SCHEDULE OF MEDICAL RESEARCH
GRANTS AND SCHOLARSHIPS AWARDED FOR 2013

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 forty-two applications were received by Kidney Health Australia for funding support in the calendar year 2013. Our Medical and Scientific Advisory Committee awarded eighteen separate grants and scholarships to the value of $491,000 into kidney related research projects in University departments, medical research institutes and hospitals throughout Australia. Support to investigator driven research totalled $401.000, plus an additional $75,000 funding for strategic targeted research.

In 2013 our Nursing Scholarship program entered its sixth 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 the withdrawal 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 2013, two Medical Research Scholarships were awarded continued funding. Three new Science Research Scholarships were newly awarded. Funding allocated was valued at $151,000.

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 Advisory Committee 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 2013

Dr Kevin Chow supervised by A/Prof Andrew Lew (*Medical)*
Walter and Eliza Hall Institute of Medical Research, VIC
The molecular regulation of monocyte derived dendritic cells

Islet transplantation provides a potential cure for patients with type 1 diabetes. Successful transplantation requires the use of life long anti-rejection treatment that can be associated with significant side effects. A better understanding of the immune response to transplantation may allow for the development of improved anti-rejection treatments. We are investigating the role that monocyte derived dendritic cells play in transplant rejection. These cells are important in activating other components of the immune system and have been shown to play a role in the immune response to infection. We have developed methods to deplete these monocyte derived dendritic cells in diabetic mice that have received an islet transplant in order to understand the role that they play in transplant rejection.

Dr Veena Roberts supervised by Dr Karen Dwyer (*Medical*)
University of Melbourne - St Vincent's Hospital VIC
Reducing chronic kidney scarring

During the process of transplantation, the donor organ (such as kidney) is starved of blood (ischemia) at the time of donor kidney procurement. This initiates a series of cellular events which are detrimental to the donor organ. To minimise these effects the donor organ is stored on ice which slows the metabolism of the donor organ minimising such adverse effects. Engraftment and reperfusion of the donor kidney with blood although essential to halt the effects of ischemia promotes an inflammatory injury. Together this injury is ischemia reperfusion injury (IRI). IRI impacts on both the short and long term function of the graft and therapeutic strategies to minimise the effect of IRI are the basis on intense ongoing research.

Adenosine is a substance normally produced in the body by the action of the enzyme CD39 and can protect against IRI. We have preciously shown that donor kidneys from mice that over-express CD39 are protected from acute injury following IRI and in renal transplantation. The aim of this study is to determine if the acute protection conferred by CD39 over-expression translates into improved long term outcome.

Dr Scott Wilson supervised by Prof Stephen Harrap (*Medical)*
Department of Nephrology – University of Melbourne, Royal Melbourne Hospital VIC
Understanding changes in blood pressure in dialysis patients with chronic renal failure – a comprehensive clinical and genetic analysis

Over the past 3 years we have been investigating the patterns and mechanisms of how blood-pressure (BP) behaves in kidney patients requiring dialysis, and how this is different from non-dialysis requiring patients, both with, and without kidney disease. Our results thus far have been strarling, revealing that significant, clinically silent BP fluctuations are both common and unrecognised in standard dialysis practice. These observations go some way towards explaining the significantly increased risks of cardiovascular disease and death to which dialysis patients are exposed. Our data has highlighted some limitations in the way clinicians have historically considered BP behavior on dialysis, and we have developed a set of revised definitions which can be considered more clinically helpful to both medical teams, and patients, going forward. These ideas are the subject of a peer-reviewed paper that will be presented at the American Society of Nephrology meeting in San Diego (November 2012), with the underlying data being presented at both local and international meetings over 2011 and 2012. We remain grateful to Kidney Health Australia for their support of our research, which is helping us to improve the quality of care and potential life-expectancy of our kidney disease patients.

Newly awarded scholars for 2013

Mr Thomas Rogerson supervised by Dr Angela Webster (*Science*)
The Centre for Kidney Research - The Children's Hospital Westmead NSW
Evidence based testing and outcomes in renal transplantation

In transplant medicine clinicians rely on diagnostic tests to identify disease and guide treatment. In particular, diagnostic tests play an important role in pre-treatment assessment to determine the compatibility of potential donors and recipients, and detect infectious diseases. Continuing on from previous research, the first three projects of this PhD will focus on diagnosis test evaluation. These projects include a pilot stage of larger primary study to determine accuracy of test for latent tuberculosis and their cost-effectiveness in Australia, and a review of new technologies for donor-recipient

tissue matching. The second theme of this PhD will focus on the issue of organ scarcity in Australia and the potential for so called 'high risk' donor organs to be utilised in select groups of patents. This theme will encompass two projects, the first of which is a study of kidney transplant in patients with chronic infectious diseases (hepatitis C/B and HIV) using pre-existing registry data. The second project is a review of the literature of kidney transplant recipients that have received an organ from a 'high risk' donor.

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.

Miss Brooke Huuskes supervised by A/Prof Sharon Ricardo (*Science*)
Monash immunology and Stem Cell Laboratories - Monash University VIC
Investigating the use of stem cells in conjunction with anti-fibrotic treatment to reverse scarring of the kidney

The incidence of kidney disease is increasing at a rate approximately 7% per year worldwide. Kidney transplantation remains the preferred method of treatment for patients with end-stage renal disease. However due to the significant cost associated with this treatment and that fact that there is a severe shortage of available organs, it is imperative that cellular based therapies aimed at restoring kidney function are offered as alternatives. Mesenchymal stem cell (MSC) therapy has been reported to relieve kidney injury and promote structural repair, however their viability is thought to be hampered by scar formation. The use of anti-fibrotic factors, such as the hormone relaxin, reveres scar formation in many fibrotic disease, including renal pathologies. Background studies demonstrate that the combination of MSC and relaxin was more effective in preventing renal fibrosis than either treatment alone.

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.

One renal nurses were awarded scholarships valued at $3,000 each, for a maximum of three years –total of $12,000 for calendar year 2013.

Continuing Nursing scholars for 2013

Mrs Wendi Bradshaw - Master in Nursing Practice - Deakin University, VIC
Ms Toni East - Master of Nursing - Nurse Practitioner - Flinders University, SA
Ms Anthony Perkins - Master of Nursing - Advanced Practition – University of Newcastle, NSW

Newly awarded scholars for 2013

Ms Laura Austin - Master of Nursing (Nursing Education) - Charles Sturt University, NSW

SUMMER VACATION SCHOLARSHIPS

These scholarships are now valued at $3,000 each, and are designed to provide assistance to undergraduates undertaking summer vacation research in the area of kidney and urinary tract.

Miss May Wong supervised by Prof Carol Pollock
Kearnes Facility, Kolling Institute of Medical Research, Royal North Shore Hospital NSW
The role of anti-inflammatory agent in renal fibrosis

Renal fibrosis is a progressive process that ultimately leads to end-stage renal failure, a devastating disorder that requires dialysis or kidney transplantation. The pathogenesis of renal fibrosis represents a failed wound-healing process of the kidney tissue after chronic, repeated injury. Several cellular pathways have been identified as the major avenues responsible for the recruitment of inflammatory cells. Recent evidence suggests that reactive species oxygen, the by-products of these inflammatory processes, initiate a vicious cycle of injury and repair. Currently, the agents we have at our disposal are only partly effective and thus targeting the early phases of cellular response to injury and inflammation may be a promising means to limit tubulointerstitial fibrosis in the kidney.

Targeted or Strategic Research

This year $75,000 was awarded by the Medical and Scientific Advisory Committee 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

PROJECT GRANTS

Project grants worth $45,000 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 2012

Chief Investigator: Dr Rachael Morton
Co-Investigators: Dr Nicholas Gray & Prof Peter Kerr
Associate Investigators: A/Prof Kirsten Howard, Dr Paul Snelling & Dr Angela Webster
School of Public Health, Sydney Medical School – University of Sydney NSW
Patient Information About Options For Treatment (PINOT) follow-up study

Lay Report
Aim: The primary aims of the Patient INformation about Options for Treatment (PINOT) Follow-up Study are to determine the proportions of patients, identified in the 2009 PINOT cohort that: (i) Made the transition to home dialysis, after an initial start on centre-based haemodialysis; (ii) Commenced dialysis, or a time-limited trial of dialysis within 3 years, after confirmed plans for conservative care. **Background:** The Australian observational study Patient INformation about Options for Treatment (PINOT), collected data from 66 of 73 Australian renal units about the initial and planned treatment of an incident cohort of patients with stage 5 CKD (n = 721). The results showed 443 of 721 (61%) new patients initially commenced centre-based dialysis, 146 (20%) commenced a home therapy and 102 (14%) planned for conservative care. In 2011 a Kidney Health Australia grant was awarded for follow-up of the treatment(s) and health services utilised by the original cohort. **Methods:** All participating renal units will complete a web-survey detailing PINOT patients' treatment history, dialysis access and mortality. Additional questions will collect data on reasons for non-initiation of planned home dialysis and end-of-life-care for conservative care patients. The hypotheses to be tested are that: a) 50% of stage 5 CKD patients who plan for home dialysis do not commence home dialysis within 3 years, and instead remain on centre-based haemodialysis; and b) less than 15% of stage 5 CKD patients who plan for conservative care commence dialysis within 3 years. **Results:** The survey has been developed and will be piloted at 4 test centres. **Conclusions:** The PINOT follow-up study will provide valuable insights into determinants of the uptake of and barriers to home dialysis and planned conservative care.

Chief Investigator: Dr Lynelle Moon
Co-Investigator: A/Prof Stephen McDonald, Ms Frances Green & Ms Claire Sparke
Health Group, Australian Institute of Health and Welfare (AIHW) ACT
Agreement of hospital admitted patient diagnoses with cause of death diagnoses for patients with end-stage kidney disease

Our study aims to use linked hospital and mortality data to establish whether mortality records in Australia reflect the actual disease pattern of people with ESKD. In the absence of a full validation study, it is possible to use existing linked health data from New South Wales (NSW) and Western Australia (WA) to compile a full profile of a patient's hospitalisations and death records and assess the agreement between hospital diagnoses and causes of death.

Detailed planning, including of the analysis scope and methods, has been undertaken. Each of the states has complex processes that need to be followed in order to obtain the linked data. These have been completed for WA, and remain in progress for NSW. Obtaining these data has taken many months, as it has required a number of ethics applications and approvals. We have recently received data from WA and initial documentation and validation of the data is in progress. We continue to follow the various steps needed to obtain the NSW data, including ethics applications. Once NSW data arrive, we expect to be able to quickly apply what we have learned with the WA data.

Chief Investigator: Dr Martin Gallagher
Other Investigators: Prof Alan Cass, Dr Sradha Kotwal & Dr Angela Webster
Renal and Metabolic Division, The George Institute for Global Health NSW
Outcomes and burden of renal disease in NSW

We gained ethical approval for this project in the first part of this year through the NSW Population & Health Services Research Ethics Committee. Approval of all the relevant data custodians was subsequently obtained and the data extraction is now complete. The data has recently been transferred to the secure servers of The George Institute for Global Health. The data analysis has now commenced and we anticipate the first round of results by early 2013. We anticipate the first publication from this project in quarter 2 of 2013 as well the presentation of results at the World Congress of Nephrology in May 2013 and the ANZSN Annual Scientific Meeting later in 2013. Our original progress planned to conduct the project over the two years 2012-2013 and progress to this point suggests that this timeline remains appropriate. We have also furthered our collaboration with investigators from the School of Public Health at the University of Sydney (Drs Angela Webster and Phillip Masson) to further extend the analyses of the dataset. This collaboration has the potential to enhance the scope and impact of the project substantially.

Chief Investigator: Dr Germaine Wong
Co-Investigators: Prof Jonathan Craig, Dr Steven McTaggart & Dr Allison Tong
Associate Investigators: Dr Gabrielle Williams, A/Prof Kirsten Howard, Dr Andrew Hayen & A/Prof Philip Clarke
Centre for Kidney Research, Kids Research Institute, the Children's Hospital at Westmead NSW
Wealth and health in kids with CKD

We would like to inform Kidney Health Australia that the proposed research project funded by Kidney Health Australia has gone according to our proposed plan with good progress to date. We have received ethics approval to conduct this study from the two participating research sites, The Children's Hospital at Westmead in Sydney and the Royal Children's Hospital in Brisbane. We have designed questionnaires to measure outcomes of wealth and health in chronic kidney disease patients that involves reporting of child factors, caregiver burden and the impact of chronic kidney disease on their quality of life. We have also designed semi-structured interview schedules to measure their experience of chronic kidney disease, social and financial support during follow-up of these patients. We have planned clinical follow-up of the study participants and data-linkage with ANZSN registry at the completion of the study. Currently, we are enrolling pilot study patients from both Sydney and Brisbane and we are well on track. We are grateful to Kidney Health Australia for supporting this research project.

Chief Investigator: A/Prof Nicole Isbel
Co-Investigators: A/Prof Carmel Hawley & Dr Rathika Krishnasamy
Associate Investigators: A/Prof Grahame Elder, Dr John Coucher, A/Prof Jeff Coombes & Prof David Johnson
Department of Nephrology, Princess Alexandra Hospital QLD
A study investigating relationship between bone and vascular health in patients with Chronic Kidney Disease

Patients with chronic kidney disease (CKD) have a higher risk of cardiovascular disease (CVD). Treatments already in use for CVD may not work as well in CKD patients because of the complex problems these patients suffer such as blood vessel

stiffness and calcification. There is evidence of an important link between changes in bone density and CVD in these patients, but a better understanding of how and why these changes occur is needed. We will look at whether a new scan technology using low radiation exposure can detect changes in the bones of CKD patients that predict the risk of CVD. By detecting changes in the bones earlier, better treatments can be offered to prevent CKD patients developing loss of bone density and to prevent blood vessel calcification.

Newly awarded Project Grants for 2013

Sixteen applications were received with five awarded funding by the Medical and Scientific Advisory Committee with a total funding of $225,000.

Chief Investigator: A/Prof Martin Gallagher
Co-Investigators: A/Prof Josette Eris & Dr Bruce Cooper
Associate Investigators: A/Prof Stephen McDonald, Prof Alan Cass, Dr Sradha Kotwal & Dr Paul Snelling
Renal & Metabolic Division - The George Institute for Global Health NSW
Using novel health service data to improve the outcomes of dialysis patients

Increasing numbers of Australian patients and families are bearing the burden of dialysis. The outcomes for these patients remain poor, driven in part by factors such as dialysis preparation and the type of dialysis used. Our understanding of how health services impact upon these outcomes has been limited by the absence of an effective means of collecting and analysing data from the outpatient sector. This project will undertake a 'proof of concept' expansion of the ANZDATA Registry to include data from the outpatient and hospital sector and use this to understand how outpatient resource use impacts upon patient outcomes.

Chief Investigator: Dr Allison Tong
Co-Investigators: Prof Jeremy Chapman, Prof Jonathan Craig
Associate Investigators: A/Prof John Kanellis, Prof Steve Chadban, Dr Scott Campbell, Dr Grant Luxton & Dr Wai Lim
Sydney School of Public Health – The University of Sydney NSW
Investigating barriers and disparities in 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 remains unexplained. This study will identify a range of barriers and reasons for the disparities in the rates of living donor kidney transplantation. National surveys will be administered to adults eligible for a kidney transplant to assess the associations between socio-economic factors with knowledge about living donor kidney transplantation and identification of potential live donors. A survey will be conducted in all transplant centres to assess the relationship between centre characteristics and the probability of living kidney donation. Qualitative interviews will be conducted with patients and clinicians to gain a range and depth of insight about perceived barriers and disparities in living kidney donor transplantation. The findings will inform targeted efforts for reducing disparities in living donor transplantation.

Chief Investigator: Dr Meg Jardine
Co-Investigators: Prof Bruce Neal, Prof Vlado Perkovic, Dr Jicheng Lv, Dr Lijing Yan, A/Prof Martin Gallagher
Renal Division – The George Institute for Global Health NSW
Impact of Salt Reduction on Proteinuria

Reducing dietary salt may reduce albuminuria, a risk factor for both heart and kidney disease, although this has not been proven. The largest randomised trial of salt reduction worldwide is due to conclude in 2013 and will definitively establish the impact of dietary salt reduction on high blood pressure in 2700 high risk people from rural China. This application proposes to measure albuminuria and measures of kidney function in these participants at the end of the study. The impact of salt reduction on kidney function and albuminuria will therefore be clearly established. As the largest salt reduction trial ever undertaken, this proposal provides a unique opportunity to establish the role of a cheap and widely available intervention on the kidney. The results are likely to be of high impact within the medical and public health community.

Chief Investigator: Dr Karen Dwyer
Co-Investigators: A/Prof Glenn Ward
Associate Investigators: Prof Richard MacIsaac & Prof Frank Alford
St Vincent's Hospital Melbourne VIC
Pre-diabetes in patients with chronic kidney disease

Type 2 diabetes mellitus (T2D) results from a complex interplay between hereditary and environmental influences resulting in an increase in insulin resistance and the inability of the insulin-producing β-cell in the pancreas to secrete sufficient insulin. Recently a severe reduction in biological incretin effect has been recongnised as a mediator of this β-cell dysfunction. The incretin hormones are intestinal hormones released in response to nutrient ingestion. Both hormones enchance glucose-induced insulin secretion from the beginning of a meal, the incretin effect. Unrecognised pre-diabetes in patients with chronic kidney disease (CKD) is common (up to 69% in a Turkish population, Basturk & Unsal 2011) and insulin resistance can be demonstrated in patients with CKD and increases as renal function declines. However, there is limited data on the incretin effect in CKD. Cardiovascular events remain the single biggest cause of death of patients with CKD. In the general community an increase in insulin resistance has been associated with incident cardiovascular events. Further in both the general and renal transplant populations pre-diabetes is a potent risk factor cardiovascular mortality.

This project will determine the prevalence of unrecognised pre-diabetes in an Australian cohort of patients with CKD and examine the biological incretin effect in these patients. The advent of novel anti-diabetic therapeutics that augment the incretin effect and which are safe to use in patients with CKD may improve the metabolic and cardiovascular risk profile of these patients.

Chief Investigator: Prof David Johnson
Co-Investigators: A/Prof Carmel Hawley, Prof Nick Topley & Dr Yeoungjee Cho
Associate Investigators: Dr David Vesey
Princess Alexandra Hospital - The University of Queensland QLD
A study investigating the role of biological markers in determining peritoneal injury in peritoneal dialysis (PD) patients

PD uses exchange of solutions against the patient's own peritoneal membrane and is the predominant form of home-based dialysis. Despite its simplicity, cost-effectiveness and numerous advantages compared with haemodialysis, PD is underutilised. A major barrier to greater uptake is progressive peritoneal membrane injury by conventional PD solutions with 'unfriendly' features. Although there are no markers available to readily identify patients at higher risk with of peritoneal injury, MMP-2 is a strong candidate. The aim of this study, which involves international collaboration with a leading expert in the field of peritoneal membrane injury (Prof Nick Topley), is to demonstrate the pattern serial MMP-2 levels and its association with clinical outcomes in patients receiving conventional or novel biocompatible solutions. This study will use samples obtained during the balANZ trail, a multi-centre study of biocompatible versus conventional PD solution in 185 new PD patients over 2 years. In MMP-2 is able to accurately identify PD patients 'at risk' of peritoneal injury, it may prove to be an invaluable tool for clinicians allowing timely intervention, improved quality of life on dialysis and enhanced access to patients to home dialysis.