Awarded Grants 2016-7

The following grants have been awarded in 2016-17:

1. Dr S O Reilly
Disecting the role of Gremlin-1 in kidney fibrosis

2. Drs Kanagasundaram, Bevan, Yates, Narayanan, Gibbins
Development of an evaluation framework for actute kidney injury computerised clinical decision support

3. Mr A Sewpaul, Mr C Wilson, Prof N Sheerin, Prof S Ali
miRNA and antisense oligonucleotide therapy in renal transplant ischemia reperfusion injury using an Ex-vivo Normothermic Perfusion model

4. Dr K Marchbank
Reversing the phenotype of the C3 GOF mouse model

5. Prof J Sayer & Dr C Miles
Characterisation of a novel Joubert Syndrome model with emphasis on cystic disease phentype and novel therapies.

6. Prof C Harris & Dr K Marchbank
Complement biomarkers for diagnosis, prognosis and stratification.

7. Dr Lynne Stobart
Exploring patients' knowledge and views of decision making regarding kidney transplantation

In the UK, there is a shortage of useable 'ideal' kidneys to meet the needs of patients on the kidney transplant waiting list and sadly, patients continue to die while waiting.

One way to tackle this shortfall is to use new techniques that allow kidneys which would not previously been considered 'ideal' - and therefore not usable - to be transplanted. Research suggests that some patients might benefit from an earlier transplant of a less than ideal kidney rather than waiting for an 'ideal' one. Decisions must be made considering risks and benefits of the options and it is recommended that patients are involved in these discussions.

Our aim is to explore what patients already know about the kidney transplant process. We will interview (up to) 40 adult patients who have made, or are about to make, a decision about managing their kidney disease. We will ask them about what they know and understand about the treatments available to them (e.g. haemodialysis, peritoneal dialysis, deceased donor transplant, living donor transplant, pre-emptive transplant and palliative management). We will look at existing research on the topic and compare this with our own data. In this study we will review the timing and type of information which patients are currently given to see if this meets their needs in the right way at the right

time. We will also ask patients what they understand about the process of getting onto the waiting list, how organs are allocated and their thoughts about the possible use of poorer quality kidneys.

As well as being involved in the study as participants, we will ask patients and members of the public to take an active part in carrying out the research and sharing findings. We will ask for their help in designing information and consent forms and also in selecting the best and most useful questions for the interviews. We will ask their advice on the best way to recruit patients, and finally we will ask them to help us to publicise findings of the study to members of patient and public groups so that they are up to date with developments in this area. Following on from this work, we will ask patient and public representatives to join the steering committee for a much larger piece of work where we will develop tools to help patients consider and make decisions about the best way to manage their kidney disease.

8. Dr Sayer
Investigation of inherited ciliopathies – use of biobanking

Inherited ciliopathies are a group of genetic conditions resulting in cystic kidney disease, progressive renal failure, blindness and neurological defects. Although significant progress has been made over the last few years in the diagnosis of these overall rare conditions, the genetic defect and the underlying pathological abnormality remain unknown in some cases.

Therapeutic strategies including gene therapy in some ciliopathies are promising, with some good results in relevant animal models and in cultured human cells. A number of experimental approaches are now becoming closer to clinical application. Cell culture models such as primary cell cultures from affected individuals could be used to evaluate response and potential benefits. The Newcastle MRC Centre Biobank based at the Institute of Genetic Medicine is a repository of high quality human biomaterial aimed at facilitating research into rare disease. Originally set up for neuromuscular diseases, we now will add biobanking of samples related to inherited renal diseases to make use of the existing biobanking infrastructure and resources.

The principal objective is to be able to collect human cells, and other biological samples such as plasma and serum from patients affected by rare ciliopathies. From tissue samples (e.g. skin and urine) cells may be cultured, frozen and stored in a specialist lab at the Institute of Genetic Medicine, Newcastle University. From blood samples DNA may be obtained and stored. Samples will be used for research n compliance with the Human Tissue Act. This award will allow kidney research in Newcastle to remain at the cutting edge, using the latest techniques and allowing new insights into rare renal diseases.

9. Dr Ana Moles

Worldwide kidney disease is the 12th leading cause of death and the 17th cause for loss of quality "healthy" years of life. It affects 8-16% of the population worldwide and in the UK it is estimated that there are 3.5 million people with kidney disease.
Kidney disease is a term which encompasses acute (short-lasting episode) and chronic (developing over years) pathologies. Specific treatments for acute or chronic kidney disease are limited. Due to this, many patients progress to the point where they need dialysis or kidney transplant (>2 million). This not only represents a significant reduction in their quality and years of life but also a substantial cost for the NHS which is estimated to be around 2.5% of the total annual budget (£2 billion). For all of these reasons specific therapies to treat kidney disease are urgently needed.
In order to find new and more specific drugs, we first need to improve our understanding about kidney biology during disease progression. My research to date has focused on the study of proteases, which are proteins that alter and modify the function of other proteins. They are implicated in many normal (e.g. wound healing and cell death) and pathological (e.g. cancer and rheumatoid arthritis) processes in the body.
My team have discovered that one of these proteases, cathepsin D, is a key player in the development of acute and chronic kidney disease. Our data suggests a dual role for cathepsin D during disease progression. In acute disease, cathepsin D contributes to cell death, a process which, if reversed, will improve kidney function and disease outcome. At the same time, it appears to contribute to the scarring of the kidney in chronic disease, a process also called fibrosis which can lead, if uncontrolled, to loss of function and kidney failure.

Our preclinical studies have revealed that a drug that blocks cathepsin D improves the outcome of both acute and chronic kidney disease. Inhibition of CtsD lead to a reduction of cell death and an improvement in kidney function during both nephrotoxic and ischemic acute kidney injury. This can be relevant not only for acute kidney injury patients, but also to improve donor organ viability. Any kidney donor organ will inevitably suffer a level of injury due to ischemia, lack of blood and oxygen perfusion. Despite it is still early days inhibiting CtsD could have the potential to improve kidney donor organ viability. In addition, we have discovered that inhibition of CtsD in chronic kidney disease reduces scar formation and slows disease progression.
We are very excited about these results and plan to take forward our biological understanding about CtsD and other proteases to develop new and better drugs for kidney disease.

10. Dr Sayer, Dr Miles and Dr Ramsbottom
Novel treatments in nephronophthisis

Nephronophthisis is a childhood form of cystic kidney disease which leads to kidney failure in teenage years. There is no treatment.

We have shown that in a mouse model of nephronophthisis that we have developed here in Newcastle, cyst development can be halted. Also when we

study kidney cells grown from patients with nephronophthisis, the disease can also be treated. However, the therapy used in mice cannot be translated directly to clinical trials in children because the drug has serious side effects. This has caused us to rethink the problem.

In this project we will measure how all the genes within the kidney change during disease development with/without drug treatments using this established mouse model - to find out how the drug works as a step to developing new treatments (with less side effects) for children with nephronophthisis. This generous award combined with funding from Kidney Research UK will allow us to work on this key area for the next 3 years.

11. Dr Caroline Wroe and Dr David Reaich
Teesside 'Extra-Life' Organ Donor Register Study: Saving lives by changing attitudes to organ donation through work place education

The 'Extralife' partnership consists of South Tees NHS Trust, Teesside University, Middlesbrough College, Tees, Esk and Wear Valleys NHS Foundation Trust, Middlesbrough Council and Middlesbrough Football Club. This group employs over 20,000 people in Teesside, North East England. This project is led by Dr Caroline Wroe and Dr David Reaich from the Renal team at South Tees NHS Trust in partnership with representatives from each organisation and the Graphics Design Team at Teesside University.

What is the problem?

- On average 3 people die each day in the UK because an organ donor cannot be found for them.
- Currently in England when someone who has recently died is thought to be a potential organ donor, consent is requested from their family. Permission is given in 57% of cases, but this increases significantly to >90% if the potential donor has previously spoken to family members about their desire to be an organ donor or is on the organ donor register (ODR).
- Analysis of data from NHS Blood and Transplant indicates that the vast majority of the population are in favour of donation in principle, however only 35% of the population are on the organ donor register.

How can this project make a difference?

One of the key aims of the NHS 2013 strategy 'Taking Organ Transplantation to 2020' is to change public attitude so that donation becomes a normal and expected part of end of life care.
The aim of this project is to:

- Create thought provoking ways of engaging the public about organ donation with novel design solutions in partnership with Teesside University Graphics Design Department.
- Test the effectiveness of and response to these ideas in the different workplaces in the 'Extralife' partnership.