SCHEDULE OF MEDICAL RESEARCH
GRANTS AND SCHOLARSHIPS AWARDED FOR 2015

Kidney Health Australia's vision
To save and improve the lives of Australians affected by kidney disease.

SUPPORT FOR KIDNEY RESEARCH

Kidney Health Australia is one of the main non-government supporter of kidney and urinary tract biomedical research in Australia. In 2010 the Board of Directors determined that in the future there should be a shift in the focus of our research support program towards project grants in the public health area of CKD.

A total of fifty-four applications were received by Kidney Health Australia for funding support in the calendar year 2015. Kidney Health Australia awarded eighteen grants and scholarships to the value of $500,000 into kidney related research projects in University departments, medical research institutes and hospitals throughout Australia. Support to investigator driven research totalled $388,000, plus an additional $75,000 funding for strategic targeted research.

In 2015 our Nursing Scholarship program entered its seventh year. This program aims to support Renal Nurses pursuing a Masters Degree, to encourage nurses to pursue a career in renal nursing, in any of its components - clinical practice, education or research - across the continuum of CKD, from prevention to early detection to renal replacement.

Dr Tim Mathew
Medical Director

Investigator Driven Research Grants and Scholars

BIOMEDICAL SCHOLARSHIPS

The new direction of KHA research funding aimed at a public health agenda included a reduction in the number of new scholarship offers. The nephrologists are in general well supported in post-graduate study by funds specifically targeted at medical graduates and scientists have access to a variety of sources for PhD support.

These scholarships permit talented researchers to pursue full-time research for up to three years, qualifying them to obtain a doctoral degree or equivalent at the end of this period. Individual scholarships are valued at $27,000 for scientists and $35,000 for medical graduates, per annum. These scholarships are tax free to the holder and are an investment in the future of Australian medicine.

In 2015, two new Medical Research Scholarship were awarded. Three Science Research Scholarships and one Medical Research Scholarship were awarded continued funding. Funding allocated was valued at $186,000.

We actively encourage students receiving KHA funding, to apply for NHMRC scholarships each year, to make the most of our research dollar.

Sponsored Scholarships: Kidney Health Australia encourages groups and individuals to consider supporting research in this manner. Funding biomedical scholarships is a most valued and meaningful way to ultimately promote better health outcomes in kidney patients. We are always interested in hearing from individuals wishing to donate funds for scholarships or grants. All offers are valued and presented to the Medical and Scientific Advisors for consideration. If you wish to find out more, contact the Medical Director's Office and we would be delighted to discuss this with you.

Continuing PhD scholars for 2015

Dr Qi Cao supervised by Prof David Harris (*Science*)
Westmead Millennium Institute – University of Sydney NSW
Defining the role of the major subsets of renal mononuclear phagocytes

Renal mononuclear phagocytes (rMP), conventionally comprising macrophage and dendritic cells, play a central role in health and disease of the kidney. We have identified four subsets of rMP in mouse kidney. However, the role of subsets of rMP in chronic kidney disease (CKD) is unclear. We will assess the phenotype and function of rMP subsets in different mouse models of CDK, including adriamycin nephropathy and anti-glomerular basement membrane nephritis. The studies will provide therapeutic potential by using regulatory type of rMP subsets or targeting pro-inflammatory type of rMP subsets to treat CKD.

Mr Aowen Zhuang supervised by Prof Josephine Forbes (*Science*)
Mater Research QLD
Problems with protein folding and trafficking are novel mediators of kidney disease

Kidney disease leading to heart attacks and strokes affects up to one third of Australian individuals with diabetes (~400,000 persons) and is one of the most deadly and poorly understood chronic complications, with current therapies only slowing the progression. When proteins are manufactured in cells they receive a number of tags which direct them to fold correctly and traffic to the right location. Oligosaccharyltransferase-48 (OST-49) facilitates the addition of one of these protein tags, via a process called N-glycosylation which is essential for cell survival. There are many important proteins which need N-glycosylation for their normal function in the kidney including the protein receptor for the hormone insulin and cell transporters which help kidney cells to take up sugars for energy production such as GLUT1 and GLUT4. This project aims to investigate if changing the amount or location of OST-48 in kidney cells contributes to the development of kidney disease in diabetes and ultimately if this can be targeted to improve kidney health. We will use a number of approaches including mouse models of diabetes where OST-48 has been altered in specific kidney cells, as well as human cells lines and kidney tissues taken from diabetic patients.

Dr John Whitlam supervised by Prof David Power (*Medical*)
Austin Health VIC
A simpler, less invasive test for monitoring kidney transplant rejection

Kidney transplantation is a treatment for kidney failure. 20% of transplanted kidneys undergo rejection. This can damage or destroy the transplant. Presently, rejection is identified when the kidney function deteriorates. This can occur late after rejection has started. To confirm the diagnosis, an invasive biopsy associated with discomfort and risks is required. This study will evaluate the use of a simpler blood test to monitor for rejection, allowing earlier and safer identification and treatment.

Miss Camilla Hanson supervised by Dr Allison Tong (*Science*)
University of Sydney NSW
Disparities in access to living donor kidney transplantation

Kidney transplantation improves life expectancy and quality of life in patients with end-stage kidney disease, compared with being on dialysis. However, the wide variation in living kidney donation rates across Australia remain unexplained. This study will identify patient, clinician, and structural barriers to living kidney donation, and describe both patient and clinician perspectives on barriers and disparities in Australia. Interviews and surveys will be used to collect data, and the results will provide evidence-based recommendations for changes to policy and clinical practice to increase access to living kidney donation.

Newly awarded scholars for 2015

Dr Emma O'Lone supervised by A/Prof Angela Webster (*Medical*)
University of Sydney NSW
Heart disease: priorities and outcomes for people with chronic kidney disease

This thesis will investigate the patterns, causes and effects of heart disease in patients with chronic kidney disease. Firstly we will look at how heart disease impacts on hospital admission patterns and mortality over time. We know that heart disease and kidney disease can both contribute to changes in the brain, affecting cognition. We will summarise the current

evidence to try and establish exactly how cognition is affected and how this then contributes to patient outcomes and quality of life. Finally, we will explore how well current research funding reflects disease burden, research output and the stated priorities of patients with chronic kidney disease.

Dr Peggy Teh supervised by Dr Axel Kallies (*Medical*)
The Walter and Eliza Hall Institute of Medical Research VIC
The role of immune cells in the kidney

Kidney disease is a major public health problem. The number of patients with kidney disease is rising. We need to understand why some individuals are at risk of having kidney disease that will require kidney replacement therapy. We believe that a special population of immune cells called T cells that live in the kidney serve an important role in maintaining a fine balance and preventing damage to this important organ. This research will investigate the details of the development the regulation of these T cells and provide an explanation for the variability observed in the individual's response following kidney injury and the development of chronic kidney disease.

SCHOLARSHIPS FOR NURSES PURSUING MASTERS DEGREE

Kidney Health Australia provides grants for Registered Nurses wishing to study for a Masters Degree in Nursing or Public Health. The aim of the program is to encourage nurses to pursue a career in renal nursing in any of its components - clinical practice, education or research - across the continuum of chronic kidney disease from prevention to early detection to renal replacement.

Six renal nurses were awarded scholarships valued at $3,000 each, for a maximum of three years – total of $18,000 for calendar year 2015.

Continuing Nursing scholars for 2015

Mrs Tania Burns - Master of Nursing (Research) - University of Wollongong, NSW
Mr Grant Ramke - Master of Nursing (Clinical Education) - James Cook University, QLD
Mrs Debra Turner - Master of Nursing (Leadership and Management) - University of South Australia, SA
Mrs Gethsy Jayaseelan - Master in Clinical Practice (Renal Stream) - Australia Catholic University, VIC
Ms Laura Austin – Master of Nursing (Nursing Education) - Charles Sturt University, NSW

Newly awarded scholar for 2015

Mrs Jo-Anne Moodie - Master of Nursing (Nurse Practitioner) - University of Melbourne, VIC

SPECIAL PROJECT FUNDING

Prof Melissa Little
University of Queensland QLD
Kidney mesenchymal stem cells in tubular development, repair and turnover

The objective of the research is to generate induced pluripotent stem (iPS) cell lines from renal patients identified as carrying a disease causing mutation responsible for their renal disease. Funding will initially support the whole exome sequencing of patients identified by Dr. Andrew Mallett. It will then support the derivation of an iPS cell line from such a patient for further characterisation in comparison to normal iPS cells.

Targeted or Strategic Research

This year $75,000 was awarded to targeted areas deserving support and assisting Kidney Health Australia in its mission to free Australia of kidney disease.

ANZDATA REGISTRY

The internationally acclaimed ANZDATA Registry has been funded substantially by Kidney Health Australia since its formation. It is one of the major accomplishments of the Australian and New Zealand nephrology community and has contributed importantly to knowledge, planning and best practice in clinical care over many years. For calendar year 2007, MSAC awarded ANZDATA Registry $75,000 annually towards its general operating costs. Learn more at www.anzdata.org.au

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PROJECT GRANTS

Project grants worth $43,200 each for use over 1-2 years were a new addition to the KHA program. The competition was strong and most applications were considered suitable for support should more funds be available.

Previous Project Grants 2014

Chief Investigator: A/Prof Josephine Clayton
Co-Investigators: Prof Carol Pollock, Dr Tim Luckett, Dr Rachael Morton, A/Prof William Silvester, Dr Karen Detering, Ms Lucy Spencer
Northern Clinical School, Sydney Medical School – The University of Sydney NSW
Investigating barriers and facilitators to advance care planning for dialysis and pre-dialysis patients

Recent guidelines have emphasised the importance of providing better support for communication and decision-making about end-of-life (EOL) issues for people with end-stage kidney disease (ESKD) and their families. Advance care planning (ACP) provides a potential solution by promoting discussion between patients, families and healthcare teams regarding values, goals for care, prognosis and EOL issues, as well as facilitating documentation of the patient's wishes for EOL care. International research, however, suggests that ACP may not be widely implemented in renal units due to various barriers. The proposed project aims to describe current Australian practice in, and attitudes to, ACP for people with ESKD and building an understanding of barriers, and facilitators to ACP implementation, as well as patient, family and health professional preferences for content, timing and mode of delivery of ACP. We have designed an online survey of renal clinicians' views on these topics. Ethics approval has been obtained and the survey has been disseminated to renal clinicians via the Renal Society of Australian and the Australian and New Zealand Society of Nephrology through their newsletters and at the Annual Scientific meeting and Conference. So far there have been 246 respondents to the survey. Ethics approval has been sought for qualitative interviews with ESKD patients, their families and renal clinicians. Qualitative semi-structured interviews will commence as soon as the final ethics approval has been obtained. The findings will inform design, refinement and implementation of ACP programs for renal units in Australia.

Chief Investigator: Dr Jeff Coombes
Co-Investigators: Miss Kassia Weston, A/Prof Nicole Isbel, Prof Rob Fassett,
School of Human Movement Studies – The University of Queensland QLD
Exercise training in chronic kidney disease

The optimal exercise prescription for patients with chronic kidney disease (CKD) has not been established. Current guidelines suggest that patients perform moderate intensity continuous exercise, however this is not based on high quality evidence. High intensity interval training has been shown to be superior to moderate intensity continuous training in improving cardiorespiratory fitness, improving cardiovascular risk factors, increasing muscle function and is more enjoyable. This has been shown in healthy individuals and patients with heart disease, obesity and diabetes. This type of exercise is yet to be studied in CKD patients. Therefore, the aims of this study are to investigate the effects of high intensity interval training on cardiorespiratory fitness, muscle function, muscle wasting and exercise adherence in CKD patients. The aim is to allocate thirty patients with CKD to either high intensity interval or moderate intensity continuous. To date, 14 participants have completed the 12 week training program (5 in the moderate intensity training group and 9 in the high intensity interval training group). Recruitment is still currently underway to enrol the remaining participants in the study. Anecdotally, patients in the high intensity interval training group enjoy the variety of the different exercise intensities. We hope that the findings from this study will have important implications for exercise prescription and understanding the effects of exercise training on muscle wasting in the CKD population.

Chief Investigator: Prof Peter Ebeling
Co-Investigators: A/Prof Craig Nelson, Dr Mahesan Anpalahan
Department of Medicine– The University of Melbourne NSW
Nitrates for bone protection in Chronic Kidney Disease

Studies have consistently shown that low trauma fractures are widely prevalent among patients with chronic kidney disease (CKD). However, the management of this condition remains controversial because the safety and efficacy of most currently available treatments for the prevention of fractures have not been adequately tested in patients with CKD. Further, many of these treatments are potentially toxic to kidneys and may also have deleterious effects in certain types renal bone disease. Therefore, there is a need for investigating new therapies for bone protection in CKD, using drugs that are safe and effective in patients with CKD. Recent evidence suggests that nitrates have all the necessary attributes to be a postmenopausal women, although not specifically in patients with CKD, and their safety in CKD, including in patients with advanced CKD, is well established. The current study is designed to assess the efficacy of isosorbide dinitrate, a commonly available oral nitrate preparation in Australia, in the prevention of bone loss in patients with moderately severe kidney disease.

Chief Investigator: Prof Josephine Forbes
Co-Investigators: Prof Anthony Russell, A/Prof Nicki Isbel, Prof Carmel Hawley, Prof Arnold Ng, Prof Andrew Cotterill, Prof Mark Harris, Prof Kim Donohue, Dr Michael Ward, Horst Joachim Schirra
Glycation and Diabetes – Mater Research QLD
Can disturbances in energy production provide biomarkers for kidney disease in diabetes?

Diabetic individuals with kidney disease make up the greatest proportion of person requiring a kidney transplant or dialysis in Australia. We therefore need to find early detection markers as well as develop a better understand of why diabetic kidney disease occurs to design more effective treatments. It is understood, however, that maintaining the function of our cell power stations, the mitochondria, is important for kidney function, since kidneys have a very high demand for energy production from fuel sources such as sugars, lactate and simple fats. In diabetes, this fuel balance is thought to be interrupted which may cause damage to kidneys. Hence within this proposal, we will examine fuels and fuel production waste products in the urine giving us a "finger print" of kidney energy metabolites at that time. Here we aim to assess if we can detect differences between individuals with and without diabetes, as well as those with impaired kidney function. Secondly, we will use medical imaging to look at the fuel "content" of the kidney and see how this relates to urine profiles in these individuals. Overall, we aim to understand if certain fingerprints of fuel metabolites in urine and associated with kidney disease in diabetes and therefore may be worth testing as predictors of disease in larger populations.

Chief Investigator: A/Prof Nicole Isbel
Co-Investigators: Dr Michael Burke, Dr Christine Staatz, Dr Katherine Barraclough, Prof Adele Green, Dr Scott Campbell
Department of Nephrology – Princess Alexandra Hospital QLD
Identifying genetic and pharmacological predictors for non-melanoma skin cancer in kidney transplant recipients

Australian kidney transplant recipients have a twenty times greater risk of developing skin cancer compared with general population and may suffer from hundreds of cancerous lesions during their lifetime. Surgical removal of skin cancers can be disfiguring, and if they are not detected early, the cancers can be fatal. Skin cancers in transplant patients develop secondary to both past sun exposure and the unwanted side effects of immune suppressing medications that are used after the transplant to protect the kidney. This study aims to identify how genetic differences between transplant patients influence the risk of skin cancer following treatment with immunosuppressant medications. The proposed study has the potential to guide long-term treatment choices in at risk individuals and to identify patients who might benefit from more intensive skin cancer checks. This has the potential to enhance the duration and quality of life for thousands of Australians who have received a kidney transplant.

Newly awarded Project Grants for 2015

Thirty-eight applications were received. Four were awarded funding, a total of $184,000.

Chief Investigator: A/Prof Grahame Elder
Co-Investigators: A/Prof Jacqueline Centre, Prof Tuan V. Nguyen & Dr Lorraine Pereira
Westmead Hospital VIC
Has the introduction of non calcium-based phosphate binders reduced mortality for patients on dialysis in Australia?

This study will look at whether newer and more costly non calcium-based phosphate binding drugs, used to reduce dietary phosphate absorption by patients requiring dialysis, reduce the risk of cardiovascular events and mortality. In the 1970s, patients had been treated with aluminium-based phosphate binders, but owing to potential aluminium toxicity, most patients were changed to calcium-based phosphate binders. Calcium based drugs remain the most prescribed phosphate binders, but two newer non calcium containing drugs, sevelamer hydrochloride and lanthanum carbonate, were introduced 6 and 7 years ago. This corresponds to a period during which concerns have been raised at the risk high doses of calcium may pose for increased vascular calcification, cardiovascular complications and death. The proposed study is a retrospective study of all adults who have undergone dialysis since the new drugs were introduced in 2007, to determine whether their introduction and progressive displacement of calcium-based binders has influenced mortality and cardiovascular events amongst Australians on dialysis.

Chief Investigator: Prof Zoltan Endre
Co-Investigators: A/Prof Philip Peake, Dr Grant Luxton & Ms Heather Hall
Prince of Wales Hospital
Establishing a simple blood test able to detect subliminal kidney injury

The kidney can increase the filtration rate in response to increased blood flow. This renal reserve capacity is critical when a kidney is removed in organ donation, or when damaged. Reserve decreases but is not fully lost as kidney function declines with disease and age. However, reserve is rarely measured since it has not been standardised, and current measurements of kidney filtration rate [GFR] are expensive and cumbersome. This project aims to develop a simple and cheap test of the kidney's ability to increase filtration rate in response to a protein meal challenge. We will evaluate serum cystatin C concentrations before and after protein loading to determine renal reserve in normal volunteers and in patients with chronic kidney disease (CKD). This measurement will be validated against current gold standard measurements of GFR. If validated, this test will allow us to assess marginal kidney donors and patients with suspected subliminal kidney disease. Most importantly, defining renal reserve should allow us to define prognosis more accurately in patients with CKD, and in the larger number of elderly patients with reduced GFR, who may have either progressive CKD, or simply have 'old' but healthy kidneys.

Chief Investigator: Prof Craig Gedye
Co-Investigators: Dr Nikola Bowden & Prof Rodney Scott
University of Newcastle NSW
Destroying kidney cells that evade current treatments

Advanced kidney cancer is incurable. Tablets that block blood vessels help many patients, but inevitably fail. My research has revealed that kidney cancer is better understood as a difference kind of cancer than we previously through; a "sarcoma' rather than a "carcinoma". I have also found that it highly adaptable, with some cancer cells able to act as either "hunters" or as "gatherers". When tablet treatments fail, the "hunter"-type cells predominate. My research program will investigate how kidney cancer cells adapt, identify critical targets to block this adaptation, and identify and "repurpose" old, approved drugs that work with blood-vessel blocking tablets to improve the survival of patients with advanced kidney cancer.

Chief Investigator: Prof Angela Webster
Co-Investigators: Dr Philip Masson, Prof Jonathan Craig, Prof Rustam Al-Shahi Salman, Dr Emma O'Lone, Dr David Roy & Dr Patrick Kelly
University of Sydney NSW
Death from stroke and heart disease in people with end-stage kidney disease

People with ESKD have greater risk of heart attack and stroke than the general population. General population deaths from stroke and heart disease have each declined by 2%/year since 1970, because of effective prevention and treatment. The commonest cause of death for people who are on dialysis or have a transplant is heart disease and stroke. What is not

known is if the death rate from stroke and heart disease has decreased at the same rate as for the general population. While not proven decisively, it seems likely that prevention drugs driving improvements from the general population don't have the same benefits for people with kidney failure. We don't know if clot busting treatments for heart attack or stroke work in people with kidney failure, as they have been excluded from trials. Large numbers needed to observe treatment differences mean new trials are impractical and logistically impossible. While this project can't answer some of the questions of prevention or treatment response directly, by looking at the pattern of deaths from heart disease and stroke over time, if we see the same improvement in death rate as the general population this will be very reassuring. If we see a lack of improvement, it will be another single that prevention and treatment options might be at best ineffective, or at worse harmful to people with kidney failure. This project will generate new evidence to either underpin current practice, or to drive new research about the treatment response of heart disease and stroke in people with kidney failure. Whatever the findings, the results will be relevant to healthcare providers, policy makers, researchers and people with kidney failure.