Annual Report 2009

ANZAC Research Institute
“We do not know his rank or his battalion. We do not know where he was born, or precisely how and when he died. We do not know where in Australia he has made his home or when he left it for the battlefields of Europe. We do not know his age or his circumstances – whether he was from the city or the bush; what occupation he left to become a soldier; what religion, if he had a religion; if he was married or single. We do not know who loved him or whom he loved. If he had children we do not know who they are. His family is lost to us as he was lost to them. We will never know who this Australian was. Yet he has always been among those we have honoured. We know that he was one of the 45,000 Australians who died on the Western Front. One of the 416,000 Australians who volunteered for service in the First World War. One of the 324,000 Australians who served overseas in that war; and one of the 60,000 Australians who died on foreign soil. One of the 100,000 Australians who have died in wars this century.” Dedication to the Unknown Soldier.

Don Watson

“Perhaps the most drastic effect of the war on Australia would never be enumerated: it was the loss of all those talented people who would have become prime ministers and premiers, judges, divines, engineers, teachers, doctors, poets, inventors and farmers, the mayors of towns and leaders of trade unions, and the fathers of another generation of Australians. It was a war in which those with the gift of leadership, the spark of courage, and the willingness to make sacrifices often took the highest risks. The Australians were all volunteers. It may be that on Gallipoli and in France we lost the most generous spirits of a generation.”

Geoffrey Blainey

He is all of them. And he is one of us.

Just as the Unknown Soldier represents the sacrifice made by our forebears and symbolises the ANZAC spirit, the ANZAC Health and Medical Research Foundation will, in perpetuity, add to our Nation’s understanding and confidence about our place in the world and our capacity to play a creative and humane part in it. The Foundation’s vision will encourage us to recognise how important it is for our Nation to believe in great ideas and to have them at the forefront of our ambitions.

Vision

To provide leadership and excellence in health and medical research activities throughout Australia, with a focus on ageing, to improve the future health and medical care for the Australasian community. In so doing, the Foundation will provide a lasting legacy to the veterans and their families who have created the society we have today.

Mission

- To establish and operate a state-of-the-art biomedical research institute on the campus of Concord Hospital that is affiliated with the University of Sydney.
- To encourage, collaborate in and undertake basic, clinical and epidemiological research, with a particular focus on ageing, that aims to improve health and medical care and is dedicated to the memory of our war veterans and their families.
- To gain and optimise support from the wider community in order to facilitate our vision.
- To provide leadership and excellence in biomedical research in national and international arenas.
- To foster education and training in relevant research and health disciplines.

Cover image: Courtesy Charles Taranto
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Once again, securing and maintaining funding for the ANZAC Research Institute have been the main concerns of the Board of the ANZAC Health & Medical Research Foundation in the 2008-09 financial year. The standard of excellence achieved by the scientific research teams has brought success in winning grant funding, but has also increased demand for technical, administrative and infrastructure support funding. Investment strategies devised by the Board in earlier years have needed adaptation to the difficult circumstances of the global financial crisis. However, I am pleased to advise that overall the Institute’s finances remain in good shape, as you will see from the financial statements later in this report. We are particularly grateful for the strong support of the University of Sydney, the Federal Government and the Sydney South West Area Health Service for our work and the extension to the Institute’s premises.

Recent moves from government to review the many levels of funding arrangements for health and medical research have been cautiously welcomed in the sector. There is no doubt that funding programs could operate more effectively to facilitate and encourage world-class research. The Board remains concerned that in making efforts to streamline funding approaches, stakeholders will take the opportunity to insert more centralised controls on funding and stifle the independence of research teams. We will continue to monitor developments with interest and to make our views known in relevant circles.

In the meantime, I would like to acknowledge the success which the Institute’s scientists have again achieved in the past year under the leadership of the Director, Professor David Handelsman. The Institute’s early successes soon after opening in 2000 have proven a sound indicator of the high standards of research being undertaken by the scientific teams, with long-term programs now delivering consistent results. The Institute’s name has now appeared in many of the most prestigious journals; care is being taken to ensure that research teams invited to take up space in the new laboratories are capable of making worthwhile contributions to enhance the Institute’s international reputation.

Members of the Board join me in thanking the Director and his administrative team, especially Julie Taranto, Annet Doss and Tracey Dent for their support to the Board. I would also like to thank my Deputy Chair, Danny O’Connor, the members of the Finance Committee Mrs Eve Bosak and Prof David Cook for their efforts in this difficult year and to pay tribute to all members of the Board for their commitment to the future of the ANZAC Institute.
Welcome to the ANZAC Research Institute’s Annual Report, with updates from our 9th year of operation. In moving towards the end of our first decade, we complete another year of research discoveries, continued success in competitive external grant funding, training new research scientists and publishing papers in top international journals. An overview of this exciting work is outlined in the following pages from the Institute’s research groups, each an international leader. With much to be proud of, it remains a challenge to maintain such an excellent record.

Since opening in 2000, the ANZAC Research Institute is among Australia’s top medical research institutes and the fastest growing in NSW. Located on the grounds of Concord Hospital, it has earned a reputation for scientific excellence within its overall theme of Ageing with work covering andrology, burns, cancer, cardiovascular disease, osteoporosis, neurodegenerative disease and dementia, and population research into ageing and the health of veterans. Recognized by the NHMRC and NSW government as a independent medical research institute, we provide a scientific home to over 130 scientists including 40 graduate (PhD) students. Altogether we earn an annual external grant-based income of over $7 million and produce 150 scientific papers per year in top journals. The ANZAC continues to maintain a high success rate with over 50% success in NHMRC Project Grants.

A major milestone this year was Prime Minister Rudd opening the Bernie Banton Centre in January 2009. Located next door to the ANZAC Research Institute, the Bernie Banton Centre houses the Asbestos Disease Research Institute (ADRI), a world’s first research facility dedicated to research into asbestos related diseases especially mesothelioma, on the ground floor with an extension to the ANZAC Research Institute laboratories on the upper floor. At the opening, PM Rudd announced the Commonwealth’s contribution of $5 million to complete the Centre including construction of a new translational research facility. The ANZAC Research Institute’s scientists are eagerly looking forward to supporting ADRI in its start-up phase under its inaugural Director, Professor Nico van Zandwijk and principal scientist Dr Glen Reid.

The ANZAC Research Institute’s role is to serve as the dedicated medical research institute for Concord Hospital. Each research group is headed by individuals closely affiliated with Hospital departments. Such strong linkages ensure a close alignment of research with the needs to improve medical practice through translational research. We are therefore ideally placed to drive the best research from basic discovery science to applications in clinical, translational, public health and health services research. Such a tight integration of active medical research is the only guarantee for any modern teaching hospital of maintaining highest standards of medical care through continual fresh input from discoveries all over the world. A medical research institute with high academic standing serves a Hospital by attracting top academic physicians, researchers and trainees from around the country and overseas. This model of mutual enrichment between a teaching hospital and its medical research institute is, however, under threat from not only the general climate of economic uncertainty but also specific pressures from the government sector that threaten the vital infrastructure funding which keeps our doors open and our scientists working in their labs. Doing high quality medical research is costly in the short-term but makes an exceptional long-term investment in better health and medical care. Only strong community support which recognizes the value of medical research can keep the Institute going strong.

"DIRECTOR’S REPORT 2008-9"
This Report is my chance to give public thanks to the many who make this work possible. The Institute could not work as successfully without the skill, commitment and untiring work of our terrific administrative team - Justin Crosbie, Tracey Dent, Annet Doss, Candice Chang, Mark Jimenez, Mamdouh Khalil, Pam McDowell, Julie Taranto & Lilian Tay. They make the necessary work go lightly - it is a pleasure to thank them most sincerely. Thanks also to the General Managers of Concord Hospital, Danny O’Connor and Gary Miller, for their reliable support on behalf of the Sydney South West Area Health Service. Similarly, the support of the University of Sydney Medical School, and Professor David Cook in particular, is gratefully appreciated. Thanks are also due to John Gatfield for editing of our newsletter Discovery. Finally, it is a pleasure to thank Felicity Barr, the Chair and her Board, for their unwavering support and commitment to making the Institute grow to be the best it can. Above all, it is a privilege to work in the challenging and productive environment created by the Institute’s scientists and I am grateful to them always for their quiet, inspiring efforts which make all obstacles worth overcoming.
ANDROLOGY

Group Leader: Professor David Handelsman

Senior Scientists: Dr Charles Allan, Dr Tim Harwood, Dr Ulla Simanainen, Dr Kirsty Walters

Visiting Scientists: Dr Gideon Sartorious (Switzerland), Dr Thilee Sivananathan

Staff and Students: Omar Akram (with Heart Research Institute), Lydia Andres, Fay Bacha, Frank Bathur, Assoc Prof Ann Conway, Irene Di Pierro, Carolyn Fennell, Ellen Gao, Amanda Idan, Dr Veena Jayadev, Mark Jimenez, Patty Kapelaris, Lucy Liu, A/Prof Peter Liu (till March 2009), Dr Lam Ly, Dr Kisten McTavish, Keely McNamara, Jennifer Spaliviero, Sasa Spasevska, Leo Turner, Ljubica Vrga.

What is Andrology? Andrology is literally the study of man (Greek andros, man). Androgens (male hormones), the main one being testosterone, occur naturally in the body and play far-reaching roles in many body systems, particularly in male reproduction, fertility and sexuality. They exert important influence on most non-reproductive tissues especially the prostate, cardiovascular system, bone and the brain, throughout the entire male lifespan and may also influence women’s health.

The Andrology group focuses on both the biological and clinical effects of androgens on male health, in particular men’s reproductive and general health across all ages.

The Andrology group is a collaboration of the:
• Andrology Laboratory at the ANZAC Research Institute where the focus is on the physiology and pharmacology of androgens in males and also in females, by undertaking research using experimental animal models and laboratory bench research
• Department of Andrology at Concord Hospital, where patient and community centred research is carried out and translated into improvements in patient care. The focus is on the therapeutic use of androgens such as to treat hormone deficiency states in adolescence and adulthood, in certain chronic diseases, for male contraception and for ageing men. In addition we also study the relatively widespread misuse/overuse and abuse of androgens for many wishful or harmful non-medical reasons.

Highlights for 2008-2009
• Dr Kirsty Walters: Young Investigator Award from Australian Menopause Society, 2009
• Prof David J Handelsman: Honorary life membership, Endocrine Society of Australia 2008
• Dr Ulla Simanainen: Australian Women in Endocrinology Young Investigator Award 2008
• Dr Ulla Simanainen: International travel award, Endocrine Society of Australia, 2008

Physiology and Pharmacology of Androgens

Clinical Pharmacology of Testosterone
A Conway, C Fennell, L Turner, DJ Handelsman

The Department of Andrology at Concord Hospital provides testosterone replacement therapy to testosterone deficient men. As an international leader in research into the physiology and pharmacology of androgens, we continue to research the best and most acceptable forms of delivery of testosterone treatment for men who are testosterone deficient. Our extensive research into the implantation of testosterone pellets has provided unique information in defining how best to minimise the problem of pellet extrusion, how long the treatment lasts, why and how it varies between men and at what threshold of blood testosterone levels people become aware of returning symptoms of insufficient blood testosterone levels. A newer 3 month injectable form of testosterone has been introduced into clinical practice and we have completed the first long-term, head-to-head comparison study between the implantable and injectable depot testosterone products. Our findings show that, although injectable and implanted testosterone differ in their hormonal profile, their overall effects are comparable and well accepted. Ongoing quality assurance initiatives including the regular review of biochemical parameters in the blood help us monitor the effects and side effects of testosterone therapy and provide evidence to inform our clinical practice. Further studies are planned to further customize and improve testosterone delivery.

Measuring Steroids in Serum and Biological Samples
T Harwood and DJ Handelsman

Accurate measurement of steroid hormones from clinical and biological samples is essential for the diagnosis and monitoring of reproductive disorders as well
as being invaluable for a variety of applications within the research laboratory. Traditionally, either radioimmunoassay (RIA) or gas chromatography mass spectrometry (GC/MS) has been used for this purpose. However, there are problems associated with using these techniques. These include large amounts of sample being required for GC/MS and problems with cross-reactivity for RIA. Recently there has been growing interest in developing liquid chromatography mass spectrometry-based methods to measure steroid hormones from biological samples as affordable quantitative bench-top mass spectrometers which now match the sensitivity of immunoassays while maintaining reference level specificity.

Androgen Misuse and Abuse: Testosterone Overprescribing & Sports Doping

A Idan, C Fennell, M Jimenez, DJ Handelsman in collaboration with A Death, L McRobb, K McGrath (Heart Research Institute) and C Goebel, R Kazlausakas, G Trout, C Howe (National Measurement Institute)

Androgens play a major role in muscle strength, energy and quality of life in men. This can be dramatic in men with testosterone deficiency where testosterone replacement therapy often provides striking benefits.

Androgens, synthetic forms of testosterone, have major effects on muscle size and strength so that abuse of these well known effects has become entrenched in small pockets of the community among men and women seeking performance or image enhancement or as a panacea against ageing.

Androgens remain the most effective and popular drugs abused in sports doping. In recent years new designer androgens and indirect forms of androgen doping have been developed to evade detection of androgen doping. Maintaining effective bans on androgens requires continual vigilance in detection of illicit androgens and of indirect androgen doping. We are now undertaking World Anti-Doping Agency (WADA) and Australian Sports Anti-Doping Authority (ASDA) supported clinical and laboratory studies to develop new and more powerful detection tests for such novel androgens and other means to evade detection of androgen abuse.

Together with our collaborators at NMI, we continued to undertake studies to develop novel methods to detect abuse of other potential anabolic agents that act through increasing androgen output (such as hCG, and recombinant LH) or through other mechanisms (such as insulin). A recently completed pilot study revealed that short term use of an injectable GnRH analog produces a sustained increase in testosterone levels which may not only go undetected using the current method of sports doping urine tests but may also serve to “mask” the abuse of other androgens at the same time. Based on these important findings, a larger study has recently been funded by WADA to extend and detail these findings so as to develop more effective detection tests.

We developed a national, state-based surveillance of PBS-funded testosterone prescribing patterns. This has identified patterns of over-use that call for heightened surveillance and increased professional and public education to make clear the differences between valid evidence-based use of testosterone treatment and deterring misguided overuse lacking reliable evidence of safety and effectiveness. Fortunately, surveys of Australian high school students we have reviewed indicate that androgen abuse has remained at steady, relatively low levels during the last decade.
Healthy Male Ageing: The Health Man Study

G Sartorious, S Spasevska, AJ Conway, PY Liu, DJ Handelsman with Prof RI McLachlan and Dr C Allan (Prince Henry's Institute of Medical Research, Melbourne)

Why do some men remain healthy well into old age and others do not? Our Healthy Man study aims to determine the role of circulating androgen levels in maintaining good health and to explore the reasons why testosterone concentrations vary in one man compared with another through the observation of up to 400 healthy men. This study will also define age-specific reference ranges for testosterone in an “elite” healthy male population. This project will extend our established reference panel methodology from our study of young men to middle-aged and older men with the addition of multiple sampling and use of a reference testosterone assay using our new tandem-mass spectrometry method.

Measuring Progress of Puberty in the Community

T Sinvananthan, F Bathur, A Idan, A Conway, DJ Handelsman

Male sexual development and fertility develop relatively rapidly over a few years during adolescence, a period of time referred to as puberty. The triggers for puberty remain a mystery and the age at which it starts and its rate of progression vary widely between individuals for largely unknown reasons and have hardly ever been studied in the community. When boys pass the usual time for puberty without experiencing the expected body changes, the so-called secondary sexual characteristics (such as voice change and growth of muscle and body hair) that are the distinctive features of a man’s body, this is called delayed puberty. Delayed puberty can have deep and lasting effects on a developing man’s psyche because of the difficulties it creates in “fitting-in”, on how they are perceived as immature by others and themselves, creating difficulties in finding a social niche and forming life-long conjugal partnerships. Delayed puberty in boys is a common problem presenting to paediatricians and treatment is often further deferred while doctors and parents wait in hope that puberty may “catch-up” naturally. More pro-active and effective treatments for delayed male puberty are important area for further study.

The Andrology department is developing several study of male puberty. In one, the Department is coordinating a large multi-centre study of pubertal failure involving all major Australia and New Zealand pediatric endocrinology centres to test whether new recombinant gonadotrophin treatment is superior to the conventional form of testosterone treatment currently used world-wide. This study has the potential to change medical practice in the management of delayed puberty in adolescent boys. The Department is also supporting the ARCHER study, a rural community based adolescent cohort study of puberty, its variations and the impact of these on the development of health and wellbeing in young adults.
In order to conduct studies of male puberty in the community, better objective and quantitative measures of progress of male puberty are needed. While blood tests are very useful, they are invasive and hard to get in large community-based studies and they also only provide a single instantaneous measure of hormones levels, rather than an integrated measure over time. Furthermore there are is it is not possible to tell the onset of male sexual activity or of sperm production by any objective tests. We are therefore developing novel ways to measure these important, but difficult to study, endpoints by examining urine specimens.

**Androgens and the Prostate**

**Origins of Prostate Disease**

*K Griffiths, G Sartorious, B Jin, L Chan, A Conway, DJ Handelsman*

Our clinical studies on the origins of prostate disease have also focussed on early life factors (such as pre-birth or during puberty) that may predestine the development of prostate disease decades later.

We are undertaking two long-term clinical cohort studies. In one, we are following a cohort of 570 men studied 5-10 years previously to measure the growth rate of the human prostate by ultrasound and to identify lifestyle, hormonal and genetic factors that may influence it. In the second study, we are focussing on how events before and soon after birth may determine the susceptibility of the prostate to diseases such as prostate cancer and hyperplasia in later life. In this project, we are establishing a birth cohort of young men born ~1970 in inner Sydney and who are now in their early 30’s. The latter study requires us to trace young men born in Sydney around 1970 using hospital birth records. In contrast to a birth cohort of girls developed by collaborators in Adelaide, the recruitment of boys in Sydney has proved to be much more difficult, due, at least in part, to the requirement for an invasive transrectal ultrasound. As a response, we developed and validated a new less invasive method, transperineal ultrasound, which we showed to be as reliable as the standard transrectal methods. This new method published in the top Urology journal should facilitate future population studies of healthy men prior to onset of overt prostate disease.

**Tissue-selective Role of Androgens in the Prostate**

*U Simanainen, K McNamara, E Gao, CM Allan, DJ Handelsman*

The androgen receptor (AR) has a crucial role in both normal prostate development and the emergence and progression of prostate cancer. Ulla Simanainen (PhD, Finland) has joined the laboratory to study the AR and prostate function by applying innovative transgenic approaches to selectively disrupt AR function in defined cell types within the mouse prostate. We have created a model targeting AR in the prostate epithelium to explore the role of androgen in the development of structures fundamental to normal functioning prostate, as well as in prostate proliferative diseases of benign prostate hyperplasia and cancer that develop in later life. Our ongoing research will also investigate the influence of selective AR deprivation on long-term steroidal sensitivity of the prostate, noting that early hormonal exposure and deprivation may have long-range influences and essential roles in the subsequent development of prostate cancer later in life. Our research may provide new clues for targets for prevention, screening and/or treatment for prostate diseases including prostate cancer.
**Andrology**

**Androgens and the Testis**

The Department of Andrology is interested in researching all available avenues to help those men seeking fertility but also the development of safe effective male contraception.

**Gonadotrophin Replacement Therapy in Treatment for Male Infertility**

*A Idan, A Conway, DJ Handelsman*

Most causes of male infertility are unknown and consequently there are very few treatment with proven effectiveness in treatment of men unable to produce pregnancy in their wives. Gonadotrophin deficiency is the most effectively treatable cause of male infertility. The Andrology Department has published the largest and most detailed analysis of gonadotrophin treatment for this condition. It also was a major participant in the clinical registration studies for the new recombinant (genetically engineered) FSH hormone which is one of two key hormones necessary for treatment of gonadotrophin deficient men.

The other key hormone required for treatment of gonadotrophin-deficient men is human chorionic gonadotrophin (hCG). For the last 5 decades this has traditionally been produced by purifying urine from pregnant women but in recent years it has become possible to produce recombinant hCG commercially via genetic engineering. As this recombinant hCG remains under patent to a single multinational company who market it solely for use in IVF, despite the clinical need it has not been tested in men. To rectify this deficit, the Andrology Department has conducted the only studies of recombinant hCG in men aiming to discover the most effective manner to use it in men. Currently we are conducting a study to compare the effects of the new recombinant hCG with the older standard form of hCG purified from pregnancy urine. If as expected this proves the rhCG as safe and effective in healthy males as the conventional form of purified hCG, this may open the way for this newer form of treatment for men with gonadotrophin deficient and infertility as well as in boys with pubertal failure.

**Male Hormonal Contraception**

*L Turner, C Fennell, AJ Conway, PY Liu, M Jimenez, DJ Handelsman*

A major practical application of knowledge about how hormones control sperm production is the development of a male hormonal contraceptive. Following a decade of preliminary feasibility and path-findings studies, in 2003 the Andrology Department published a proof of principle study establishing very high reliability of a depot combined hormonal male contraceptive. Through many preliminary studies using a depot form of testosterone, we defined the lowest effective dose of testosterone having sufficient suppression but avoiding undesirable side effects and tested it with a progestin to identify the best combination. The excellent result for our prototype hormonal combination was a major advance and made international headline news. These path-finding studies have led progress in optimising the approach to develop a practical hormonal male contraceptive regimen. Currently, based on our 2003 study, we are extending our clinical experience with the combined depot approach in providing first medical male hormonal contraceptive service offered anywhere in the world. Furthermore, a major CONRAD and WHO sponsored international multicentre trial is using a similar injectable depot androgen-progestin combination to extend and refine the findings on contraceptive effectiveness for this “leading candidate” approach for a marketable male hormonal contraceptive.

**Hormonal Control of Sertoli Cell Function and Spermatogenesis**

*CM Allan, L Courcoran, J Spaliviero, M Jimenez, DJ Handelsman*

Collaboration: J Couse, K Korach (National Institute of Environmental Health Sciences, Research Triangle Park NC, USA) & M Griswold (Washington State University, Pullman USA); G Denyer (University of Sydney); P Stanton (Prince Henry’s Institute of Medical Research)

Reproductive hormones such as sex steroids and gonadotrophin proteins control testis development and sperm production (spermatogenesis). We have a major research focus (through external NHMRC-funding) on the functional development of Sertoli cells, vital cells that surround and nurture developing sperm cells. Our
research has contributed to fundamental understanding of the specific roles of key hormones and their receptors found in Sertoli cells (SC), which coordinate the complex hormonal responses required for spermatogenesis and normal male fertility. New genetic models were created to study the androgen receptor (AR) and its role in SC function, in particular the direct binding of AR to DNA (ie. target genes). The specific loss of AR DNA-binding function in SC revealed that genomic AR interaction is vital for sperm development. In this model, the expression levels of two SC androgen-regulated genes, Rhox5 and Eppin known to be important for full male fertility, were reduced in the pre-pubertal testis. However, in the adult testis, Rhox5 remained low whereas Eppin expression became elevated, revealing differential developmental control for distinct AR-regulated genes. Expression of a known androgen-repressed gene (Ngfr) showed maintenance of a non-classical AR pathway independent of DNA binding, however the incomplete spermatogenesis in this model suggests such pathways are secondary, or play no major independent role in SC function. Other genetic models have been established to study the role of SC AR during development, and will allow the dissection of the AR-regulated pathways essential for initiating normal spermatogenesis and male fertility.

Another key research interest (supported by an external ARC Discovery grant) is to determine the role of sex steroids, such as androgens (eg. testosterone), estrogens (eg. estradiol) and progestins in testicular development and function. We use genetic models deficient in sex steroids (hypogonadal hpg model) or specific hormone receptors such as the AR and estrogen receptors (ERs) to dissect specific roles and actions of these major steroids. Recent analysis showed that estradiol, the classic female sex steroid, can stimulate spermatogenesis in the hpg model, and requires the presence of ERalpha but not ERbeta. This rather paradoxical estradiol-induced spermatogenic response also involves follicle-stimulating hormone (FSH) secretion, and requires the presence of a functional AR. In combination, these research projects are increasing our fundamental knowledge of the underlying biological pathways that control (or inhibit) spermatogenic development. Such research is predicted to provide valuable genetic targets for therapy (eg. male infertility) or for the treatment of testicular tumours, or to develop novel strategies for male contraception.

Androgens, Ageing and Female Reproductive Physiology

Androgens and the Ovary

K Walters, CM Allan, DJ Handelsman in collaboration with L Salamonsen (Prince Henry’s Institute of Medical Research, Monash University)

Enhanced understanding of ovarian and uterine physiology and function is of great importance as infertility occurs in 1 in 6 Australian couples, with 50% attributable to female factors. Androgens are essential for male reproduction and traditionally are regarded as a defining characteristic of masculinity. However, in recent years, studies have shown that androgens can influence female reproduction. We and others have shown experimentally in mouse models, that androgen actions mediated by the androgen receptor (AR) have a previously unrecognized influence on female fertility. These may provide long overdue new insights into the basis of the timing of menopause and androgen associated female reproductive disorders such as polycystic ovary syndrome (PCOS), premature ovarian failure (POF), endometriosis, and uterine hyperplasia, a precursor of endometrial carcinoma.

Androgens and Post-testicular Control of Male Fertility

U Simanainen, K McNamara, E Gao, DJ Handelsman

Action of male hormones, androgens, is essential not only for maintenance of spermatogenesis, but also in the post-testicular control of fertility. So far, it has not been possible to dissect in vivo the role of androgens in post-testicular fertility due to the close relationship and high androgen dependency of spermatogenesis in the testis. We have created a mouse model with tissue-selective androgen receptor (AR) inactivation in prostate, seminal vesicle, epididymis and vas deferens, while the testis is unaffected displaying normal spermatogenesis and testosterone production. This model will provide novel, in vivo information of androgen action in post-testicular male fertility, with specific data on molecular mechanisms underlying the reduced function of androgen deprived, post-testicular glands.

The dichotomy of reduced sex accessory gland structure and functions with normal testis development and function provide a so-far unique opportunity to develop novel insight into the molecular determinants of androgen-dependent, post-testicular sperm functional maturation. This model could identify hitherto unexplained causes of male infertility as well as creating novel targets for development of post-testicular, male fertility regulation mechanisms. This new knowledge could make new inroads into the detection, diagnosis and treatment of unexplained male infertility as well as in developing new male-based, hormonally targeted but non-hormonal contraceptives (neo-hormonal) for both human and animal application.
Currently we are identifying the precise mechanism how the AR influences female reproductive physiology, notably in the ovary, brain and female reproductive tissues (ovary, breast, uterus). We have created a unique transgenic model whereby the AR gene has been selectively inactivated (ARKO), resulting in female mice functionally unable to respond to any androgens. Using this novel model Dr Walters has revealed defects in ovulation (Fig. 1) and late-stage follicle growth as the major contributors to the observed reduced fertility. Furthermore, more recent work provides strong direct evidence that as well as intra-ovarian AR-mediated actions, extra-ovarian AR-mediated functions also play a central role via neuroendocrine signalling in maintaining female fertility. In addition, we have shown a role for AR-mediated actions in the regulation of uterine growth and development, which may have important long-term functional consequences for hormone dependent uterine disorders such as endometrial hyperplasia and cancer. This work aims to further enhance our understanding of how androgens regulate female reproductive function, and unravel disruptions in androgenic mechanisms which may be involved in the establishment of androgen-associated reproductive disorders.

FSH and Female Reproductive Ageing

K McTavish, K Walters, DJ Handelsman, CM Allan

Collaborations: R Kalak, H Zhou, M Seibel, C Dunstan (Bone Biology, ANZAC)

In women, reproductive ageing (declining fertility) coincides with an accelerated decline in ovarian follicles (cells that contain the developing eggs). An early sign of reproductive ageing is increasing levels of serum FSH, which may occur several years prior to cessation of menstrual cycling (menopause). High FSH levels are associated with premature ovarian failure or onset of menopause, reduced ovarian reserve and reduced success of assisted reproduction. We established a unique transgenic mouse model with increasing levels of FSH and premature infertility. Current research (via NHMRC funding) employs this model to determine whether or not high FSH is a passive marker or actively contributes to reproductive ageing. Kirsten McTavish successfully completed her PhD investigating this high FSH expressing model, and is now a postdoctoral fellow with Prof Shunichi Shimasaki at UCSD (San Diego). This research showed that premature infertility due to elevated FSH occurs despite estrous cycling, follicle development and ovulation (similar to reproductive ageing in women), but appears not to be linked to early depletion of the non-renewable ovarian follicle pool. Ongoing research is investigating the effects of high FSH on the ovarian follicle reserve. Premature infertility in transgenic FSH females was due to reduced embryo-fetal survival, which can be rescued using pharmacological (anti-progesterone) or genetic (AR-deficiency) approaches showing elevated FSH disrupted progesterone-androgen signalling pathways. Higher levels of transgenic FSH in another line produced earlier infertility as well as ovarian cysts. Thus, our transgenic FSH model provides a valuable opportunity to study female reproductive ageing, gonadotrophin-induced hyper-stimulation and ovarian dysfunction.

Recent research has also focussed on the role of FSH in bone loss, after the recent but controversial proposal that elevated levels of FSH can induce bone loss in ageing hypogonadal women, a major problem in our ageing population. Our recent work has studied age-related changes to bone structure and dynamics in our transgenic FSH female mouse models. This work suggests that increased FSH alone does not directly stimulate overall bone gain or loss but depends on complex ovarian-dependent mechanisms to influence overall bone dynamics. Continued analysis of these models has major clinical relevance to the onset of age-related diseases (eg. osteoporosis) associated with loss of ovarian function (eg. estradiol deficiency) due to menopause.
**Group Leader:** Professor David Le Couteur

**Scientists:** Dr Victoria Cogger, Dr Alessandra Warren, Dr Aisling McMahon, Dr Svetlana Zykova, Dr Dmitri Svistounov, Dr Mimi Sabaretnam, Vicky Benson, Jennifer O’Reilly, Samantha Solon, Professor Robin Fraser.

The Biogerontology Laboratory in the ANZAC Research Institute is the laboratory component of the Centre for Education and Research on Ageing (CERA) at Concord Hospital. The Biogerontology Laboratory performs research into the biology of ageing and age-related diseases. Our motivation is to develop strategies to delay ageing and age-related disease, thus improving the quality of life of older people.

**Ageing Biology and the Ageing Liver**

Old age is the main risk factor for disease and disability. Our research studies the effects of ageing and disease on the hepatic microcirculation. We discovered that with advancing age there are major changes in the liver microcirculation that we called pseudocapillarization. These changes influence the liver metabolism of lipoproteins, thereby providing an explanation for why old age is the major risk factor for cardiovascular diseases such as heart attacks and strokes. Currently we are working towards therapies that prevent or reverse these age-related changes in the liver microcirculation and we believe will have a dramatic impact on the prevalence of vascular disease in older people. This work involves an NHMRC-supported drug discovery programme in collaboration with the Eskitis Institute.

In addition, we are studying other factors that link the ageing liver with age-related diseases, such as diabetes mellitus, apolipoprotein E, caloric restriction and the sirtuin pathways. We are also studying the effect of a severe premature ageing disease, called Werners syndrome in transgenic Werners mice.

**Ageing Biology, Diet and Sirtuins**

Diet has a profound effect on ageing. The ageing process can be markedly delayed by caloric restriction and by altering the ratio of protein to other dietary constituents. These effects are in part mediated by a cellular switch called sirtuins. We are studying the blood samples from CHAMP (Concord Health and Ageing in Men Project) to determine whether changes in sirtuins are associated with frailty, ageing and death. In collaboration with David Sinclair and Rafael de Cabo in the USA, we are studying the role of sirtuins in the ageing liver. In collaboration with Steve Simpson we are studying the effects of different protein dietary regimens on the ageing process in mice. We have just gained a new NHMRC grant to escalate the study of dietary protein and ageing in humans. These studies will provide new targets for delaying ageing and age-related disease.

**Highlights for 2008-2009 include:**

- Our group were involved in five successful new NHMRC grant applications during this period, including two grants studying ageing and the liver, and two grants studying the effects of diet and sirtuins on ageing in mice and humans.
- We were invited to contribute the chapter on fenestrations to the leading international book on the liver (Arias et al, The Liver: Biology and Pathobiology 2009) as well as generating numerous scientific publications in international journals. We were invited to present our discoveries on ageing and the liver endothelium at a plenary session of the American Association of Anatomists, FASEB annual conference in the USA.
- There were three PhD students who completed theses in our laboratory: Dr Rajkumar Cheluvappa, Dr Mimi Sabaretnam and Dr Hamish Jamieson.
- We developed successful new international collaborations with Professor Bard Smedsrod (Norway), Professors de Cabo and Sinclair (USA) and Dr Lebel (Canada). The Norway collaboration has led to a successful EU grant to support this collaborative research. In addition, two senior medical post-doctoral scientists, Dr Svetlana Zykova and Dr Dmitri Svistounov have joined our laboratory for a one year sabbatical to further their studies on ageing and the liver microcirculation.
A Scanning electron micrograph showing a Kupffer cell travelling through a liver sinusoid.

A Scanning electron micrograph of the liver. A large blood vessel lies next to the intricate network of liver sinusoids, which perfuse the liver with blood.

A Scanning electron micrograph of the liver sinusoidal lining. The endothelial cells perforated with many fenestrations.

Immunofluorescence studies of apoE (red) and tubulin (green) in hepatocytes isolated from a young rat. The nucleus is shown in blue.

Immunofluorescence studies of actin (red) and golgi (green) in hepatocytes isolated from a young rat. The nucleus is shown in blue.
Group Leader: Professor Markus J. Seibel

Senior Scientists: Dr Hong Zhou

Staff and Students: Dr Robert Kalak, Dr Yu Zheng, A/Prof Colin Dunstan (associated), James Modzelewski, Janine Street, Colette Yee, Mystie Mak, Li Laine Ooi, Holger Henneicke, Agnes Weber, Anastasia Mikuscheva, Shaoxin Yu, Julian Pavey.

Visiting Fellows: Dr Markus Herrmann, Saarland University, Homburg, Germany, Dr. Cornelia Spiess, Humboldt University Berlin, Germany, Professor Martina Heer, German Aerospace Centre, Cologne, Germany.

The Bone Research Program pursues research in Basic Bone Biology, Applied Bone Metabolism and Clinical Research in Metabolic Bone Disease. In addition, our laboratory has a strong interest in the development and evaluation of transgenic models of bone disease.

In 2008/2009, the program has supported postgraduate and doctoral studies of Yu Zheng (completed in April 2008), Mystie Mak (under review), Laine Ooi, Agnes Weber (Humboldt University Berlin), Anastasia Mijuseva (Humboldt University Berlin), Holger Henneicke (Humboldt University Berlin) and Shaoxin Yu (Shanghai Jiao Tong University). Julian Pavey participated as undergraduate summer student.

In addition, we had the opportunity to build productive scientific partnerships and collaborations with international researchers: Prof Frank Buttgerie, Humboldt University Berlin, Germany, Prof Di Chen, University of Rochester, NY, USA, Prof Paul Stewart and Dr Mark Cooper, University of Birmingham, UK, Prof Yungjun Wang, Shanghai University of Traditional Chinese Medicine, PRC, and Prof Wim van Hul, University of Antwerp, Belgium. These collaborations have in the past lead to important publications and successful grant applications, including NHMRC Project Grants.

Further collaborations with Australian groups include those of Prof. Phil Sambrook, RNSH, Sydney; Prof. John Eisman and Dr Paul Baldock, The Garvan Inst of Medical Research, Sydney, Profs Bruce Armstrong, Rebecca Mason, Robert Cumming, David Handlesman and Arthur Conigrave, The University of Sydney, Prof. John Wark and Terrence O’Brian, The University of Melbourne, Dr Tania Winzenberg, The University of Tasmania, Prof Chris Nordin, The University of Adelaide, Dr Robert Day, Medical Engineering & Physics, Royal Perth Hospital. We have also established co-operative industry links through research partnerships with Amgen, Sanofi-Aventis (USA and Australia), MSD Merck, Sharp & Dohme (Switzerland, Germany, Australia), Roche Pharmaceuticals (Switzerland, Australia), Novo Nordisk (Switzerland), Servier (France, Australia) and Novartis Pharma (Australia).

Our ongoing research is supported through funding from within Australia and overseas. With our collaborators, we have current and future funding to a total value of over $6,000,000, including seven NHMRC project grants.

Our group is well represented at national and international scientific meetings (e.g. American Society for Bone and Mineral Research, European Society for Calcified Tissue; Australian and New Zealand Bone and Mineral Society; Cancer and Bone Society and others). At all of these meetings, our group had multiple oral presentations, reflecting the high standard and international recognition of our research. This year, our group has seven oral presentations at international conferences and received the “ASBMR Young investigator award” of the American Society of Bone and Mineral Research.

Our plan is to further develop our comprehensive research program, making use of the multi-disciplinary opportunities provided by the ANZAC Research Institute, and to intensify our collaborations with both basic and clinical research groups locally and around the world.

Following is a short description of our current research projects.
The Role of Glucocorticoids in Bone Metabolism

H Zhou, R Kalak, M Mak, C Spiess, J Street, C Yee, C Dunstan, MJ Seibel

Glucocorticoids have been of great benefit to countless patients suffering from diseases such as rheumatoid arthritis, asthma, inflammatory bowel disease and malignancies, or who have undergone organ transplantation. It is, however, well known that glucocorticoids may also exert deleterious effects on bone causing osteoporosis.

The Bone Research Program investigates the effects of glucocorticoids on bone using novel transgenic mouse models. One of these models is characterised through a transgene that results in a local inactivation of glucocorticoids in the bone forming cells, the osteoblasts, by directing these cells to produce an enzyme known as 11beta hydroxy-steroid dehydrogenase, normally found in the kidney. Using this and other genetically modified mouse models, we are currently working on the following research projects:

The Role of Endogenous Glucocorticoids in Bone Development

H Zhou, M Mak, R Kalak, J Street, C Yee, X Shao, C Dunstan, MJ Seibel

We have discovered a novel mechanism by which glucocorticoids regulate mature osteoblast in their control of mesenchymal progenitor lineage commitment through Wnt signalling (Zhou et al J Biol Chem 283: 1936-45, 2008).

Furthermore, we have identified a delay in the development of the skeleton in newborn mice and determined that glucocorticoid signalling in osteoblasts is required for normal development of calvarial bone structures (Zhou et al. Development 136: 427-436, 2009).

In a current NHMRC funded project, we are investigating the interaction of glucocorticoid and Wnt signaling in osteoblasts controlling mesenchymal lineage commitment. In the long term, we hope that these studies will point the way to strategies for the prevention of the detrimental effects of cortisone on bone.

The Role of Endogenous Glucocorticoids in Immune Arthritis

H Zhou, F Buttgereit, R Kalak, C Spiess, J Street, C Dunstan, MJ Seibel

Synthetic glucocorticoids (GC) are of great importance in the treatment of rheumatoid arthritis (RA) and other inflammatory rheumatic diseases. However, the role of endogenous GC action in contributing to the susceptibility and/or severity of RA is unknown. With our collaborators led by Prof Frank Buttgereit at Humboldt University, Berlin, Germany, we investigated the effect of osteoblast-targeted transgenic disruption of GC signalling on joint inflammation and bone catabolism in the serum transfer model of autoimmune arthritis. We made the surprising observation that arthritis was attenuated in the transgenic mice, indicating that endogenous glucocorticoids modulate inflammatory responses through direct effects on osteoblasts and pointing to a central role of local endogenous GCs in arthritis (Arthritis & Rheum 60:1998-2007, 2009).

In ongoing studies, we are investigating the mechanisms involved in the attenuation of arthritis, which may point to novel strategies for the treatment of autoimmune arthritis.

Changes in Bone and Fat Metabolism Induced by Exogenous Glucocorticoid-Induced

H Hennecke, M Herrmann, R Kalak, J Street, C Dunstan, H Zhou, MJ Seibel

The bone-related effects of exogenous glucocorticoids at pharmacological levels are of major research interest. Continuous glucocorticoid delivery at a constant rate is a major requirement for this research. We have developed a method of long-term glucocorticoid treatment that enables us to deliver a sustained pharmacological dose of corticosterone, the major glucocorticoid in mice (Steroids. 74:245-9, 2009). Using this method in our transgenic mice, we found that exogenous glucocorticoid-induced bone loss could be prevented in these mice. We also found, that the transgenic mice lacked the body fat deposits normally seen during high-dose exogenous glucocorticoid treatment. These findings indicate that osteoblasts are an important cellular target for exogenous glucocorticoids, mediating not only the deleterious effects of glucocorticoids on bone but also those on fat metabolism. This work has been accepted as two oral presentations at ASBMR conference in Denver, US this year. We will utilise these transgenic mice to identify the mechanisms that govern the changes in bone and fat metabolism induced by exogenous glucocorticoids.
BONE RESEARCH PROGRAM

Preventing the Spread of Malignant Tumours to Bone


Breast cancer and prostate cancer each have a particular preference to form secondary tumours (metastases) in bone. Breast cancer in bone is associated with bone destruction that frequently results in significant pain and disability. Prostate cancer cells in bone induce high rates of bone formation and bone resorption, resulting in disorganisation of bone structure and severe pain. In both cancers, tumour cells grow in bone and induce normal bone-resorbing cells of the bone marrow to destroy the surrounding bone. It has been proposed that destruction of bone releases factors that help cancer cells grow faster, thus creating a vicious cycle that contributes to the serious consequences of bone metastases.

In this study, we are studying mice with transplanted breast cancer cells to understand what makes the bone marrow a receptive site for breast cancer metastasis. We are manipulating bone remodelling rates in mice see how this impacts the ability of circulating cancer cells to target bone and to establish destructive tumours there.

To date, we have determined that anti-resorptive treatments inhibit tumour growth in bone indirectly through effects on osteoclasts, rather than directly through effects on tumour cells (Zheng et al. Bone 2007). After discovering that increasing bone resorption through a low calcium diet enhances breast cancer metastasis to bone in mouse models (Zheng et al, Cancer Res 2007), we are now investigating how vitamin D deficiency affects the growth of breast cancer metastasis to bone. It appears that low Vitamin D levels enhance human breast cancer growth in the bone of mice through both indirect and direct effects. This may have clinical implications as vitamin D deficiency contributes to the serious consequences of breast cancer metastasis.

Effects of FSH on Bone Structure and Metabolism

R Kalak, C Allan, H Zhou, C Dunstan, DJ Handelsman, MJ Seibel

In collaboration with Dr Charles Allan and Prof David Handelsman (Andrology), we are studying the phenotype of female transgenic mice overexpressing human FSH. We have determined that these mice develop high bone density. This study shows for the first time an apparent anabolic effect of human FSH on mouse bone. Further studies are planned to investigate in more detail the mechanism for the bone changes in these mice. The principle ideas behind this research have been outlines in a letter to Cell (Seibel et al., Cell, 127: 1079. 2006).

Study into the Genetic Determinants of Bone Loss and Osteoporosis in an Affected Family

M Kozlowska, C Meier, W vanHul (Belgium), MJ Seibel

Osteoporosis is a common multifactorial disorder of reduced bone mass. Osteoporosis treatments are currently limited in terms of efficacy and drug classes available. Identification of new therapeutic targets is a high priority. Although multiple environmental factors are involved in the pathogenesis of osteoporosis, genes also play a major role as reflected by heritability of many components of bone strength. The common form of osteoporosis is generally considered to be a polygenic disorder arising from the interaction of common polymorphic alleles at many loci. However, a few recent publications have reported a major gene pattern of BMD inheritance in several ethnic populations. Identification of major genes contributing to osteoporosis would be valuable for assessment of risk in individual patients.

In collaboration with Prof Wim van Hul, University of Antwerp, Belgium, we are currently studying a large family with an autosomal dominant inheritance pattern of low bone mineral density. We have obtained DNA samples and clinical data from this extensive family and are examining the results to determine the best approach for identification of candidate genes.

Studies on Biochemical Markers of Bone Metabolism

J Modzelewski, MJ Seibel

All metabolic bone diseases are characterised by changes in bone formation and in bone re-absorption, the two major processes that keep bone alive, healthy and strong. Measurement of specific ‘bone markers’ in serum and urine determines the activity of these processes and the results of these simple tests can help the clinician assess the severity, and monitor the treatment of bone diseases such as osteoporosis.

Although these “bone markers” have been developed only recently and are still being refined, they are already widely used amongst clinicians worldwide. Led by Markus Seibel, we are focusing on the development and experimental and/or clinical validation of novel or improved markers of bone turnover.

Present studies focus on the evaluation of bone turnover in the very elderly (with Philip Sambrook, RNSH), the effect of androgens on male bone health (with David Handelsman, Andrology), the effect of anti-epileptic drugs and smoking on bone turnover (with John Wark, University of Melbourne), and other topics.
BONE RESEARCH PROGRAM

Studies into the Influence of Serum Testosterone Levels and its Longitudinal Changes on Different Target Tissues of Androgen Action

C Meier, M Jimenez, J Modzelewski, DJ Handelsman MJ Seibel

In men, serum testosterone levels decrease progressively with ageing. Changes seen with ageing (such as decreased bone mass and decreased muscle strength) are also seen in individuals with hypogonadism. Hence, diminished testosterone levels have been associated with a variety of chronic conditions in elderly men, and formed the basis for trials investigating the effects of androgen replacement therapy in elderly men with partial androgen deficiency.

However, the impact of different degrees of androgen deficiency on age-related conditions remains unclear and, specifically, the influence of longitudinal changes in serum testosterone on the occurrence of androgen-related diseases is unknown. This includes the effect of partial androgen deficiency on musculoskeletal measures (i.e. fractures, rate of bone loss, muscle strength), quality of life and overall mortality.

In collaboration with John Eisman (Garvan Institute), we are studying the large population of elderly men in the Dubbo Osteoporosis Epidemiology Study. This project, assessing the impact of androgens on men’s health, will help us to understand the physiological role of sex hormones in elderly men and could lead to more effective treatment of osteoporosis in men. A first study, on the relationship between serum sex hormone levels and fracture risk, has shown that circulating testosterone but not oestradiol levels are associated with incident fractures in older men.

Awards:

Best Abstract Award: 18th Australian & New Zealand Bone & Mineral Society (ANZMBS) annual Scientific Meeting, Melbourne, Australia, to Robert Kalak, 2008, $1,000

Chunhui Plan Award: The Ministry of Education-funded. organization, Ministry of Education, China, to Hong Zhou, 2008

Concord Clinical Week Research Award: Concord Hospital, NSW, to Holger Henneicke, 2008

ASBMR Young Investigator Award: 30th Annual Meeting of the American Society for Bone and Mineral Research (ASBMR), Denver, USA, to Li Laine Ooi, 2009

University of Sydney Short Term Visiting Fellowship, to Dr. M Cooper (Sponsor: M. Seibel) 2009

Highlights:

Hong Zhou, Invited International speaker, Western China Health and Environment Forum, Yinchuan, China September 4-8, 2008.


Micro-CT analysis of 6 month old female mouse bone:

The bone mass is dramatically increased in one of our genetic modified transgenic mouse line compare to their non-transgenic (wild type) littermates.
Group Leader: Professor Peter Maitz

Scientists: Dr Zhe Li, Dr Yiwei Wang and Kate Nieuwendyk

Co-investigators & Collaborators: Dr Alex Phoon, Sue Taggart, Dr Alaina Taylor, Dr Peter Kennedy, Dr Peter Haertsch, Dr John Harvey, Dr John Vandervord, Dr Anthony Weiss, Jelena Rnjak, Jessica Almine, Amy Lee, Dr Clive McFarland and Dr David Millis

The group researches all aspects of Burn Care and specialises in tissue engineering of 3 dimensional skin substitutes for sear burns patients. Cultured Epithelium Autografts (CEA) is a well established technique to create large numbers of skin cell for resurfacing of wounds. Unfortunately these cultured cells do not have the same physical properties as normal human skin cells as they are missing the interaction with deeper tissue layers.

Our laboratory is committed to improve the cultured skin autograft technology by developing three-dimensional dermal substitutes and skin equivalents for treating deep burn wounds. Using technologies including tissue culture, cell biology, molecular biology and, cellular and tissue engineering, we have been trying to produce different biological scaffolds that are biologically compatible, safe and suitable for skin cells to attach and grow. The scaffold could be used for repairing the damaged dermal bed or for engineering autologous skin substitute with skin structures comparable to normal human skin, which includes epidermis, dermal components, pigment cells and microvascular vessels under laboratory conditions. The research and development of tissue-engineered scaffold, dermal and skin equivalents will benefit not only the burns patients but also the patients with other skin defects such as chronic, diabetic and pressure skin ulcers.

A Randomized Multi - Centered Trial to Evaluate Efficacy and Safety of Cultured Epithelial Autografts (CEA) in Combination with a Meshed (4:1) Split Skin Graft (SSG) after Debridement of a Burn Wound.

P Maitz, Z Li, K Nieuwendyk, J Harvey, J Vandervord, S Taggard, P Kennedy

Thin split thickness skin biopsies are taken under sterile conditions and transported to the Concord Skin Laboratory where the biopsies are processed. A piece of thin-split skin biopsy (about 4 cm²), taken from the available donor site under sterile condition, will be transported in biopsy transport medium to Skin Laboratory at Concord Hospital. Keratinocytes will be isolated from the separated epidermis following enzymatic digestion. The cells will be seeded into two cell culture flasks and cultivated under established laboratory condition. The cells in one flask will be allowed to grow and differentiate into cultured epidermal autograft (CEA) sheet while the cells in another flask will be maintained at sub-confluent phase for preparing CEA suspension.

Prior to surgery the patient will undergo a Laser Doppler on the burn that will be in the study to diagnose depth.

The suspension will be randomly allocated to syringe A or B with the control syringe containing only transport media. On the day of surgery, both CEA sheet and suspension will be harvested under sterile condition one hour before the surgery starts, labelled and then transported to the operating room in an esky with an ice brick.

On operation day (day 0) the burn wound will be debrided and a meshed SSG (4:1) will be applied and secured. Children will be in a separate study group and a suitable mesh size will be chosen by the surgeon. Four 10cm x 10cm window dressings (Surfasoft®) will then cover the SSG. Syringe A and B and a CEA sheet will then be applied to three of the windows and the forth will receive no additional treatment. The wounds will then be covered by a piece of Urgotul® (except the graft with the CEA sheet as Urgotul® is all ready in situ as the carrier dressing) and Surfasoft® secured dressings as per protocol. The dressings will remain intact for 5, days and assessed/redressed until healed. Scarring will then be monitored at 26 weeks and finally at 52 weeks.

A Clinical Evaluation of Efficacy and Safety of Cultured Epithelial Autograft (CEA) Suspension Applied to a Donor Site on a Burn Injured Patient.

P Maitz, P Kennedy, Z Li, S Taggart, T Leong, K Nieuwendyk.

A patient with severe burn usually needs skin grafting, a surgical procedure that involves transplanting split skin grafts harvested from healthy donor site to wound area.
The management of the donor site is, therefore, a very important issue in severe burn patient care. Rapid healing allows the repeat use of the same donor site in patients with large burns. But any delay in donor site healing could lead to complications such as infection and compromise the recovery process of burns patients. This study is designed to examine if the delivery of cultured autologous keratinocytes to donor site wound could facilitate or speed up its healing process.

Burn patients with a donor site ≥ 2% total body surface area will be recruited to join the trial subjecting to informed consent. The two donor sites of each patient will be divided into CEA group and control randomly. Participants will consent to a skin biopsy from which keratinocytes will be isolated and cultivated in Skin Laboratory at Concord Hospital. On operation day, the cultured keratinocytes will be harvested and spray-delivered to the donor site in CEA group while control site wound receive control vehicle solution only.

Evaluation of wound healing will occur by various methods including the measurement of evaporative water loss on different days post surgery and on each dressing change until the donor site has fully reepithelialized. Data will be analysed statistically to determine the effectiveness of cultured CEA suspension in donor site healing.

Skin Repair: Tissue Engineering using Synthetic Elastin
J Rnjak, Z Li, P Maitz, AS Weiss

Synthetic human elastin is among a range of bioengineered materials aimed at mimicking native host connective tissue. Synthetic elastin scaffolds (Fig 1), produced by chemically cross-linking recombinant human tropoelastin, and is a logical choice for a skin substitute matrix.

Synthetic human elastin has the potential to overcome difficulties associated with other matrices including animal-derived collagen or irradiated cadaver-derived dermis, as it is a human protein, and therefore not expected to be rejected. An additional benefit is that it is recombinant and therefore not extracted from humans, eliminating the risk of contamination, especially with agents that are difficult to eradicate such as latent viruses and prions.

The current project aims to grow human skin cells on synthetic human elastin scaffold (both sheets and electrospun 3D structure) in an attempt to develop an autologous skin substitute for treatment of burns injury.

Identifying the Diffusible Factor(s) Produced by Skin Cells Grown on Tropoelastin Scaffolds
J Almine, Z Li, P Maitz, AS Weiss

The main aim of this project is to study the cell-scaffold interaction and identify the diffusible factor(s) produced by skin cells cultured on the scaffold, which promotes cell proliferation and possible keratinocyte differentiation. Identifying the diffusible factor(s) responsible for the proliferation of keratinocytes and fibroblasts would be important progress in the treatment of burns and the development of a suitable skin graft. The treatment of burns patients involves the rapid coverage and closure of the wounds, which is dependent on cell proliferation and differentiation, ultimately re-establishing the epidermis and dermis. This process can be facilitated by the addition of a diffusible factor(s); consequently achieving rapid wound closure, reducing the chance of infection and re-forming skin with minimal scarring.

Skin Tissue Engineering Using a Biodegradable Polymer
D Martínez Tobón, A Taylor, P Maitz, Z Li.

Engineered skin substitutes, resembling natural human skin structure and containing living skin cells, would provide excellent alternatives for severe burn wound management.

The aim of this study is to construct a bioactive, hybrid scaffold that is biodegradable, biocompatible and porous in structure to support skin cell growth. This project is designed to develop a composite using collagen, and FDA-approved biodegradable polyester, polycaprolactone. The scaffold will be used to generate 3D skin substitute under laboratory condition. More importantly, the scaffolds will be made bio-active containing protein factors to facilitate wound healing.
Porous bio-scaffolds are developed by lyophilization technique (Fig 2) or fabricated by electrospun nano-fibres (Fig 3).

The aims of this study are therefore to establish a mouse model to assess the role of engineered skin products or dressings in wound healing. The animal host response of each mouse as the recipient of skin products or dressing materials will also be examined at cellular and molecular levels. This study will provide significant information on the efficacy and safety of laboratory-developed bio-scaffold, skin substitutes and dressing materials.

Efficacy and Safety of Engineered Skin Substitute and Dressing Materials on Skin Wound Healing: A Mouse Model Study

Z Li and K Nieuwendyk, J Rnjak and P Maitz

Lack of autologous skin graft is always a major issue in treating patients with large and deep burns injuries. Clinically, it is still quite often to observe delayed wound healing, which could lead to wound infection, scar development, deterioration of patient’s well-being and even death.

Cultured autologous skin cells or substitutes are emerging as an important alternative for wound coverage and closure. The advance in biotechnology has enabled us to grow different types of skin cells and skin substitutes by skin tissue engineering technology in our laboratory. Skin tissue engineering involves using different biomaterials such as recombinant collagen and elastin or bio-compatible polymers as porous scaffolds to support skin cell attachment, growth and differentiation into skin tissue. Various wound dressing material and dressing regimes are also designed in our laboratory in an attempt to provide favourable growth condition for cultured skin cells and to speed up the wound healing process. Wound healing is a very complicate process in which host factors and metabolisms play critical role. Although the engineered skin looks structurally similar to normal human skin containing epidermal and dermal layers, the bio-safety and efficacy of engineered skin and wound dressing products will need to be tested in an animal model before proceeding to further clinical trial.

The mechanisms of bacterial wound invasion and burn wound sepsis, and therefore help the management of burn wound.

Biofilm and Infection of Burn Wound

P Kennedy, S Brammah and E Wills

One of the most significant problems in burn care is that of infection. Following a burn injury the defensive mechanisms of the skin are impaired or destroyed and colonization by micro-organisms rapidly occurs. Many of the micro-organisms commonly found on the burns wound are known to produce biofilms, a collection of organisms attached to a surface and surrounded by matrix containing polysaccharides known as extracellular polymeric substances (EPS).

Biofilms are the cause of significant morbidity and mortality in relation to implanted medical devices and septic complications associated with indwelling intravenous catheters. The organisms within biofilms are well known to develop resistance to antibiotics and to the immune system.

It is estimated that two third of all chronic disease are biofilm related. Biofilm formation (Fig 4 and Fig 5) in burn wounds has not been thoroughly examined. This ongoing study will help to understand the mechanisms of bacterial wound invasion and burn wound sepsis, and therefore help the management of burn wound.
Group Leader: Professor Stephen Clarke
Senior Scientists: Assoc Professor Graham Robertson, Dr Kellie Charles, Dr Patsie Polly

Staff and Students: Phillipa Camilleri, Candice Clarke, Dr Wei Chua, Anthony Corradin, Haryana Dhillon, Dr Michael Evtushenko, Chantal Gebbie, Dr Lucy Jankova, Dr Marina Kacevska, Dr Stephen Kao, Melissa Lloyd, Marko Matic, Melissa Moore, Anthoulla Mohamudally, Arran Painter, Dr Viet Phan, Dr Jane Reid, Dr Anneliese Rittau, Angie Shum, Cindy Tan, Ryland Taylor, Lili Truong, Dr Maria Tsoli, Dr Janette Vardy, Catherine Xu, Mark Baker - APAF; Pierre Chapuis, Les Bokey, Owen Dent, Tsoli, Janette Vardy, C Xu, [Mark Molloy, Matt Mackay & Mark Baker - APAF; Pierre Chapuis, Les Bokey, Owen Dent, Charles Chan Caroline Fung & Betty Lin - Depts of Surgery & Pathology, CRGH].

The Cancer research group has successfully established itself at ANZAC, following the appointment of Prof Stephen Clarke to the Chair of Medicine. Since joining three years ago, the team has significantly increased cancer research activities on the Concord campus in multiple areas. These include clinical trials of new cancer treatments, nutritional and psycho-oncology research and the establishment of a molecular-based cancer pharmacology laboratory. In addition, a strong collaboration with the Australian Proteome Analysis Facility at Macquarie University has enabled our scientists to search for new biomarkers for Colorectal cancer. This has led to a successful Cancer Institute NSW translational program grant for $3.75 million over 5 years. The appointment of Prof Andrew McLachlan (Faculty of Pharmacy, Uni of Sydney) to the Chair of Geriatric Pharmacy on the Concord campus strengthens the pharmacokinetic and analytical expertise required for clinical drug studies in cancer patients. Recently Dr Kellie Charles rejoined the group as a Senior Scientist after 4 years Post-Doctoral Training in London.

Colorectal Cancer Biomarker Studies and Clinical Trials

Stephen Clarke, Haryana Dhillon, Chantal Gebbie, Luc Jankova, Jane Reid, Graham Robertson, Lili Triuong, Maria Tsoli, Janette Vardy, C Xu, [Mark Molloy, Matt Mackay & Mark Baker - APAF; Pierre Chapuis, Les Bokey, Owen Dent, Charles Chan Caroline Fung & Betty Lin - Depts of Surgery & Pathology, CRGH].

In collaboration with the Australian Proteome Analysis Facility, many potential protein biomarkers have been identified that will provide better assays for diagnosis and prognosis as well as help to predict the response of colorectal cancer patients to anti-cancer agents. Such biomarkers will guide the development of individualised treatment regimes which will take into account the variability in efficacy and toxicity to drugs experienced by many cancer patients. In addition some biomarkers will be used to identify patients at risk of developing the muscle wasting associated with the cancer cachexia syndrome. Medium throughput mass spectrometry-based assays have been developed to assess the utility of these proteins before high through-put screening using the Concord Colorectal tissue and data banks collected by Departments of Surgery and Pathology, CRGH. Immuno-staining for the presence of specific proteins in colorectal tumours using tissue microarrays have enabled validation of potential biomarkers for colorectal cancer. We have that the proteins fascin and GST-pi are prognostic markers for survival while maspin did not show an association with clinical outcome despite previous reports for many cancers including colorectal.

Concord has become a major Australian centre for clinical trials in colorectal cancer patients with particular emphasis on the angiogenesis inhibitor bevacizumab. In nutritional cancer research, we have evaluated the prognostic value of nutritional assessments and demonstrated that patients with advanced colorectal cancer and a poor nutritional status have a shorter survival than well nourished patients. Studies into the cognitive function and fatigue in cancer patients after chemotherapy will be carried out by oncologist Janette Vardy. In psycho-oncology research, among other projects, we are assessing whether education and counselling might improve end of life decision making.

Cancer Pharmacology and Cachexia

The focus of the cancer pharmacology laboratory is to explain inter-patient differences in response and toxicity to anti-cancer drugs. The treatment of cancer patients with drugs is difficult due to the fine balance between killing tumour cells and causing toxicity to normal cells. Therefore the huge variability between patients in clearance of anti-cancer agents has a significant impact on the success of chemotherapy. Anti-tumour action may be lost if the drug is cleared too rapidly, while slow drug excretion may lead to extreme toxicity. A better understanding of the source of this variability should lead to improvements in the manner in which chemotherapy is administered and would represent a welcome advance for cancer patients.

Cancer cachexia is experienced by up to 80% of all cancer patients and involves muscle wasting and depletion of fat reserves. It is directly responsible for the death of 30% of cancer patients. A better understanding of the complex factors responsible for cancer cachexia would help to identify those patients who will be susceptible to developing cachexia as well as better management of this debilitating condition.
Do Tumour-Derived Cytokines Repress Drug Clearance in the Liver?

Stephen Clarke, Marina Kacevska, M Matic, Arran Painter, Viet Phan, Graham Robertson, Anneliese Ritau, Prof Andrew McLachlan, Faculty of Pharmacy, USyd

The rate of breakdown and elimination of drugs from the body is largely determined by the levels of enzymes called cytochrome P450s (CYPs) in the liver as well as specific drug transporters which move drugs in and out of cells. In humans CYP3A4 is responsible for the disposal of more than half of all drugs including many important anti-cancer agents. Clinical studies carried out by our group found that CYP3A4 levels are reduced in some cancer patients, leading to greater toxicity. The source of repressed hepatic CYP3A4 levels appears to be linked to tumour-derived cytokines. Therefore a major goal of our research is to study the links between cytokines released by tumours and down-regulation of drug clearance pathways in the liver. Ultimately we hope to be able to predict which patients will suffer toxicity and to develop anti-inflammatory treatments that will normalise drug handling and improve patients’ response to anti-cancer drugs.

As it is difficult to study these processes in the livers of patients, we created a transgenic mouse model of human CYP3A4 regulation. Using these mice we have carried out experiments to analyse the signalling pathways and molecular mechanism involved in mediating the inflammatory response of the liver to tumours. We have found that this process is linked with the growth of several different cancers, including melanoma, breast, colon and sarcoma, indicating that this may be a general feature of many different cancers. In addition to repression of CYP3A metabolism, hepatic drug transporters for several important anti-cancer drugs are also switched off in the presence of cancer, leading to even slower clearance of drugs from the body and greater toxicity. In collaboration with APAF (Macquarie University) we have carried out extensive proteomic profiling and found that all aspects of drug clearance pathways are altered, including many CYP and phase II enzymes and drug transport proteins. Pharmacokinetic and biodistribution studies are underway to assess the impact of these changes on clearance of anti-cancer drugs and probe reagents.

Detailed analysis of cytokine signaling cascades and nuclear receptors which control metabolic pathways has shown that there is crosstalk between IL-6 and impaired nuclear receptor action. The use of mouse tumour models has enabled us to perform pre-clinical testing of anti-cytokine interventions aimed at normalising drug clearance. In preliminary experiments we have found that using antibodies to IL-6 has partially restored the levels of CYP3A.

Ethnic Differences in Drug Clearance.

Stephen Clarke, Viet Phan, Anneliese Ritau, Cathy Xu, [Prof Prof Andrew McLachlan - Faculty of Pharmacy, University of Sydney, Prof Micheline Piquette-Miller, University of Toronto]

Compared to Caucasians, cancer patients from an Asian background have greater difficulty tolerating chemotherapy and suffer from more adverse events due to toxicity. Clinical studies are being carried out in breast and lung cancer patients to examine the genetic differences (single nucleotide polymorphism or SNPs) in genes involved in drug metabolism which may be related to altered clearance of anti-cancer drugs. Pharmacokinetic analysis of commonly used chemotherapy drugs such as paclitaxel and doxorubicin are being developed to determine the rate at which they are eliminated from the body. The inter-patient and ethnic differences in drug clearance will be correlated with genetic differences and toxicity.
CANCER PHARMACOLOGY

Cancer Cachexia, Cytokines and Altered Metabolic Pathways?
Stephen Clarke, Dan Gardon, Lucy Jankova, Marina Kacevska, Patsie Polly, Graham Robertson, Maria Tsoli, Ryland Taylor, Anthony Corradin, Marko Matic, Phillipa Camilleri, Angie Shum. [Mark Molloy - APAF; Edna Hardeman - UNSW; Frances Sladek Uni of California, Riverside]

Cancer cachexia is a complex condition involving disturbances in energy balance and metabolism in several organs of the body. The release of cytokines into the blood by tumours is a likely link between tumour cells and the major metabolic tissues of the body - muscle, fat and liver. Mouse tumour models have been used to study the regulation of metabolic pathways during the development of cachexia. As these pathways are primarily controlled by nuclear receptors, we have profiled the expression of all 50 nuclear receptors, their cofactors and a representative set of their target genes in liver as well as a subset in muscle and fat. This has given valuable insights into the alterations in many metabolic pathways due to the impact of tumour-derived cytokines on nuclear receptor expression. In particular it appears that brown adipose tissue (BAT) becomes inappropriately activated resulting in excessive energy expenditure while the liver is unable to process and redistribute nutrients including lipids and carbohydrates. Such changes may contribute to aberrant energy balance leading to cancer cachexia.

The morphology of muscle fibres and fat deposits has been examined to characterise the changes that occur during cachexia. These changes in muscle and fat cells reflect alterations in metabolism and the molecules that control energy balance in the body.

Highlights
(Scholarships)
• Anthony Corradin: APA Scholarship $55,000, 2006-2008
• Anthony Corradin: Cancer Institute NSW Research Scholar, $50,000; 2007-2008
• Angie Shum: APA Scholarship 2009-2011

(Grants)
• NHMRC: $296,950, 2007 - 2009
• NHMRC: $315,000 Ethnic Differences Study, 2008 - 2010
• Cancer Institute NSW Translational Program Grant: $3.75 million, 2007-2011.
• Cancer Institute NSW Infrastructure Grant: $182,000. 2005-2007

Molecular Analysis of Nuclear Receptors PXR, RXR and HNF4
Anthony Corradin, M Kacevska, Marko Matic, Patsie Polly, Graham Robertson, [M Molloy - APAF Macquarie Uni; Frances Sladek - University of California Riverside]

To understand the regulation of genes involved in drug clearance pathways, we are carrying out detailed molecular studies into the nuclear receptors PXR, its binding partner RXRa and HNF4a. An important step is to identifying which domains of the PXR protein are necessary for interactions with other molecules in liver cells after PXR is activation by drugs. We are especially interested in defining specific interactions with other protein co-factors which move PXR into the nucleus and form the active multi-protein complex required to switch on target genes. Specific modifications of the PXR RXRa and HNF4a proteins, such as phosphorylation, are likely to play a critical role in modulating such interactions with other proteins. We anticipate that this information will help to understand how different diseases which have a marked inflammatory component, such as cancer, impact on nuclear receptors by altering their phosphorylation state.
ANZAC Research Institute

GERIATRIC EPIDEMIOLOGY: CONCORD HEALTH AND AGEING IN MEN PROJECT (CHAMP)

Group Leader: Professor Robert Cumming

Co-investigators: Professor David Handelsman, Professor Markus Seibel, Dr Helen Creasey (CERA), Dr Vasi Naganathan (CERA), Dr Louise Waite (CERA), Professor Philip Sambrook (Royal North Shore Hospital), Professor David Le Couteur (CERA)

Staff and Students: Melisa Litchfield, Janet Gilchrist, Maggie Hayes, Angeline Koh, Janice Koh, Golnar Mousavi, Diane Pinkerton, Suzanne Todd, Fiona Blyth, Stephane Rochat, Kerrin Bleicher, Noran Hairi, Chris Hoon, Anita Sharma, Fiona Stanaway

CHAMP is a population-based longitudinal study designed to provide a wide range of new information about the health of older men. The study is funded by a 5-year NHMRC Project grant. A total of 1705 men were recruited into CHAMP between January 2005 and May 2007. Two year follow-up examinations are almost complete, with more than 1300 men having been seen.

Despite the fact that men who reach the age of 65 still have much lower life expectancy than women of that age, very little research has been done on the health of older men. CHAMP was designed to fill this gap and is one of the world’s most comprehensive studies of the health of older men. Investigation of the role of reproductive hormones, including testosterone, in ageing in men is an important part of CHAMP.

Men were invited to participate in CHAMP if they were aged 70 years or older and lived in the community in one of three Local Government Areas near Concord Hospital: Burwood, Canada Bay and Strathfield. Fifty four percent of the men we contacted agreed to participate.

The study involves questionnaires and a wide range of tests. Prior to attending the study clinic in the Medical Centre at Concord Hospital, subjects complete a detailed questionnaire. They then spend two to three hours at the study clinic, where a series of tests is done, including dual energy x-ray densitometry (DEXA) to measure bone, fat and lean mass; the Addenbrooke’s Cognitive Examination; tests of muscle strength, balance and gait; spirometry; and uroflowmetry and measurement of post-void residual urines. Blood tests include assays for reproductive hormones, vitamin D, PTH, and markers of bone turnover, and measurement of Prostate Specific Antigen (PSA). Blood is being stored for DNA testing.

A paper describing the methodology used in CHAMP has been published in the International Journal of Epidemiology. A number of other papers are in press or have been submitted for publication. These include papers on: pain and frailty; a drug burden index; depressive symptoms in Italian migrants to Australia; the effect of urinary incontinence on quality of life; anxiety and pain; normal values of Prostate Specific Antigen; equations for estimating lean body mass; treatment of osteoporosis and frailty and health service use.

Papers about CHAMP have been presented at several international meetings during the past year. The paper on treatment of osteoporosis in older men that Kerrin Bleicher presented at the International Bone and Mineral Society meeting in Sydney attracted a great deal of scientific and media interest. Three CHAMP papers were presented at the International Association of Geriatrics and Gerontology meeting in Paris.

Assays for levels of testosterone and other reproductive hormones will be completed soon and the investigators will then be able to address one of CHAMP’s central questions: what are the effects of endogenous reproductive hormones on the health of older men?
The Northcott Neuroscience Laboratory, headed by Professor Garth Nicholson is internationally renowned in the field of molecular genetics of human hereditary neuropathies. The group has continued to make important contributions to finding gene mutations causing neurodegeneration of peripheral nerve and motor neurons. The identification and characterisation of these genes discovered in our families is furthering our understanding of the mechanisms causing degenerative nerve disease.

Inherited Peripheral Neuropathies

M. Kennerson, O. Albulym, A. Aziz, M. Brewer, R. Chaudhry, S. Chu, B. Kowalski, M. Simone, G Nicholson

Charcot-Marie-Tooth (CMT) disease CMT is a degenerative disorder of the peripheral nerve affecting both sensory and motor neurons. It is the most common inherited peripheral neuropathy with one in 2,500 people affected. Due to the chronic nature of these disorders, the hereditary neuropathies are a poorly recognised and silent health burden with a lifetime cost to Australians measured in billions of dollars.

Motor and sensory neurons represent a unique cell type with long axons (up to 1 metre) that require continuous maintenance from the cell body to the neuromuscular junctions. This organisation requires that systems be in place to maintain efficient cellular communication over these long distances. When these systems breakdown ‘dying back’ of the nerve ends (axonal degeneration) occurs is a common feature seen in many neurodegenerative disorders. The long term aim of our research is to identify the biological pathways leading to axonal degeneration with the ultimate goal of developing therapeutic treatments to prevent this process from occurring. Our strategy to identify these pathways is to locate the gene mutations in families with inherited peripheral nerve disease.

The laboratory continues to lead the world in mapping genes for X-linked forms of both CMT and distal motor neuropathies. This year we have utilised state-of-the-art genome technologies to identify the CMTX3 gene with next generation deep sequencing and targeted microarrays for copy number variation (CNV). Our laboratory is leading an international collaboration with groups from, Australia, United States, Belgium and Brazil to map the gene for a distal motor neuropathy locus on chromosome Xq13.1-q21 (DSMAX). We are currently validating sequence variants identified in a candidate gene in two families linked to the DSMAX locus.

Motor Neuron Disease

I Blair, S Yang, C Cecere, J Durnall, K Williams, J Solski, A Drew, S Warrach, A Thoeng, K Allen, G Nicholson

The motor neurons are nerves that extend from the brain to the muscles and provide the stimulus through which we move, breathe, eat and drink. The motor neuron diseases (MND) are a group of related neurodegenerative diseases that cause the progressive death of motor neurons. These diseases range from slowly progressive, non-fatal forms to the rapidly progressive fatal disorder amyotrophic lateral sclerosis (ALS). ALS typically leads to death within 3 to 5 years of first symptoms. ALS causes progressive paralysis and the cause of death is usually respiratory failure.

There is no specific diagnostic test for MND and treatment is extremely limited. The only known causes of MND are mutations in particular genes that lead to death of motor neurons. The known MND genes only account for about 2% of all cases. We are working to understand the biological basis of MND through identification of defective genes that cause the death of motor neurons. This understanding is a prerequisite to effective diagnosis, treatment and prevention of MND.

Recent highlights of our research include the identification of two new genes that cause MND when mutated. These breakthroughs, in collaboration with scientists from the UK, were recently reported in the journal Science. These discoveries have opened a new chapter in MND research and offer hope for the development of better diagnostic and therapeutic tools for this devastating illness.

These images showed the expression of TDP-43, a protein that plays important roles in motor neuron disease pathogenesis, in a motor neuron-like cell line NSC 34. The TDP-43 protein was shown in red and the outline of the cells was shown in green. The image on
the left shows the expression of normal TDP-43 protein whereas the image on the right shows the expression of mutant TDP-43 protein. As we can see, the location between the normal and mutant TDP-43 protein is different. The normal TDP-43 protein localised in the centre of the cell, where the cell nucleus are. By contrast, the mutant TDP-43 was excluded from the nucleus, a phenomenon that has been found in many MND patient cells. The photos were taken using a confocal microscopy and the magnification is 60X.

Immunostaining of NSC34 cells following transient transfection with TDP-43-HaloTag construct. Cytoskeleton stained with phalloidin-FITC (green), nuclei stained with DAPI (blue), and TDP-43-HaloTag fusion protein stained with TMR (red).

Parkinson’s Disease

N. Page and G. Nicholson

Parkinson disease (PD) is the second most common neurodegenerative disease, affecting approximately 100,000 Australians. Recently, the importance of genetic factors causing familial and some sporadic cases of PD has been realised, with mutations in eight genes known to be involved in the development of the disease. A major concern for families affected by PD is ascertaining which family members are carrying gene mutations, and thus have an increased risk of developing disease. Therefore affordable genetic diagnostic options are an important aspect of patient care. We have developed a novel method for the detection of all known PD mutations using the BeadXpress (Illumina). This method allows us to simultaneously detect point mutations and copy number variations. To date we have identified seven point mutations and four copy number variations in PD patients using this method. Thus, the BeadXpress system provides us with state of the art technology for mutation screening, providing the speed and high throughput capacity to process gene mutations in an accurate and competitive fashion.

Students:

The laboratory had three summer research students as part of the Sydney University Faculty of Medicine (2008-2009) Summer Scholarship program. Vanessa Thomas worked on a new MND candidate gene and was awarded the ANZAC Research Institute award for the best Summer Student presentation. Shannon Chu and Keta McDowall performed genetic analysis and mutation screening of candidate genes for our X-linked CMT families. Shannon Chu commenced his PhD in 2009 and will be examining the molecular cell biology of an X-linked form of distal hereditary motor neuropathy. The laboratory currently has four students (Obaid Albulyum, Megan Brewer, Alex Drew and Sadaf Warraich) in the second year of their PhD and two Masters students (Ann Aziz and Martin Simone). Ann is studying the genetics of Bells Palsy (BP). Her project was awarded a grant from the James N. Kirby Foundation which has funded a genome wide scan for mapping a BP gene in a larger family the laboratory has identified. As part of our efforts to map new loci for X-linked CMT the laboratory hosted a Turkish Master’s student from the Bogazici University. Irem Akat was awarded an Endeavour Award from the Australian government and visited the laboratory for five months as part of her Masters candidature.
**VASCULAR BIOLOGY**

**Head:** Professor Ben Freedman

**Senior Scientists:** Dr Paul Witting, A/Prof Len Kritharides, A/Prof Harry Lowe, A/Prof David Brieger

**Staff and Students:** Dr Julie Redfern, Dr Chang-Jie Song, Dr Raymond Sy, Dr Andrea Szuchman-Sapir, Dr Gabrielle Pennings, Dr Wei Zhao, Susan Hua, Dr Andy Yong, Dr Mohammed Moharram, Vicky Benson, Shane Antao, Sarah Parry, Sarah Wood, Ben Rayner, Hong Duong, Anu Shau, Lis Neubeck, Alana Mohamed, Rhoda Ascanio, Anna Jackson, Vincy Li, Roshanak Aran, Marzy Nikanami, M Sabaretnam, Alex Rosenov and Jasmin Voitl.

**Investigation of Inflammatory Mediators and the CHOICE study**

B Freedman, C Song, P Witting, S Hua, A Mohammed, J Redfern, L Neubeck, A Siney, R Ascanio, A Jackson, V Li,

Our main aim is to demonstrate novel mechanisms of initiation of inflammation, and to define links between inflammation, arterial thrombosis, and atherogenesis. We have shown that both CRP (C-reactive protein) and SAA (serum amyloid A) which are acute phase inflammation markers predictive of death or infarction in both normal populations and those with coronary artery disease, can stimulate blood monocytes to produce tissue factors, the initiator of in vivo coagulation. There is a non-specific up-regulation of monocyte responsiveness to both CRP and SAA in patients with coronary artery disease. The higher concentrations of these proteins seen in patients who have events indicates that both CRP and SAA are not just markers of inflammation, but may play a role in thrombosis which precipitates adverse events.

We have further investigated the mechanism whereby SAA is pro-inflammatory, and found very early and potent up-regulation of many pro-inflammatory cytokines by SAA and monocytes are the principle source. This is even greater in monocyte-derived macrophages present in atherosclerotic coronary artery vessel walls, and appears to be mediated by the nuclear switch NF-κB, and may be an important amplifier of both inflammation and thrombosis in acute coronary syndromes (including heart attack) and sudden coronary death. We have also shown that SAA is released into the coronary circulation in patients with coronary artery disease but not in controls. Our recent investigations have focused on the role of SAA in initiating vascular dysfunction. We have shown that exposure of blood vessel lining cells (endothelial cells) to pathological SAA induces endothelial dysfunction by affecting Ca2+ signal transduction pathways, stimulating the production of reactive oxygen species (e.g. O2•−), up-regulating the expression of pro-inflammatory genes and genes involved in the coagulation cascade, and decreasing cGMP which is involved in the synthesis of the blood vessel vasodilator nitric oxide.

We have also demonstrated an important protective effect of HDL, part of the ‘good cholesterol’ that has other protective actions against atherosclerosis. Part of these studies won an award of 200,000 Yen at the English Session of the 41st Conference of Japan Atherosclerosis Society, in 2009. We are beginning to study the protective effect of HDL on SAA-induced endothelial abnormalities, under high-glucose conditions to simulate diabetes. The group continues its longstanding collaboration with Prof Carolyn Geczy (UNSW) in these projects, and in other projects to ascertain the role of S100 proteins in atherosclerosis.

The CHOICE group has had productive year and now comprises a team of 7 staff members with the support of a HCF Research Foundation Grant and a NHMRC NICS-Heart Foundation Fellowship for Julie Redfern. We have had several publications in 2008-2009 including results of our original 12 month RCT in Heart (Redfern et al 2009), our current study protocol in BMC Cardiovascular Disorders (Neubeck et al 2008) and a systematic review (Neubeck et al 2009) of telehealth interventions for cardiovascular disease management that attracted international media attention. Our program and staff also appeared on national ABC Television news, and in the Sydney Morning Herald. Lis Neubeck (PhD Candidate) presented her systematic review at the EuroPrevent Conference, Stockholm Sweden with a CRGH Travel Scholarship in May as well as poster at the University of Sydney Cell To Society Conference in November 2008 where she was awarded a prize for her poster presentation. In our current study across 4 hospitals we have enrolled around 100 patients who have survived a coronary event but have elected not to participate in traditional cardiac rehabilitation. Following these patients will tell us whether a brief intervention will have long lasting effects on multiple risk factors.
Lis Neubeck (PhD Candidate) presented her systematic review at the EuroPrevent Conference, Stockholm Sweden with a CRGH Travel Scholarship in May as well as poster at the University of Sydney Cell To Society Conference in November 2008 where she was awarded a prize for her poster presentation.

Heart Attack and Stroke

P Witting, A Szuchman-Sapir, S Hua, B Rayner, H Duong, S Parry, S Wood, S Antao, M Sabaretnam, A Shanu, M Nikanami, R Aran

Dr Witting and his staff and students interests include ischemic injury to the heart (heart attack) and brain (Stroke) and effects of myoglobinurea on kidney function. The main research thrust involves design and testing of potential (synthetic antioxidant) inhibitors of damage to myocardial and neuronal tissues in the setting of acute heart or brain attack. In recent times, a large ARC grant awarded to investigators Hugh Harris (Adelaide University) and Witting (ANZAC) has opened new areas of research in the use of synchrotron radiation to characterize biochemical changes in heart and brain cells. The research has gained funding from a variety of sources including philanthropic Foundations, mainstream government bodies such as the ARC, Diabetes Australia, the National Heart Foundation of Australia and Industry (Servier). Importantly, the lab continues to support young undergraduate and postgraduate researchers with Dr Witting acting as supervisor for four current PhD students, two Honours students and one Vacation Scholarship awardee (Roshanak Aran) in 2009. During 2009, Shane Antao (working under the supervision of Dr Witting) was awarded a prestigious nationally competitive Heart Foundation scholarship; Hong Duong received a nationally competitive travel award from the Australian Neuroscience Society and Sarah Wood gained a research travel award from the Society for Free Radical Research to attend the annual meeting held in Melbourne.

Coronary Disease, Endocarditis and Echocardiography

L Kritharides, G Pennings, W Zhao, R Sy, A Yong, A Mohamed

Drs Yong (MBBS) and Pennings (PhD) have continued to study platelet and leukocyte activation in coronary artery disease (CAD) both in peripheral and intracoronary sampling. They have identified upregulation of leukocyte CD147 in patients with coronary disease, and found upregulation of platelet activation markers across coronary stenoses. Current work will include studies of the regulation in GPVI in collaboration with Drs Elizabeth Gardiner and Robert Andrews, Monash University.

Alana Mohammed, supervised by Prof Cris dos Remedios and Prof Ben Freedman, is utilizing a novel approach to examine patterns of multiple leukocyte and inflammatory markers with a slide based array. Preliminary findings indicate different activation patterns in patients with stable angina or acute coronary syndrome. She recently won an award at the 2009 Bosch Annual Scientific Meeting.

Ray Sy has continued his PhD studies on risk stratification in infective endocarditis on a part time basis. He has demonstrated that the risk factors for adverse outcome change over the first two weeks of treatment. He has achieved three publications on his work in the last year in highly regarded international journals (J Am Coll Cardiol, Eur Heart J, and Circulation: Quality and Outcomes), and is currently extending his studies into endocarditis through a data linkage project supported by the University of Sydney.

Dr Zhao is a cardiac sonographer who has joined our laboratory in the last 12 months. In the clinic, Wei has established novel methods for non-invasively assaying pulmonary vascular resistance and pulmonary arterial compliance in patients with pulmonary hypertension. In the laboratory, Wei has established mouse echocardiography at the ARI using highly sensitive high frequency transducers and together with the group of Professor Handelsman will investigate the role of androgen deficiency on cardiac size and function in mice.

Gene targeting for heart attack and studies of saphenous vein graft disease

H Lowe, V Benson, M Moharram

Vicky Benson, supervised by A/Prof Harry Lowe and Dr Aisling McMahon (Biogerontology), is examining novel gene-targeting techniques using short strand catalytic DNA molecules to provide knockdown of the transcription factor Early Growth Response Factor-1 (Egr-1) in models of acute myocardial ischemia in the setting of diabetes. It builds on our own recent demonstrations that this approach provides potential therapeutic benefit in non-diabetic models of...
myocardial ischemia: work attracting international recognition, and our own recent data suggesting the same approach may be even more relevant in the presence of diabetes.

Egr-1-targeting DNAzymes are sequence-specific enzymes that cleave Egr-1 mRNA, thus preventing expression. Using in vitro models of diabetes and myocardial ischemia, and our own recently developed animal model of myocardial ischemia in diabetes, we are examining the effects of DNAzyme delivery on Egr-1 expression, molecular pathways of ischemic injury, and infarct size. This work has the potential to provide novel “diabetes specific” therapies for heart attack. Vicky recently presented her findings at the European Society of Cardiology Heart Failure Congress held in Nice, France. She received a travel scholarship from the European section of the ISHR to attend the meeting. She has also published a review article in the British Journal of Pharmacology.

Dr Moharram is investigating saphenous vein graft disease. Coronary bypass grafts (saphenous vein grafts or SVGs) have a tendency to develop narrowings in the years following coronary surgery, leading to further symptoms of heart attack. The nature of these narrowings remains poorly understood, but is thought to be distinct from the atheroma that develops in native coronary vessels. We are trying to determine the nature of atheroma in SVGs and whether it is similar to or different from atheroma in native coronaries. This will help us understand, and possibly tackle, the atherosclerosis process in these conduits in a better way. Mohamed is a recent addition to the group; his work so far has culminated in a poster presentation at the annual Australian and New Zealand Cardiac Society meeting.

Inflammatory Mechanisms and Mediators in Acute Coronary Syndromes
D Brieger, A Rosenov, J Voitl

Studies under the direction of A/Prof Brieger have focused on the utility of novel measures of haemostatic function in characterising therapeutic responses to anti-platelet agents in patients with coronary disease. Patients undergoing invasive cardiac procedures receiving anti-platelet therapies have their overall haemostatic function determined by assays include the Overall Haemostatic Potential (OHP) Assay and calibrated automated thrombogram (CAT). These have been developed in collaboration with the Haematology Departments at Concord Hospital and Royal North Shore Hospitals. The impact of different anti-platelet agents and combinations of these agents on these assays are being evaluated and compared against conventional functional studies of platelet function. This work is currently being performed by Alex and Jasmin who are visiting students from Austria.
ANZAC
Research Institute

VETERANS EPIDEMIOLOGY:
AUSTRALIAN VIETNAM VETERANS
FAMILY HEALTH STUDY

Group Leader: Dr Brian O’Toole

Co-investigators: Professor Stanley Catts (Univ of Qld), Dr Sue Outram (Univ of Newcastle), Kate Pierse, Prof Jill Cockburn (Univ of Newcastle, deceased)

The Australian Vietnam Veterans Health Study was begun in the late 1980s and has followed a cohort of veterans for over 30 years. With Army assistance, a random sample of 1,000 veterans was identified and, with assistance of the Australian Bureau of Statistics and the Department of Veterans Affairs, the first health assessments were undertaken in 1990-92 with funding received from the NHMRC. Over 25 publications have come from the first wave of the study, the most recent in 2008, which continues to provide a solid evidential base for data analysis into the future.

In 2005-06 the study assessments were repeated, again with the assistance of the Bureau of Statistics and the Department of Veterans Affairs, and funding from NHMRC. This has added to the data lode and opened up a much richer prospect for scientific contributions to the knowledge about the long term effects of war service. Many discrete projects are under way, supported by modern and sophisticated data analysis techniques. A few of these are described below, and arise from published or under-review manuscripts from the study. Each describes a project that is aimed at providing important insight into the etiology, maintenance and treatment of war-related illnesses and the warriors who endure them.

In 2006-07 the study was expanded to include wives and partners of the veterans, with additional funding support from the Australian Rotary Health Research Foundation. In this study, veterans’ wives/partners were assessed using the same procedures as used for the veterans, and the assistance of the Bureau of Statistics was also available to the study. Thus, the study has extended from veterans to their wives/partners, and is now seeking funding to extend the study to veterans’ children.

Factors Associated with Civilian Mortality in Australian Vietnam Veterans Three Decades After The War.

Mortality studies of Australian veterans have produced mixed results. On the one hand, the mortality rates in the whole veteran force (Army, Navy, Air Force) were not different from Australian population expectations, yet when National servicemen were compared with NSM who did not go to Vietnam. There was a much higher rate of head-and-neck cancers, lung cancers, and alcoholic liver disease. In our cohort of 1,000 Australian Army Vietnam veterans we determined deaths using the Institute of Health and Welfare National death Index. We also analysed risk factors for post-war mortality using information from Army records and personal interview assessments of physical and mental health measured approximately 15 years earlier. We especially wanted the opportunity to examine any associations of post-war civilian mortality with combat, military service, health risk factors (smoking, alcohol) and psychiatric status including post-traumatic stress disorder (PTSD). Factors predicting mortality were identified using multivariate statistical methods including logistic and Cox regression. Mortality was associated with principally with age, enlistment route (Regular soldiers had higher mortality rates than National Service conscripts) and conduct while in service in the whole cohort. Additional analysis using interview data revealed that mortality was predicted by age, smoking status, chronic diabetes, bronchitis and blood diseases and treatment for cancer and heart disease. Psychiatric status including PTSD diagnosis was not associated with mortality, nor were data describing military service such as rank and duration of deployment. Veterans’ causes of death and mortality risk factors seem commensurate with the normal aging process but also indicate the need for risk factor reduction both in-service and post-service.

The Physical and Mental Health of Australian Vietnam Veterans Three Decades after the War and Its Relation to Military Service, Combat and PTSD.

The long-term health consequences of war service remain unclear despite burgeoning scientific interest. The cohort study of Vietnam veterans was designed to assess veterans’ post-war physical and mental health 36 years after the war and examine its relation to Army service, combat and post traumatic stress disorder that was assessed 14 years previously. Prevalence of disease in veterans was compared with prevalence in the Australian population. Veterans’ Army service and data from the first assessments were evaluated using multivariate logistic regression prediction modelling.

Veterans’ general health and some health risk factors were poorer, and medical consultation rates were higher than population expectations. Of 67 long term conditions, 47 were higher and only 4 were lower when compared with population expectations. Half of all veterans took some form of medication for mental wellbeing. Eleven of
VETERANS EPIDEMIOLOGY: AUSTRALIAN VIETNAM VETERANS FAMILY HEALTH STUDY

17 psychiatric diagnoses were in excess of Australian population expectations. In a multivariate predictive analysis, military and war service characteristics and age were the most frequent predictors of physical health endpoints, while PTSD was the most strongly associated with psychiatric diagnoses. Draftees had better physical health than regular enlistees, but no better mental health. We conclude that Army service and war-related PTSD are associated with risk of illness in later life in Australian Vietnam veterans.

The Health of Partners of Australian Vietnam Veterans Three Decades after the War and its Relation to Veteran Military Service, Combat and PTSD.

Women living with male veterans who are suffering from Post Traumatic Stress Disorder (PTSD) and other war-related conditions may be at higher risk of poorer health. Using independent standardized health assessments of 240 veteran-partner couples, comparative national population data and regression modelling, we assessed the prevalence of health conditions in veterans’ partners. This was compared this to national Australian Bureau of Statistics (ABS) population data, and examined the associations of veterans’ war service, combat and psychiatric status with women’s health. Thirty of 60 ABS physical and mental health conditions assessed were significantly in excess of population expectations; 11 of 17 psychiatric conditions were significantly in excess.

Veterans’ military service and mental health were related to only few of their partner’s physical health conditions however veterans’ combat and PTSD were significant predictors of women’s depression, with combat related to women’s severe depression. We conclude that war service may have unrecognized consequences for veterans’ partners, particularly if the warriors develop PTSD.

Confounding of combat reports with PTSD: Scratching beneath the surface.

Recent evidence from the US suggests that, as time goes on, veterans’ reports of their combat exposures become enhanced, especially if they have PTSD. Our study allowed a comparison of reports of combat exposure that were gathered 14 years apart. Qualitative evidence from the interviews suggested that, under normal conditions, veterans rarely forget their war experiences when asked to recall and rank the worst events that occurred to them. However, it was found that there indeed was a tendency for reports of stressor exposures to increase over time. When examining the incidents that were subject to an increase, many were remarkably stable – enemy contact, seeing Australian dead or injured, seeing Australian wounded, and witnessing civilian deaths. On the other hand, some events were much more often reported at the second wave than the first: seeing Australians being killed, killing the enemy, and participating in a body count. Interestingly, veterans’ subjective reports of the risk of their own death dropped by a huge 63% from wave 1 to wave 2: On reflection, and more than 30 years later, the apparent risk seems less.

The US literature suggests that increases in combat reports are more likely in people with PTSD, which was tested in the current study. But the story is not as straightforward as it seems. PTSD is diagnosed using thresholds for clinical significance of each of the symptoms; each of these symptoms has a threshold below which it is not clinically significant, above which it would be termed a ‘symptom’. By using various thresholds, the diagnosis can be manipulated to assess its relationship with other items. In the current study, manipulation of the thresholds led to widely different results: It turns out that combat exaggeration may be related to PTSD but only for the least or lowest threshold: As the definition is ‘tightened up’ the association disappears. In addition, the combat-exaggeration-PTSD association does not hold for the current (disorder present in the past month) diagnosis, although it does for the lifetime diagnosis. Thus, explanations of the combat-PTSD relationship being confounded are not supported by the data in the present study.
Malevolent Environment and Mental Health: Beyond Combat

War zone experiences that are hazardous to physical and mental health go beyond traditional combat. Early US work on the essential features of traumatogenesis concluded that it was being a ‘target’ that was the essential experience for PTSD to develop. However, the changing nature of war has dictated a widening of this definition, as separate identifiable components of war-zone exposures have been identified and their independent effect on PTSD symptoms has begun to be examined. Complications caused by the various formulations of PTSD make more difficult the task of correlating observed and defined psychiatric disorder with a set of non-traditional combat stressors. For example, duration of time spent in a malevolent environment has been recognized as an important stressor, as have attempts to define the components or constituents of a ‘malevolent environment’. Drawing on several large US studies, the evidence for non-combat events to have an impact on PTSD and other psychiatric disorders such as depression was examined. The existence of ‘improvised explosive devices’ (or IEDs) are common features of modern theatres of war, but also were prevalent in Vietnam. The constant exposure to the risk of death from IEDs or mines adds to the milieu that constitutes a malevolent environment. This aspect of the study examines non-traditional combat exposures and their effect on mental health conditions including, but not limited to, PTSD.
STAFF & STUDENTS 2008 - 2009

Scientific Staff

Director
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Scientific Program Leaders
Professor Stephen Clarke MB BS, PhD FRACP, FACHPM
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Dr Hong Zhou MD (China), PhD

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Maggie Hayes RN
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Technical Support
Fay Bacha BSc
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Vicky Benson MSc
Annette Berryman
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Patty Kapelaris Business Studies
Christina Nostas Animal Attendant Cert 3
Tia Smith Cert 3 Animal Companion Services, Cert II Animal Studies
Ljubica Vrga BSc (Hons)
Matilda Webbey Animal Attendant Cert 3
Jennifer White BApp Sc, Grad Dip Education
ANZAC Research Institute

STAFF & STUDENTS 2008 - 2009

Overseas Visiting Fellows/Students
Dr Markus Hermann MD
Holger Henneicke
Anastasia Mikuscheva
Dr Gideon Sartorius
Agnes Weber

Graduate Students
Obain Albulym MSc
Jessica Almine BSc (Hons)
Shane Antao BSc (Hons)
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Kerrin Bleicher
Vicky Benson MSc
Megan Brewer BSc (Hons)
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Anthony Corradin BMedSc
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Hariyana Dhillon BSc, MAI (Psych)
Hong Duong BSc, BAA
Alex Drew BSc (Hons)
Min Li Huang BSc (Hons)
Marina Kacevska BSc (Hons)
Curtis Kuo BSc (Hons)
Dr George Lau MB BS, FRACP
Marko Matic BSc (Hons)
Melissa Moore BSc (Hons)
Keely McNamara BSc (Hons)
Alicia Neubeck BA (Hons), RN
Jennifer O’Reilly BA(Mus) BSc (Hons)
Li Laine OOi BSc (Hons)
Arran Painter BAdvSc (Hons)
Viet Phan MD MPH
Jelena Rnjak BSc (Hons)
Mimi Saba BSc (Hons)
Dr Anita Sharma DSM, AMC, FRACP
Martin Simone BSc (Hons)
Fiona Stanaway
Dr Alice Tiong BSc (Hons), MB BS, FRACP
Sadaf Warraich BMedSc (Hons)

Undergraduate Students
Honours Students 2008
Phillipa Camilleri BSc
Angie Shum BSc
Annora Thoeng BMedSc
Sarah Wood

Masters Students
Alana Mohamed BSc

Summer Scholars
2007/08
Daniel Cox
Shannon Chu
Elica Rodas
Martin Seneviratne
Alexander Treble
Giselle Yeo

2008/09
Shannon Chu
Caitlin Gillis
Sharon Hu
Keta McDowall
Li Ann Ooi
Julian Pavey
Vanessa Thomas
Mohit Tolani

Administrative Staff
Director
Professor David Handelsman MB BS, PhD, FRACP

Director, Laboratory Animal Services (MPU)
Mamdouh Khallil BSc, Ass Dip Animal Technology

Business Manager
Julie Taranto, BSc

Finance Manager
Annet Doss, Dip Acc, Dip Comp Prog

Accounts Clerks
Lillian Tay
Candice Chang

Information Systems Manager
Justin Crosbie  BSc Information Technology

Human Resources Manager
Pam McDowell

Receptionist/Administration
Tracey Dent

Growth at ANZAC Research Institute

Staff Growth at ARI

- Admin
- Sc & Technical
- Grad Students
- Post Doctoral Scientists
- Program Directors

FTE

Year

2000 2001 2002 2003 2004 2005 2006 2007 2008 2009

36
## GRANTS

<table>
<thead>
<tr>
<th>Grant/ Type</th>
<th>Scientific Title</th>
<th>Chief Investigators</th>
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<tr>
<td>NHMRC</td>
<td>Investigating the molecular basis of motor neuron disease</td>
<td>Blair</td>
<td>102,250</td>
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<tr>
<td>Career Development</td>
<td>Androgen Deficiency in Chronic Disease</td>
<td>Liu</td>
<td>102,250</td>
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<td>Equipment</td>
<td>Olympus Confocal Microscope Upgrade</td>
<td>Allan, Seibel, Myers, Handelsman, Witting, Kennerson, Freedman, Cogger, Robertson, Le Couteur, Nicholson, Zhou, Blair, Clarke,</td>
<td>63,332</td>
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<td></td>
<td>Stereomicroscope-Imaging Workstation</td>
<td>Allan, Seibel, Handelsman, Le Couteur, Kennerson, Robertson, Walters, Cogger, Nicholson, Zhou, Blair, Simanainen, McMahon.</td>
<td>24,039</td>
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<td>Fellowship</td>
<td>Patient-centred modular prevention of heart disease: a program for implementing evidence-based guidelines.</td>
<td>Redfern</td>
<td>69,597</td>
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<td>Infrastructure</td>
<td>NHMRC National Baboon Colony</td>
<td>Hennessy, O’Connel, Rasko, Twigg, D’Aspice, Le Couteur</td>
<td>120,000</td>
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<td>Project</td>
<td>Nutrition and aging</td>
<td>Simpson, Le Couteur, Raubenheimer, Ballard</td>
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<td>Old age and the liver endothelium</td>
<td>Le Couteur, Cogger, Lebel, Quinn, Hilmer, McCuskey</td>
<td>292,750</td>
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<td>Sunlight and falls (Freedom Study)</td>
<td>Sambrook, March, Cameron, Cumming, Seibel, Simpson</td>
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<td></td>
<td>How defective dynamin 2 activity causes Charcot-Tooth Disease</td>
<td>Robinson, Nicholson, McCluskey</td>
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<td>Sirtuins and the molecular epidemiology of frailty in older men.</td>
<td>Cumming, Le Couteur, Kennerson, de Cabo, Naganathan, Sambrook</td>
<td>236,140</td>
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<td>CHAMP Project</td>
<td>How are synapses lost in muscle and does this contribute to the loss of strength with age?</td>
<td>Phillips, Reddel, Noakes</td>
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<td>The role of mutant TDP-43 in ALS</td>
<td>Blair, Nicholson, Hawke</td>
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<td>Hepatic drug clearance and drug induced liver disease in aging</td>
<td>Hilmer, Jones, Cogger, de Cabo</td>
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<td>Obstructive sleep apnea and androgen dysregulation</td>
<td>Liu, Grunstein, Handelsman</td>
<td>175,900</td>
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<td></td>
<td>Metabolic and psychomotor changes after continuous positive airway pressure treatment for obstructive sleep apnea</td>
<td>Liu, Yee, Phillips, Berend</td>
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<td>Hormonal control of Sertoli cell maturation and function</td>
<td>Allan, Handelsman</td>
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<td>Glucocorticoid effects on bone: the role of the osteoblast</td>
<td>Seibel, Zhou, Dunstan</td>
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<td>AED's and fracture risk.</td>
<td>Wark, O’Brien, Sambrook, Seibel, Herkes</td>
<td>156,506</td>
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<td>Osteoblast control of mesenchymal progenitor cell differentiation: The role of glucocorticoids &amp; Wnt signalling.</td>
<td>Zhou, Seibel, Chen, Dunstan</td>
<td>143,625</td>
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<td>Pharmacogenetics of tissue androgen activation</td>
<td>Handelsman, Reichardt, Yu, Seibel</td>
<td>141,974</td>
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<td>Optimising pain management in frail older people</td>
<td>McLachlan, Nagabathan, Le Couteur, Hillmer, Gibson</td>
<td>131,250</td>
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<tr>
<td>Caloric restriction ageing and the liver sinusoidal endothelium</td>
<td>Le Couteur, Fraser, Cogger, Sullivan</td>
<td>116,268</td>
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<td>Inter-ethnic differences in tolerance of anti-cancer drugs.</td>
<td>Clarke, McLachlan</td>
<td>113,575</td>
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<td>FSH and female aging</td>
<td>Alian, Handelsman, Dunstan</td>
<td>94,440</td>
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<td>Mutation analysis of novel candidate genes for X-linked Charcot Marie Tooth (CMTX3) neuropathy</td>
<td>Kennerson, Nicholson</td>
<td>93,743</td>
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<td>Cognitive function and fatigue after chemotherapy</td>
<td>Vardy, Clarke, Tannock, Schnitzler, Dhillon</td>
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<td>Sun exposure, vitamin D and the outcome of prostate cancer</td>
<td>Armstrong, Kedda, Smith, Steginga, Kricker, Kimlin, Seibel, Clements</td>
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<td>Inflammation-associated S100 proteins: links between arthritis and atherosclerosis</td>
<td>Geczy, McNeil, Freedman, Hsu,</td>
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<td>Strategic Awards</td>
<td>Sensory impairment: causes, impacts and interventions</td>
<td>344,599</td>
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<td>Australian Research Council</td>
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<td>Linkage Infrastructure, Equipment &amp; Facilities</td>
<td>Liquid Chromatography Tandem Mass Spectrometer (API 5000 LC/MS/MS) [Total cost of equipment $560K]</td>
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<td>Project</td>
<td>Cellular response to pro-oxidative myoglobin</td>
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<td></td>
<td>Steroidal control of male meiosis</td>
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<td></td>
<td>Witting</td>
<td>141,400</td>
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<td></td>
<td>Alian, Handelsman, Griswold, Denyer</td>
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<td>Cancer Institute</td>
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<td>Fellowship</td>
<td>Early Career Development Fellowship</td>
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<td>Infrastructure</td>
<td>Supplement for &quot;Use of proteomic analysis to improve the management of colorectal cancer&quot;</td>
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<tr>
<td>Program Grant</td>
<td>Use of proteomic analysis to improve the management of colorectal cancer</td>
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<td>Project</td>
<td>Sun exposure, vitamin D and the outcome of prostate cancer</td>
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<td></td>
<td>The role of intraprostatic glucocorticoid action in prostate physiology and pathology</td>
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<td>Simanainen, Baker, Baxter, Christopherson, Clarke, Daly, Guilhaus, Kavallaris, Molloy</td>
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<td>Clarke, Robertson, Baker, Molloy, Bokey, Chapuis, Chan, Lin, Christopherson, Lee, Hong, Kohonen-Corish, Beale, Salomon, Horvath, McKay</td>
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<td>Armstrong, Seibel, Clements</td>
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<td>Simanainen (Handelsman, Zhou, Seibel)</td>
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## GRANTS

### Diabetes Australia Research Grant

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<tr>
<th>Project</th>
<th>Investigator(s)</th>
<th>Amount</th>
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<tbody>
<tr>
<td>The acute phase protein serum amyloid A promotes endothelial dysfunction in diabetics</td>
<td>Witting</td>
<td>58,820</td>
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<tr>
<td>An examination of poor outcomes following heart attack in diabetes.</td>
<td>Lowe, McMahon, Witting</td>
<td>50,000</td>
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<tr>
<td>Synthetic polyphenol antioxidants that reverse diabetes-induced vascular dysfunction</td>
<td>Witting</td>
<td>50,000</td>
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<tr>
<td>Proinflammatory activation of endothelial cells by serum amyloid in diabetes</td>
<td>Freedman,</td>
<td>30,000</td>
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### Muscular Dystrophy Association

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<tr>
<th>Project</th>
<th>Investigator(s)</th>
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<tr>
<td>Finding the gene causing x-linked Charcot-Marie-Tooth (CMTX3) neuropathy</td>
<td>Nicholson, Kennerson</td>
<td>67,767*</td>
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<tr>
<td>Effects of mutant SPTLC1 on cell biology of neuronal cells causing hereditary sensory neuropathy</td>
<td>Nicholson, Myers</td>
<td>40,540*</td>
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### OSMR

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<tr>
<th>Infrastructure</th>
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<tr>
<td>Medical Research Support Program 2006-2009</td>
<td>ANZAC Research Institute</td>
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### University of Sydney

<table>
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<tr>
<th>Bridging Scheme</th>
<th>Investigator(s)</th>
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<tbody>
<tr>
<td>Androgen mechanisms in female reproduction</td>
<td>Walters, Handelsman</td>
<td>50,000</td>
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<tr>
<td>Impact of tumour-derived cytokines on drug clearance pathways in cancer.</td>
<td>Clarke, Robertson, McLachlan</td>
<td>50,000</td>
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<tr>
<td>DVC Bridging support scheme: Role for neuroglobin in protecting neuronal cells in models of cerebral inflammation</td>
<td>Witting</td>
<td>50,000</td>
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<tr>
<td>How osteoblasts control mesenchymal progenitors</td>
<td>Zhou, Seibel, Chen, Dunstan</td>
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<table>
<thead>
<tr>
<th>Cancer Research</th>
<th>Investigator(s)</th>
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<tbody>
<tr>
<td>The role of androgens in prostate physiology and pathology</td>
<td>Handelsman, Simanainen</td>
<td>50,000</td>
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<tr>
<td>Bone and tumour necrosis following anti-resorptive treatment</td>
<td>Seibel, Dunstan, Blair</td>
<td>44,674</td>
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<table>
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<tr>
<th>Establishment Grant</th>
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<th>Amount</th>
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<tbody>
<tr>
<td>Support early to mid career Fellows (linked to A511929 NHMRC)</td>
<td>Liu</td>
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</table>

### International Visiting Research Fellow

<table>
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<tr>
<th>Project</th>
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<tbody>
<tr>
<td>Exploring the role of tRNA synthesis in neurodegenerative disease.</td>
<td>Antonellis</td>
<td>11,500</td>
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### Major Equipment

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<th>Project</th>
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<th>Amount</th>
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<tbody>
<tr>
<td>Rotor-Gene 6000 Real-time Amplification System</td>
<td>Allan</td>
<td>26,264</td>
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### Strategic Research

<table>
<thead>
<tr>
<th>Project</th>
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<tbody>
<tr>
<td>Investigation of novel protein post-translation modification in the infarcted heart</td>
<td>Witting</td>
<td>50,000</td>
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</table>

### Other

#### Contributions

<table>
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<tr>
<th>Contribution</th>
<th>Investigator(s)</th>
<th>Amount</th>
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<tbody>
<tr>
<td>ADRI start up fund</td>
<td>van Zandwijk</td>
<td>7,000</td>
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<tr>
<td>Consumables</td>
<td>Lab consumables</td>
<td>100,000</td>
</tr>
<tr>
<td>Contribution to &quot;Minimal Trauma Fracture Clinic CRGH&quot;</td>
<td>Seibel</td>
<td>25,000</td>
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</table>
## ANZAC Research Institute

### GRANTS

#### Bequest

<table>
<thead>
<tr>
<th>Organization</th>
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<tbody>
<tr>
<td>AFT-Holman</td>
<td>Bequest for muscular dystrophy research</td>
<td>Nicholson</td>
<td>33,902</td>
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<tr>
<td>Churm</td>
<td>Bequest for motor neuron disease research</td>
<td>Nicholson</td>
<td>50,000</td>
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<tr>
<td>Elaine Kendall</td>
<td>Bequest for Charcot Marie Tooth research</td>
<td>Nicholson</td>
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<tr>
<td>G &amp; C Loudon</td>
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#### Equipment

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<tbody>
<tr>
<td>Ramaciotti</td>
<td>The liver, age-related dyslipidemia and atherosclerosis, and novel therapeutic targets in a premature aging mouse model.</td>
<td>Cogger</td>
</tr>
</tbody>
</table>

#### Projects

<table>
<thead>
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<th>Description</th>
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<tbody>
<tr>
<td>ALSA</td>
<td>Identification of a novel gene causing motor neuron degeneration</td>
<td>Nicholson, Blair</td>
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<td>Anti-Doping Research Panel Grant</td>
<td>A Generic Method for Detecting Insulin Abuse in Sport</td>
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<td>Australian Rotary Health Research Fund</td>
<td>Investigating the role of the gene encoding TAR DNA binding protein (TDP-43) in ALS</td>
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<td>Brain Foundation</td>
<td>Does chronic upregulation of acetylcholine signalling at neuromuscular junction with pharmaceutical long term inhibition of acetylcholinesterase exacerbate the pathophysiological effects of anti-AChR mediated and anti-MuSK mediated myasthenia gravis?</td>
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<td>Guided choice for prevention of future heart disease</td>
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<td>HCF Grant-in-aid</td>
<td>Choice study for secondary prevention of heart disease</td>
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<td>Development of valid diagnostic criteria for age-related androgen deficiency in men</td>
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<td>Motor Neuron Disease</td>
<td>Finding genes causing familial motor neuron degeneration</td>
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<td>Identifying novel genetic loci for familial motor neuron disease</td>
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<td>Identifying new genes for familial Amyotrophic Lateral Sclerosis</td>
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<td>National Heart Foundation</td>
<td>Neuro-protective antioxidants that synergise with thrombolytic treatments for acute cerebral ischemia</td>
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<td>Concord Centre for Cardiometabolic Health in Psychosis</td>
<td>Lambert, Chen, Snars</td>
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<td>Prostate Cancer Foundation of Australia</td>
<td>Vitamin D deficiency and prostate cancer metastasis to bone</td>
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<td>World Anti Doping Agency</td>
<td>Detection of recombinant human LH as a doping agent</td>
<td>Kazlauskas, Trout, Handelsman</td>
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<td>World Health Organisation</td>
<td>Sperm suppression and contraception protection provided by norethisterone enantate (Net-En) combined with testosterone undecanoate (TU) in healthy men. Master protocol A25165</td>
<td>Handelsman, McLachlan</td>
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#### Trial Studies

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<td>Ascend/Besins Pharmaceuticals</td>
<td>Efficacy and safety of DHT to prevent prostate growth in middle aged men</td>
<td>Handelsman, Conway</td>
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GRANTS

Scholarships

**NHMRC**

- Medical Postgrad Scholarship
  Role for myoglobin in myocardial ischemia reperfusion injury. Yong 32,500

**Andrology Australia**

- Development of a postgraduate education program for a clinical fellow in Andrology Jayadev 15,000

**Bushell Foundation**

- What gene mutation causes the death of motor neurons in distal hereditary motor neuropathies? Chu 35,000
- How do mutations in serine palmitoyltransferase long chain sub unit 1, causing hereditary sensory neuropathy, affect the neuronal cell cytoskeleton Simone 30,000
- What is the gene mutation causing an X-linked form of Charcot-Marie-Tooth neuropathy (CMTX3)? (Stipend for PhD) Kennerson, Nicholson 30,000

**Reginal Maney Lake & Amy Laura Bonamy Scholarship**

- The effect of androgen action and inactivation of different prostate compartments McNamara 20,407

**Royal Australian College of Physicians**

- RACP Osteoporosis Australia Research Entry Scholarship Ching Wu 29,000

**TOTAL** $10,114,985

* AUD = USD/0.8
$ are Annualised for 2008 & 2009
Incidence and determinants of mycological infection following percutaneous coronary interventions according to the revised Joint Task Force definition of troponin T elevation. International Journal of Cardiology 2009. PMID:1913135
Allan CM, Lim P, Robson M, Spalviero J and Handelsman DJ
Transgenic mutant D657G but not wild-type human FSH receptor overexpression provides FSH-independent and promiscuous glycoprotein hormone Sertoli cell signalling. The American Journal of Physiology Endocrinology & Metabolism 296: E1022-8, 2009. PMID:19225333
Cohort profile: The Dynamic Analyses to Optimize Ageing (DYNOPTA) project. International Journal of Epidemiology 2009. PMID:19451277
Araujo AB, Kupelian V, Page ST, Handelsman DJ, Bremner WJ, and McKinlay JB.
Beautiful Study Group (SB Freedman member of International steering committee), Ferrari R, Ford I, Fox K, Steg M and Tendler M.
Benson VL, Khachigian LM and Lowe HC
Birzniev V, Meinhardt UJ, Handelsman DJ and Ho KK
Testosteron stimulates extra-hepatic but not hepatic fat oxidation: conclusion of oral and transdermal testosteron administration in hypopituitary men. Clinical Endocrinology (Oxf) 2009. PMID:19170715
Blair IP, Vance C, Durnall JC, Williams KL, Toong A, Shaw CE and Nicholson GA
Blyth FM, Cumming RG, Brnabic AJ and Cousins MJ
ANZAC Annual Report 2009

PMID:19071150


PMID:18303073


Hormonal and androgens in men. Clinical Endocrinology (Oxf) 2008. PMID:18429008

Handelsman DJ, Abernethy DR and Hilmer SN

Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep 31: 1079-85, 2008. PMID:19109348

Lee F and Seibel MJ


Saliba S, Khechen D, Feely S, Chu S, Shy M and Garbern J

Invasive management and late clinical outcomes in contemporary Australian management of acute coronary syndromes: observations from the ACACIA registry. Medical Journal of Australia 190: 162; author reply 162, 2009. PMID:19202302

Kukuljan S, Nowson CA, Bass SL, Sanders K, Nicholson GC, Seibel MJ, Salmon J and Daly RM


Lee Couteur DG and Kendig H


Old age and the hepatic sinusoid. Anatomical Record (Hoboken) 291: 672-85, 2008. PMID:18486414

Lee F and Seibel MJ

Male hormonal contraception: so near and yet so far. Journal of Clinical Endocrinology & Metabolism 94: 801-8, 2009. PMID:19060302

Lim P, Robinson M, Spaliviero J, McTavish K, Jimenez M, Zajaz J, Handelsman DJ and Allan CM

Sertoli cell androgen receptor genomic action is essential for the completion of spermatogenesis. Endocrinology (in press)

Lim PY, Baker HW, Jayadev V, Zacharin M, Conway AJ and Handelsman DJ


Lim PY and McLachlan RJ

Birthweight is affected more by the rate of gestational age than by gestational age per se: a postmortem study of 2258 stillbirths and neonates. American Journal of Obstetrics & Gynecology 191: 1311-6, 2009. PMID:19635586

Lim PY, oh doch, MacLachan RJ, Miller AD, Vannier CP, Rimm EB, et al.

Handelsman DJ, Abernethy DR and Hilmer SN


Hilmer SN, Allan CM, Notini AJ, Axell AM, Spaliviero J, Jimenez M, Davie R, McManus J, MacLean HE, Zajaz JD and Handelsman DJ


Lim P, Robinson M, Spaliviero J, McTavish K, Jimenez M, Zajaz J, Handelsman DJ and Allan CM

Male hormonal contraception: so near and yet so far. Journal of Clinical Endocrinology & Metabolism 93: 2474-8, 2008. PMID:18617702

Lowe HC and Freedman SB


Marshall NS, Wong KK, Liu PY, Cullen SR, Knuiman MW and Grunstein RR

Sleep apnea: an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep 31: 1079-85, 2008. PMID:18714779

Marshall NS, Wong KK, Phillips CL, Liu PY, Knuiman MW and Grunstein RR

Sleep apnea: an independent risk factor for prevalent and incident diabetes in the Busselton Health Study? Journal of Clinical Sleep Medicine 5: 15-20, 2009. PMID:19101756

Marshall NS, Wong KK, Phillips CL, Liu PY, Knuiman MW and Grunstein RR

Sleep apnea: an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep 31: 1079-85, 2008. PMID:18714779


Determinants of the rate and extent of spermatogenic suppression during hormonal male contraception: an integrated analysis. Journal of Clinical Endocrinology & Metabolism 95: 1774-83, 2008. PMID:18800373


Old age and the hepatic sinusoid. Anatomical Record (Hoboken) 291: 672-85, 2008. PMID:18486414

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Sleep apnea: an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep 31: 1079-85, 2008. PMID:18714779

ANZAC Research Institute

PUBLICATIONS

Matic M, Nakleh S, Lehnert AM, Polly P, Clarke SJ and Robertson GR
A novel approach to investigate the subcellular distribution of nuclear receptor in vivo. Nuclear Receptor Signaling. 7: 804-9, 2009. PMID:19471583

McLachlan AJ

McLachlan AJ, Hillmer SN and Le Couteur DG

MacLean HE and Handelsman DJ

McMahon AC, Zerig H and Lowe HC

McRobb L, Handelsman DJ and Heathaker AK
Androgen-induced progression of arterial calcification in apolipoprotein E-mice is uncoupled from plaque growth and lipid levels. Endocrinology 150: 841-8, 2009. PMID:19176022

McRobb L, Handelsman DJ, Kazlauskas R, Wilkinson S, McLeod MD and Heathaker AK

Medi C, Kalman JM and Freedman SB

Meier C, Nguyen TV, Handelsman DJ, Schindler C, Kushnir MM, Rockwood AL, Meikle AW, Center JR, Eisman JA and Seibel MJ

Meier C, Seibel MJ and Kraenzlin ME
Use of bone turnover markers in the real world: are we seeing what we think we see? Journal of Bone Mineral Research: 24: 386-9, 2009. PMID:19183133

Miller MD, Thomas JM, Cameron ID, Chen JS, Sambrook PN, March LM, Cumming LG and Lord SR

Moharram MA, Brigger D and Lowe HC

Morgan ET, Goralski KB, Piquette-Miller M, Renton KW, Robertson GR, Chalavadi MR, Charles KA, Clarke SJ, Kacevska M, Liddle C, Richardson TA, Sharma R and Sinal CJ

Severe early-onset axial neuropathy with homoygos and compound heterozygous MN12 mutations. Neurology 70: 1678-81, 2008. PMID:18492277

Niknami M, Patel M, Witting PK and Dong Q

O’Toole BI and Catts SV

O’Toole BI, Catts SV, Outram S, Fierce KR and Cockburn J
The physical and mental health of Australian Vietnam veterans three decades after the war and its relation to military service, combat and PTSD. American Journal of Epidemiology 170 (5): 318-330, 2009. PMID:19644470

Page SL, Birden HH, Hudson JM, Thistlethwaite JE, Roberts C, Wilson I, Bushnell J, Hogg J, Friedman SB and Yeomans N
Medical schools can cooperate: a new joint venture to provide medical education in the Northern Rivers region of New South Wales. Medical Journal of Australia 188: 179-81, 2008. PMID:18324119

Parry SN, Ellis N, Li Z, Mairt P and Witting PK


Ethnic differences in drug metabolism and toxicity from chemotherapies. Expert Opinions on Drug Metabolism and Toxicology 5: 243-57, 2009. PMID:19335196

Pollard RL, Kennedy PJ and Matz PK
The use of artificial dermis (Integra) and topical negative pressure to achieve limb salvage following soft-tissue loss. Acta Biomater 8: 2019-33, 2009. PMID:18078796

Ramaswamy Y, Wu C, Dunstan CR, Hewson B, Eindorf T, Anderson GI and Zreiqat H


Redfern J, Briot T, Ellis E and Freedman SB

Redfern J, Briffa T, Ellis E and Freedman SB

Roo J, Castellano JM, Navarro VM, Handelsman DJ, Pinilla L and Tena-Sempere M

Robertson GR, Grant DM and Piquette-Miller M
Pharmacogenetics of pharmacoeconomics: which route to personalized medicine? Clinical Pharmacology & Therapeutics 85: 343-5, 2009. PMID:19395528

Robertson GR, Liddle C and Clarke SJ


Sartorius G, Ly LP, Sikarsik K, McLachlan R and Handelsman DJ

Seibel MJ

Sharma R, Cunningham D, Smith P, Robertson G, Dent O and Clarke SJ
Inflammatory (B) symptoms are independent predictors of myosupression from chemotherapy in Non-Hodgkin Lymphoma (NHL) patients–analysis of data from a British National Lymphoma Investigation phase III trial comparing...
Tan JS, Wang J, Younan C, Cumming RG, Rochtchina E and Mitchell P

Thomas SR, Witting PK and Drummond GR
Redox control of endothelial function and dysfunction: molecular mechanisms and therapeutic opportunities. Antioxidants & Redox Signaling 10: 173-65, 2008. PMID:18707220

Tseng AY, Lowe HC, Freedman SB and Brigger DB

Association study on glutathione S-transferase omega 1 and 2 and familial ALS. Amyotrophic Lateral Sclerosis 9: 81-4, 2008. PMID:18422547

Sharrma R, Zucknick M, Lendon R, Kacervska M, Liddle C and Robertson G

Sharrma R, Zucknick M, Lendon R, Kacervska M, Liddle C and Clarke SJ

Sherrington C, Lord SR, Vogler CM, Close JC, Howard K, Dean CM, Clemson L, Barraugh E, Ramsay E, O’Rourke SD and Cumming RG
Minimising disability and falls in older people through a post-hospital exercise program: a protocol for a randomised controlled trial of economic evaluation. BMC Geriatrics 9: 8, 2009. PMID:19245697

Sherrington C, Whitney JC, Lord SR, Herbert RD, Cumming RG and Close JC

Simanainen U, McNamara K, Davvy RA, Zajic JD and Handelsman DJ
Severe subfertility in mice with androgen receptor inactivation in sex accessory organs but not in testis. Endocrinology 149: 3308-8, 2008. PMID:18365274

Simanainen U, McNamara K, Gao YR and Handelsman DJ


Song C, Hsu K, Yamen E, Yan W, Fock J, Witting P, Geczy CC and Freedman SB
Serum amyloid A induction of cytokines in monocyes and lymphocytes. May 2009, in press

Song C, Shen Y, Yamen E, Hsu K, Yan W, Witting PK, Geczy CC and Freedman SB
Serum amyloid A may potentiate proinflammatory and proangiogenic events in acute coronary syndromes. Atherosclerosis 202: 596-604, 2009. PMID:18571179


Tan AG, Mitchell P, Flood YM, Birlutsky G, Rochtchina E, Cumming RG and Wang JJ

Yong A, Groenesteen P, Brigger D, Lowe H and Kritharides L
Late thrombotic occlusion of a left internal mammary artery graft causing ST-elevation myocardial infarction. International Journal of Cardiology 2009. PMID:19136315

Yong AS, Lowe HC, Ng MK and Kritharides L

Population pharmacokinetics of acyclovir in children and young people with malignancy after administration of intravenous acyclovir or oral valacyclovir. Antimicrobial Agents & Chemotherapy 2009. PMID:19145797


Glucocorticoid-dependent Wnt signaling by mural osteoblasts is a key regulator of cranial skeletal development in mice. Development 136: 427-36, 2009. PMID:19141672

Zhou H, Mak W, Zheng Y, Dunstan CR and Seibel MJ

Zorzi H, James B, Brigger D, Kritharides L and Lowe HC
FINANCIAL PERFORMANCE

Income & Expenditure 2001-2009

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Felicity Barr (Chair)

Felicity Barr’s interest in the issues of ageing developed during her service with the Commonwealth Department of Veterans’ Affairs, including five years as Deputy Commissioner in NSW. She has completed master’s studies in gerontology and is now working towards her doctorate in the Faculty of Health Sciences, University of Sydney. She chairs the NSW Ministerial Advisory Committee on Ageing, is also Chair of the Board of the War Widows’ Guild (NSW), Honorary Governor of the Ageing & Alzheimer’s Research Foundation, and President (NSW) of the Australian Association of Gerontology.

Danny O’Connor (Deputy Chair)

Danny O’Connor is the present General Manager, Concord Repatriation General Hospital. His previous experience includes working as a clinician with the Community Drug Advisory Service in Surry Hills, Sydney, a research officer with the New South Wales Drug and Alcohol Authority and then State Coordinator for methadone treatment in New South Wales. He worked in the public health division of the NSW Health Department as a senior policy analyst before becoming Director of Drug Health Services in Central Sydney Area Health Service. He later moved into hospital management with Central Sydney Area Health Service as General Manager, Sydney Dental Hospital and Oral Health Services. He currently serves on various committees as Deputy Chair, ANZAC Health and Medical Research Foundation, as a Member of Ministerial Asbestos Diseases Advisory Committee and sits on the Sydney Institutes of Health & Medical Research Board.

Eve Bosak

Professional career in accounting, finance and business strategy for almost thirty years in the public, private, academic and global development sectors. International experience as CFO, South Asia region, World Bank and senior positions with major public and private sector international corporations. Serving on many public and private sector Boards in Australia including CPA Australia and NSW War Widows’ Guild. She is a member of the Institute of Chartered Accountants in Australia, a Fellow of CPA Australia, and an Associate of the Institute of Chartered Secretaries and Administrators in Australia.

Professor David Cook

Professor David Cook currently holds the Chair of Cellular Physiology at The University of Sydney. He was awarded an MD in 1995, the Gottschalk Medal of the Australian Academy of Science in 1996 and became University of Sydney Medical Foundation Fellow of the Faculty of Medicine in 1997 when he was also promoted to professor. His research interests are in the role of ion channels and other transporters in the cell membrane and how control membrane transport activity. In addition to his research and teaching within the Department of Physiology, he serves as Deputy Chair of the Central Sydney Area Health Service Human Ethics Committee and chairs the Clinical Trials Subcommittee at Royal Prince Alfred Hospital.
ANZAC
Research Institute

BOARD

Professor David Handelsman
Professor Handelsman has been Director of the ANZAC Research Institute since its inception in 1998. He is an international expert in Andrology, the study of male reproductive health, medicine and biology. While studying for his PhD, he established the first clinical Andrology centre in Australia that has eventually become the first Hospital Andrology department in the country. He has served as adviser to the WHO Human Reproduction Programme, Secretary of the International Society of Andrology and President of the Endocrine Society of Australia. He was awarded the Susman Prize from the Royal Australasian College of Physicians in 1994 and the inaugural AMA Men's Health Award in 2003. He was promoted to a Personal Chair at the University of Sydney in 1996 to become the first Professor in Andrology in Australia.

Emeritus Professor Kerry Goulston
Kerry Goulston is Emeritus Professor of the University of Sydney. Previous experience includes being Associate Dean of the Northern Clinical School of the Sydney Medical School and Chair of the NSW Greater Metropolitan Clinical taskforce (GMCT). He has been a practising Gastroenterologist for many years and has a longstanding record in research and teaching. Currently Deputy Chair of the Australia Vietnam Medical Foundation (Hocmai).

Brian Lee
Brian Lee spent his career in the medical supply industry and retired as the Area Managing Director (Australia and New Zealand) for Baxter Healthcare. He was the past National President of the Leukemia Foundation of Australia and former director of Medical Specialties Australia. Brian has been a long-time advocate and supporter of ANZAC Health and Medical Research Foundation and currently chairs the Fundraising Subcommittee on the current Board.

Dr Charles Pawsey
After Charles Pawsey graduated from the University of Adelaide in 1967, he spent three years at Queen Elizabeth Hospital in Adelaide. Later at Greenslopes Hospital in Brisbane he worked as a National Heart Foundation Research Assistant undertaking research into the Renin-Angiotensin system and hypertension. He undertook his physician traineeship at Sydney Hospital in 1972-73 and his Cardiology training at Royal Prince Alfred Hospital in 1974-75 and at Johns Hopkins Hospital in 1976. Since 1977, he has been a Staff Cardiologist at Concord Repatriation General Hospital.

Godfrey (Rusty) Priest AM
Rusty Priest was an inaugural member of the ANZAC Health & Medical Research Foundation serving as its Deputy Chair from 1995 to 2003. Rusty enlisted in the 2nd AIF in June 1945, serving in Japan with British Commonwealth Occupation Forces from April 1946 to December 1948, the Australian Regular Army from 1946 to 1967 and the Emergency Reserve until 1975. Then he undertook a management position at the University of Sydney, retiring in 1990. He is a Past President of the Returned and Services League of Australia (NSW Branch), having held office between 1993 and 2002. He is extensively involved in all matters affecting the welfare of veterans and their dependants. He serves currently as Chairman of the Board of Directors of the Kokoda Track Memorial Walkway Ltd.
Professor Bruce Robinson

Professor Robinson was appointed Dean, Faculty of Medicine, University of Sydney, in May 2007. He is an Endocrinologist and Head of the Cancer Genetic Laboratory in the Kolling Institute. While undertaking studies for a Masters of Science degree he undertook molecular research work at the Brigham and Women’s Hospital and the Children’s Hospital, Harvard Medical School from 1986-1989 and was awarded a Doctorate of Medicine from the University of Sydney in 1990. He has developed and led the Cancer Genetics’ Laboratory since 1990 and has supervised over 20 doctoral and masters students working on the genetic basis for tumour formation and gene therapy. In 2003 Professor Robinson was warded the Daiichi Prize by the Asia and Oceania Thyroid Association for this work on the pathogenesis of thyroid cancer.

Professor Robinson has a strong interest in furthering relations between Australia and Asia and he is the Founding Chairman of Hoc Mai, the Australia Vietnam Medical Foundation, which sponsors and supports medical nursing, allied health and scientific exchanges between Australia and Vietnam. He is a Fellow of the Australian Institute of Company Directors.

Professor Robert Lusby

Professor Robert Lusby is the head of the University of Sydney Clinical School at Concord Hospital and an Associate Dean of the Faculty of Medicine. He is a Vascular Surgeon and heads the vascular surgical department of Concord Hospital. He has been president of the International Cardiovascular Society Australian and New Zealand Society. Professor Lusby has served with the Australian Army Medical Corp with deployments to Rwanda with the United Nations, Bougainville and East Timor with Interfet. Colonel Lusby has been Consultant Surgeon to the Australian Army and the Australian defence Force. Professor Lusby was a Board member of Macquarie and Northern Area Health Services, a councillor of the NSW branch of the Australian Medical Association and chairman of its Ethics committee. He was a foundation member of the Post Graduate Medical Council.

Clinical Assoc Professor Kerry Russell

Clinical Assoc Professor Kerry Russell is the Area Director of Nursing & Midwifery Services at Sydney South West Area Health Service. She has held a wide range of clinical and management positions and has a keen interest in workforce, particularly staffing and recruitment, continuing education for nurses and midwives and the development of partnerships to achieve mutual benefits.

Over a period of 4 years, Kerry successfully coordinated the overseas recruitment programs for NSW Health. She has undertaken a number of nursing reviews both in NSW and interstate. Kerry is a Board Member of the College of Nursing and is a Surveyor with the ACHS. In 2008, with a colleague, Kerry completed a whole of workforce review in the Greater Western Area Health Service and the North Coast Area Health Service as well as a Nursing Workforce Review for the Fiji Ministry of Health.
## DONOR HONOUR ROLL

### Corporations
- **James N Kirby Foundation**: $22,600.00
- **Beta Sigma Phi, Delta Master Sydney**: $1,000.00
- **Breville Pty Limited**: $100.00

### Community Organisations
- **Rotary Club of Five Dock Inc.**: $8,700.00
- **Macquarie Group Foundation Limited**: $2,500.00
- **Enfield-Croydon Park RSL Sub-Branch**: $2,500.00
- **Burwood RSL Club**: $1,000.00
- **RSL - Chester Hill-Carramar Sub-Branch**: $1,000.00
- **Kingsgrove RSL Women’s Auxilia**: $850.00
- **The Returned & Services League of Australia**: $200.00
- **Combined Services RSL (Sydney)**: $100.00
- **Miranda RSL Sub-Branch**: $100.00
- **Returned & Services League of Australia Clovelly**: $100.00

### Bequest
- **CHURM Bequest**: $125,000.00

### FOTARI
- **John Loudon**: $50,000.00
- **Clare Loudon**: $50,000.00
- **Gordon Druitt**: $20,000.00
- **Mrs Margaret Graham**: $6,000.00
- **Mrs A Mildenhall**: $5,000.00
- **Annette Lemercier**: $3,000.00
- **Grand Coral Pty Ltd**: $1,300.00
- **Gregory Falk**: $1,100.00
- **John Linsley**: $1,092.00
- **Dr Charles Pawsey**: $1,040.00
- **Mrs DJ Davy**: $1,000.00
- **Andrew G Richardson**: $1,000.00
- **Steven Kalowski**: $999.96
- **Raymond Davis Paul**: $720.00
- **Lesley Cherry**: $700.00
- **Ramon Bullock**: $680.00
- **Paul Freame**: $625.00
- **Major John P. Kelly (Ret’d)**: $600.00
- **Ross Bradbury**: $520.00
- **G D Pearce**: $520.00
- **Dr Marjorie J Pink**: $500.00
- **Majorie J Pink**: $500.00
- **Richard Bloor**: $500.00
- **Eileen Maria Collins**: $400.00
- **Annette Gibson**: $350.00
- **Doreen Walker**: $300.00
- **Mr Alan Davidson**: $200.00
- **Claire Fleming**: $200.00
- **William James Forbes**: $200.00
- **Mr WB & Mrs MJ White**: $200.00
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