operating with clinical research.

It might be a change of scenery for Professor Cooper, but he’s been developing his field of research since 1998.

Prof. Cooper’s investigation is into the role of adrenal glands, which produce a range of steroids, most significantly the anti-inflammatory steroids known as glucocorticoids. These are very important when the body faces problems such as osteoporosis, obesity and rheumatoid arthritis.

“My work really looks at the hormones made by the adrenal glands, and how they work in the body, what happens if you have too little or if you have too much, how they are dealt with in the tissues.”

“We used to have this simplistic view that if the body needs steroids it gets them from the adrenal glands – the adrenal glands make more. But in the past 20 years, we have realised that the tissues themselves can up-regulate or down-regulate the amount of steroid that they need.”

About 1% of the population take anti-inflammatory steroids like cortisone – one of the most common conditions being rheumatoid arthritis.

“It wasn’t really till our research came along that people appreciated that a major contribution in rheumatoid arthritis comes from the body’s own steroids,” says Prof. Cooper.

“If you or I were to suddenly develop an inflammation of our joints, our joints themselves would switch on this little catalyst, and start to generate steroids within the inflamed tissue – and for many of us that would be enough. We might be able to dampen down inflammation and it would all get better.

“We think the inflamed tissue makes as much steroid as it can, and when eventually it gets overwhelmed, then people get the signs and symptoms of

rheumatoid arthritis. We then supplement them with extra steroids to try to use the same trick.”

Prof. Cooper’s breakthrough was to link this tissue metabolism to changes in the appearance of the body as it ages.

“We know that as people get older, they tend to lose bone. We know that when people get steroids, therapeutically, they lose bone. But no-one really thought that the two might be related. So what I’ve shown is that as you get older, your bone starts to make more steroids.

“It wasn’t really till our research came along that people appreciated that a major contribution in rheumatoid arthritis comes from the body’s own steroids”

“People who are elderly, over the age of 70 or so, the cells in their bones are probably making about four times as much steroids as people who are in their teens or 20s. This steroid is probably causing a nasty effect. We recently were involved with a research program looking at skin – we thought the same thing might happen with skin, and we went on to show that people who are in their 60s or 70s are making a lot more steroids locally in their skin than people who are younger. And this may account for some of the effects of ageing. We know that if you put steroid on the skin, the skin gets thin very quickly. But we had never really thought that the body was causing its skin to thin, through making too much steroid in the skin.”

Prof. Cooper’s ultimate goal is to develop drugs which might reduce the levels of steroids and their effects on the body.

“In the most optimistic view it might return bones to being like young bones, or it might reverse some of the changes we see in skin with age,” he says.

Staff profile:

JUSTIN CROSBIE

Information technology plays critical role

Justin Crosbie is one of the few members of staff who can claim to know everyone else at the ANZAC Research Institute, and to have a supporting role in every research project. He is the Information Systems Manager – meaning he’s responsible for ensuring that every computer and every computer-based piece of equipment is running smoothly.

“I find that more and more research involves technology, including digital data storage and analysis,” says Justin. “Every new tool seems to have a computer attached, with unique requirements.”

Justin began working at the Institute as a contractor in 2007, and moved into his current full-time role two years later.

“My role involves everything from desktop support and system administration, to supporting the most advanced scientific research computer equipment. It’s very rewarding because I meet just about every researcher here, and continually get to see the great work that’s being done.

“It’s very satisfying to see students, scientists and research groups working together and achieving such terrific outcomes, knowing that these will help improve future medical care and health in our community.”

Justin is taking his own studies further, having been granted a Sydney Local Health District scholarship for the Masters of Health Service Management degree program run by the University of Tasmania. Subjects include epidemiology and statistics, health law and ethics, and leadership and health economics. He started the course last year and hopes to graduate in 2015.

“The program is primarily run by distance education units,” he explains, “but is supported by weekend residential master-classes throughout the year, hosted at Royal Prince Alfred Hospital’s Kerry Packer Education Centre. One of the recent highlights was hearing Gail Kelly, the CEO of Westpac, speaking to us about leadership.”

Information technology is a driving factor in medical research, and Justin says it’s both exciting and fulfilling to be playing his part in the work that brings hope, health and knowledge to so many.

Macrophages in atherosclerosis

Terms such as “macrophage” and “apolipoprotein E” won’t mean much – if anything – to most Australians. But these words are extremely relevant to most Australians, because we, like so many in the western world, are battling the results of our lifestyle, and increasingly those results include high cholesterol, chest pains, strokes and heart attacks.

Dr Maaïke Kockx has spent the past ten years studying a protein known as apolipoprotein E, which has anti-atherogenic properties. Dr Kockx moved from the University of NSW about 18 months ago, along with Professors Len Kritharides and Wendy Jessup, to establish the Artherosclerosis research team at the ANZAC Research Institute.

“We study the process where you develop lesions also called atherosclerosis plaques, in the walls of your arteries,” she says.

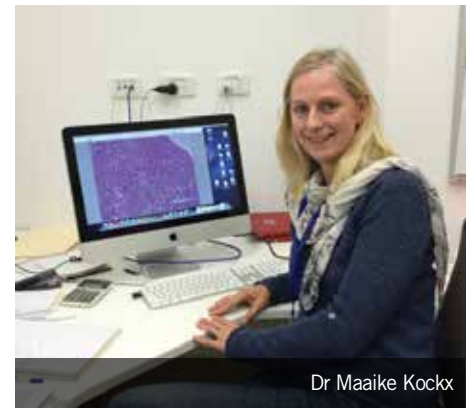
“What happens is that you get an injury

to your vessel wall, and cholesterol – lipid rich particles – accumulates in the artery wall. The monocytes that travel through your blood then move in, and they want to take care of that cholesterol. They become very lipid rich and form lipid droplets in the cell which makes them look very foamy, so we call them macrophage foam cells.”

Dr Kockx has been able to generate macrophage foam cells in the lab so she can study how they take up the cholesterol, and how we might induce removal of that excess cholesterol.

“You want them to degrade the accumulated cholesterol or move out of the lesion again, taking that cholesterol away. Because once a macrophage becomes foamy, it becomes highly inflammatory and actually makes the lesion worse.

“Part of our work is figuring out how cholesterol and also apolipoprotein E are secreted. Understanding these processes will give us ways to influence foam



Dr Maaïke Kockx

cells and combat lesion formation and progression.”

Dr Kockx points out that lesions in the vessel walls are “clinically silent” – we don’t know they exist, until we suffer symptoms. Yet studies in the US have revealed that as many as two thirds of all teenagers have these lesions – a by-product of a lifestyle that is having adverse effects on even the young.

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