

Institute Director working with WADA



The Director of the ANZAC Research Institute, Professor David Handelsman, as a nominee of

the Australian and New Zealand governments, has been appointed to a three-year term on the Health, Medical and Research Committee of the World Anti-Doping Agency.

This committee is one of four standing WADA committees and each year determines the Prohibited List of banned drugs in sport and decides on WADA research grants into anti-doping science. Chaired by Prof. Arne Ljungqvist, a 1952 Olympic athlete, the committee has played a pivotal role in developing science and research to combat doping in sport.

David Handelsman joins other committee members from Italy, Switzerland, Jordan, Malaysia, Norway, Japan, Spain, Netherlands, Greece, UK, USA and Luxembourg.

The appointment is recognition for the work that David and his colleagues in Concord Hospital's Andrology Department have performed in recent years in researching androgen misuse and abuse, together with other forms of drug cheating in sport.

The chairman of WADA until the end of 2013 is former NSW Premier John Fahey. WADA is based in Montreal, Canada.

NHMRC Grants acknowledge our achievements

The National Health and Medical Research Council has acknowledged the significant achievements recorded in the first ten years of the ANZAC Research Institute by approving five new project grants – resulting in almost \$2.5 million new funding over the next three years.

Nine applications were lodged, so this year's 55% success rate continues the Institute's exceptional results over its decade of operations of consistently more than double the overall national average of 20%-23%.

Congratulations to Garth Nicholson, Marina Kennerson and Ian Blair from the Northcott Neuroscience Laboratory, Charles Allan, Ulla Simanainen and David Handelsman from Andrology, and Brian O'Toole from the Vietnam Veterans Family Health Study. Their successful projects are outlined below.

FSH control of ovarian function

– Dr Charles Allan

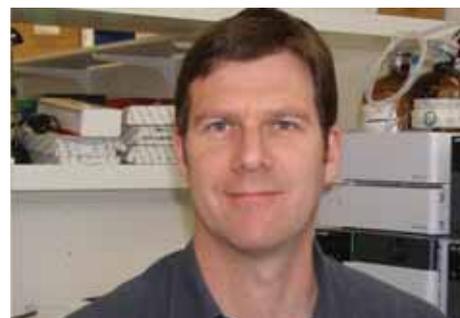
Follicle-stimulating hormone (FSH) is vital for egg development, female fertility and health and is used widely in assisted reproduction technology (IVF). But high levels of FSH are associated with premature infertility, menopause, and ovarian cancer.

Research in the Andrology lab has established unique models to investigate the possibility that high FSH plays an active role in important age-related disorders, rather than being merely a reflection of ovarian ageing and demise.

Dr Allan says this project will answer fundamental questions about the role of FSH in ovarian follicle formation, development and failure.

"Advancing our knowledge of the mechanisms that control ovarian demise, and so regulating the onset of menopause, will have a major public health impact," he says.

"Just think about the clinical implications and therapeutic possibilities for modern women, who now live half their adult lives after menopause and also exposed to post-



menopausal disease such as loss of bone density and ovarian cancer.

"We have created a transgenic mouse model that exhibits progressively rising FSH levels with age, which results in dose-dependent ovarian dysfunction and premature reproductive failure.

"Another key hypothesis of this project is that excessive FSH activity induces dysfunction in the follicles – the cells that contain the developing eggs – and this contributes to the formation of ovarian cancers," says Dr Allan.

This project is highly relevant to promoting and maintaining good health, identified as a National Research Priority and a critical element in better preventative health care.

Investigating the genetic base of Motor Neuron Disease

– Dr Ian Blair



As we reported last year in Discovery a team headed by Dr Ian Blair is making dramatic advances in our knowledge of MND, also known as Amyotrophic Lateral

Sclerosis – a nerve-destroying disease that affects one in 5000 Australians over the age of 50.

70% of patients die within 2-5 years of the onset of symptoms. About 10% of cases come in a familial or inherited form, but the other 90% are sporadic.

The ANZAC Institute team is utilising the large collection of DNA samples gathered by Professor Garth Nicholson over the past two decades from families with a history of MND. The Institute has also been recognised as a national referral centre for DNA diagnostic testing with neurologists from throughout Australia sending samples to Concord for accurate diagnosis.

"We've identified a couple of critical genes that are dysfunctional," says Dr Blair. "One gene in particular is dysfunctional in almost all the sporadic cases but is responsible for only a few per cent of the familial cases.

"All the known genes account for only 20% of familial cases so 80% of genes responsible for familial ALS are yet to be identified.

"If we can identify those then we'll look at the sporadic cases again, and we expect they'll be present there as well. It's difficult to get a grip on the sporadic cases because there must be a myriad of different causes, different environmental exposures, different genetic components, which all interact in a complex way to cause motor neurone death."

Finding these genes is now much more likely as science advances. Dr Blair points out that 10 years ago when the human genome project finished, it cost \$3 billion to map one individual's genetic sequence. That cost has now dropped to about \$30,000 and the goal is to reduce that to \$1000.

As Dr Blair pays tribute to Garth Nicholson for having had the foresight to store DNA samples from about 200 families and 1000 individuals so today it is feasible for a lab at the ANZAC Institute to DNA

sequence an individual, rather than depending on an expensive worldwide consortium.

Discovering gene mutations that cause peripheral nerve death

– Associate Professor Marina Kennerson



This project utilises state of the art genome technologies aiming to identify genes responsible for Charcot-Marie-Tooth neuropathy, the most common inherited

neurological disease that affects about 1 in every 2000 people, destroying the nerves that control hands and feet in particular.

"The project encompasses the remarkable collection of DNA from cases and families that Professor Garth Nicholson has assembled over decades of patient care," says A/Prof Kennerson. This is the basis for our leading track record. This is where we have international recognition."

"About 40 genes causing CMT are known but there are many more to be found. About 70% of cases are caused by the gene PMP22 which is found on chromosome 17, but there are more."

The team has a very strong track record of working on chromosome X so this grant will allow research with X-linked families, in which the disease is passed on from carrier mothers to sons because the mutant gene is on the X chromosome.

"By finding these genes we're identifying important biological pathways and potential therapeutic targets to try to stop the nerves dying back, to prevent it occurring or to slow it down," says A/Prof Kennerson.

"Every gene we find adds more biology to what we currently understand, and some of it can be surprising. Our recent discoveries have identified peripheral neuropathy genes that are housekeeping genes, genes we need in all of our cells, in skin cells, and in other parts of the body. But for some reason, in the nerve cells, if they're damaged, you see this effect of them dying back."

A/Prof Kennerson explains that although CMT is relatively uncommon, with about 8500 Australians affected by the disease at any time, the economic impact is enormous.

"It's estimated that each year CMT costs the nation \$220 million in paramedical and

pension support, and that lifetime loss of productivity is worth \$6.7 billion. So the potential value of our research to the Australian economy should not be underestimated."

Does PTSD in a parent increase the risk of mental health disorders in their offspring?

– Dr Brian O'Toole



This project has its roots in research conducted more than 20 years ago when Dr O'Toole's team first interviewed and assessed a random sample of 1000

Vietnam veterans. Subsequent work has tracked the mental health of the veterans and their partners, and this new research will examine the well-being of the veterans' children.

"We hope to interview up to 960 now grown children who are now aged anywhere between 19 and 59."

"This study will be about the size of the veterans' and their partners' studies put together," says Dr O'Toole, whose work is recognised internationally as the most significant examination of Vietnam veterans' mental health.

While there have been suggestions for decades that the veterans' children have higher suicide rates and above average problems with mental health, there is evidence both for and against the idea that there is a ripple effect within families.

"The problem is that the evidence so far is usually based on the veteran talking about his own kids or his partner, so you don't know whether his opinion is coloured by his own PTSD or his own depression, or whether it's a real effect," says Dr O'Toole.

More than a million Australians suffer from Post Traumatic Stress Disorder so the results of this research could have far-reaching implications for public health policy.

Studies worldwide so far have concentrated on Holocaust victims and their families, with suggestions that second generation Holocaust have similar symptoms to their parents, even though they didn't experience that trauma first hand.

"The question is, if that's happening, what is the mechanism for it? There's some evidence from Israel that mothers may be able to protect their female children or

maybe their grandchildren from the effects of the Holocaust.

"So we'll be able to look at the effects of the veteran on the child and then question whether the mother has any sort of ameliorating or intervening effects, particularly on the child's psychological health."

Dr O'Toole's research already has revealed that out of 20 psychiatric conditions, 17 are more prevalent among Vietnam veterans than in the wider Australian community, and more than 50% of veterans and their partners were diagnosed as having depression.

Androgens and prostate cancer

– Dr Ulla Simanainen



Male hormones – known as androgens – are the fuel that drives prostate cancer, so reducing levels of testosterone, the main androgen, is the standard way of

treating the disease. However it does not cure the cancer and can cause serious side-effects throughout the body.

Dr Simanainen says the goal of this project is to understand not only androgen actions in the prostate, but the cell specific actions, to understand how these male hormones act within different types of cells.

"Historically it was thought that only the testes and the adrenal glands are the hormone producing organs in men," she says. "But now it's clear that in cases when androgen production is blocked in those organs, for example in treatment for prostate cancer, then hormone dependent organs like the prostate can produce their own androgens to support the growth of the prostate and the prostate cancer.

"We want to understand how this is possible within the prostate."

Prostate is the most common organ cancer among men: 10 per cent of men in their 70s will be diagnosed and about 3000 men in Australia die from prostate cancer each year.

"Because the prostate is so androgen dependent, the first line of treatment for

advanced prostate cancer is always androgen depletion therapy," Dr Simanainen explains.

"But the major problem when men are treated with androgen depletion therapies is that after a positive response the cancer returns and then no longer responds to androgen depletion. We think that at this time the prostate itself can produce the hormones to keep the cancer growing, and that's why it is resistant to removal of external sources of androgens by medical therapies."

The researchers are using mice in which the androgen receptor has been deactivated within different cell types of the prostate. The mice are treated with different drugs and Dr Simanainen analyses the results.

"At the moment prostate cancer treatment is designed for one organ, for one human being, but we want to narrow down the focus so we know which cells are the most important so we can develop better targeted, cell-specific treatment with greater efficacy and less unintended side-effects."

Sydney Medical School Summer Scholarship students benefit from research projects at ANZAC

Once again this summer the ANZAC Research Institute has enjoyed the company of 7 highly credentialed and motivated undergraduate students, developing research projects with far-reaching potential.

We welcome these young medical researchers and wish them every success in their introduction to medical research.

The Summer Scholarship scheme, developed originally by the ANZAC Research Institute to provide undergraduate science students with an experience over the summer holidays of medical research by apprenticeship to top medical researchers, was adopted by the University of Sydney Medical School in 2005. Two years later the scheme was honoured with a national tertiary education award from the Australian Living and Teaching Council (formerly Carrick Institute) for "Outstanding Contribution to Student Learning."



The students, and their supervisors, are:

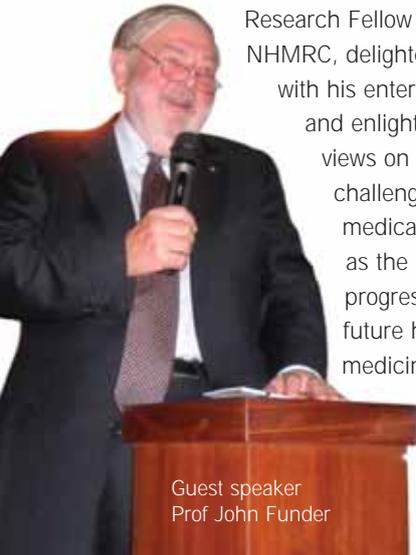
- *Eric Cheuk Kin Lee*, investigating biofilm and infection of burns wounds, with Dr Yiwei Wang
- *Richard Shaw*, examining what causes the premature death of motor and sensory neurons, with Dr Marina Kennerson
- *Tomasz Szczesnik*, investigating the development of living 3-dimensional skin equivalent by using advanced biotechnology, with Prof Peter Maitz and Dr Zhe Li
- *Sarah Kim*, investigating tea tree oil release behaviour from hydrogel, cytotoxic effect on skin cells and anti-inflammatory activity, with Dr Zhe Li and Prof Peter Maitz
- *Difei Deng*, examining vitamin D receptor and prostate cancer cell growth, with Dr Yu Zheng and A/Prof Hong Zhou
- *Pamela Ajuyah*, studying oncogenic and tumour suppressor miRNAs in the growth and survival of malignant mesothelioma cells, with Dr Lyn Schedlich
- *Leah Nayoung Kim*, investigating dendritic cells and cancer, with Prof Derek Hart

ANZAC Research Institute 10 year anniversary

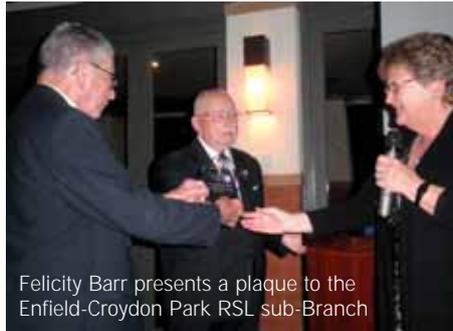
The ANZAC Research Institute's 10 year anniversary was marked on 22 October with a dinner, celebrating a decade of achievements and acknowledging the support of staff, board members and those who have given so generously in the interests of medical science.

Keynote speaker Professor John Funder, former Director of the Baker Institute and long-time Senior Principal

Research Fellow of the NHMRC, delighted guests with his entertaining and enlightened views on the challenges facing medical research as the source for progress in our future health and medicine over coming decades.



Guest speaker
Prof John Funder



Felicity Barr presents a plaque to the Enfield-Croydon Park RSL sub-Branch



ANZAC Institute Director Prof David Handelsman and Board Chairman Felicity Barr

Felicity Barr, chair of the ANZAC Health and Medical Research Foundation, and Institute Director Professor David Handelsman paid tribute to the outstanding results that staff have produced in the Institute's short history.

A special presentation was made to Russ Kenny and Frank Fyris on behalf of the Enfield-Croydon Park RSL sub-Branch, which had donated \$10,000 to the Foundation.

The Institute is grateful to the Tintilla Vineyard and Carlton and United for donating the wines and beer that

accompanied dinner and to sponsors who assisted with raffle prizes. A list of sponsors and prize winners appears below.

Thank you

The Board and staff of the ANZAC Research Institute express their gratitude to the late Mr Colin Gordon Hodges, of Inverell in northern NSW, who provided a substantial bequest in his estate that will provide vital support for our medical research projects.

ANZAC
RESEARCH INSTITUTE



10th Anniversary Raffle

Tickets: 5 for \$20.00

Drawn on 22nd October 2010 at Angelo's on the Bay

- Two nights accommodation in a deluxe room for 2 adults including breakfast staying at any Grand Chifley, Chifty, Country Comfort, Australis or Sundowner hotel of your choice in Australia. Valued at over \$440 **Prof Bob Lusby**
- A guided BridgeClimb on the arches of the Sydney Harbour Bridge for two. A day or night, Monday to Friday Climb valued at \$396 **Dr Kirsty Walters**
- 2 x Matchmaster MPEG-4 High Definition Set Top Box (Value \$229 ea) **Michael Field & Meg Nicholson**
- Angelo's on the Bay Dinner for two (value \$150) **Karen Babet**
- Two pack (1 white, 1 red) Parliamentary Wine donated by Angela D'Amore **Dr Yiwei Wang**
- Powastation Cordless Blender from Good Guys (Value \$59) **Kaylene Kritharides**
- 2 x Cartons of Fosters Crown larger (Value \$55) **Eve Bosak & Prof Andrew McLachlan**
- 2 x Johnny Walker Black Label Old Scotch Whisky (Value \$53 ea) **A/Prof Georgina Clark & Shai Joseph**
- 2 x Bunning hampers & \$20 gift voucher (Value \$40 ea) **Corine De Graaf & Mark Jimenez**
- 3 x Mirvac Rhodes/Reading Cinema Double pass (Value \$30 ea) **Anne Conway, Karen Babet & Mark Jimenez**



Thank you to our kind sponsors



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