Fellows Day 2018 Meeting Report

Kidney Research UK
Funding research to save lives

Acknowledgements

We acknowledge the below organisations for their support towards Fellows Day 2018.

This meeting has been partly funded by sponsorship from Alexion UK, but Alexion has had no input into the organisation or content of the meeting.

Amgen has provided sponsorship funding towards the meeting costs but has had no involvement in the content of the meeting or speaker selection.

BMS funding will support this meeting, but will not be used to fund any awards.

Chiesi Limited are proud to support Kidney Research UK with an unrestricted educational grant and have had no input to the meeting programme or content of the meeting.

Chiesi Limited are proud to support Kidney Research UK with an unrestricted educational grant and have had no input to the meeting programme or content of the meeting.

Janssen UK have supported Kidney Research UK with funding to support their 2018 Alumni Fellow Day. Janssen has had no input or control over the design or content of this event.

This meeting has been partially supported through an educational grant by MedImmune.

Pharmacosmos UK have supported this meeting with an unrestricted educational grant.

Sandoz Ltd has provided a grant towards this event and has no input into the contents of this meeting.

Sanofi Genzyme has provided financial support for this meeting with no input to the programme.

Vifor Pharma UK has contributed towards fees, logistics and other expenses. They have not influenced the content of the meeting.

Introduction

Professor John Feehally

Chairman, Kidney Research UK

Kidney Research UK's Fellows Day is a unique moment in the year when delegates from across the renal community come together to hear from young researchers who have been funded by Kidney Research UK, to listen to wide-ranging keynote lectures, and also to hear the perspectives of patients and carers. This would not be possible without our industry supporters, to whom we are very grateful. The last year has seen accelerating growth in kidney research made possible as more and more individuals and organisations are working with Kidney Research UK to support our aims and objectives.

At this year's event we enjoyed a diverse range of topics including superb keynote presentations from academics and from industry, as well as an inspirational talk from the mother of young children who have kidney disease. In the academic keynote presentations, Professor Dr Nine Knoers showed us the rapidly increasing impact of new genetic techniques on our understanding of rare kidney diseases. Dr Menna Clatworthy showed how recent research is refining our ability to select donor organs for transplant, and improving our understanding of the rejection process, particularly the roles of B cells and antibodies. Professor Matthew Bailey described the intimate links between salt, the kidney and blood pressure and showed how his research is interrogating mechanisms of salt-sensitivity in the kidney.

Meeting report

The 18th annual Kidney Research UK Fellows Day took place at Northumbria University on 3-4 September 2018, chaired by Professor John Sayer. Professor Sayer (Consultant Nephrologist, The Newcastle upon Tyne Hospitals NHS Foundation Trust), has clinical and research interests in inherited kidney disease. Together with Dr Colin Miles (geneticist, Newcastle University), he has discovered a cell-signalling problem that causes cystic kidney disease in Joubert Syndrome (JS) (see page 3). This discovery is helping to develop a therapy to assist sufferers with the incurable condition.

Presentation highlights

Cardiovascular disease and diabetes

Dr Rupert Major's research shows that current prognostic models used to predict the risk of cardiovascular events may be unsuitable for use in patients with chronic kidney disease (CKD). Results indicated that kidney function tests improve performance of the models. Further research will seek to understand how these models can be adapted for use in CKD.

Dr Racquel Lowe-Jones presented research which highlighted the benefits of combined clinical expertise (in a combined nephrology, cardiology and anaemia clinic), to address multiple complex medical issues in CKD patients with heart failure in a single clinic visit.

The kidneys contribute to blood pressure control by regulating the balance of salt and water in the body. Steroid hormones can alter this balance via genetic signals in response to, for example, changes in blood pressure. Dr Morag Mansley's research aims to build a complete profile of the signalling landscape involved in this process to further understand the role of the kidneys in high blood pressure.

Cardiovascular disease remains a major cause of morbidity and mortality in patients receiving peritoneal dialysis (PD). Additional sugar absorbed from dialysis fluid may be having a negative effect. Preliminary results from Dr Jennifer Williams' research indicate that flash glucose monitoring (using a sensor worn on the skin) may be useful for investigating the effect of glucose-based PD solutions on non-diabetic patients.

Dr Carlo Alberto Ricciardi's research has demonstrated that the Soluble Nogo-B (an isoform of Nogo-B protein) protects the kidney from the damage caused by diabetes, which he hopes will lead to the development of new treatments for diabetic kidney disease. Xinlu Pan's research showed that dapagliflozin reduces sugar-induced scarring in human kidney cells, thus making it renoprotective.

Chronic kidney disease

CKD and dialysis often lead to frequent hospital admissions, reduced patient well-being and quality of life. Fiona Willingham's feasibility study has demonstrated the effectiveness of a patient-centred exercise and education programme (pre-emptive rehabilitation [PREHAB]) in people approaching dialysis. Results have informed the design of an ongoing randomised trial comparing the PREHAB programme with routine care.

Tom O'Sullivan's research seeks to understand why skeletal muscle-wasting occurs in CKD and to identify measures to prevent this. Data indicate that Vitamin D deficiency may play a role in the muscle symptoms experienced by many CKD patients and supplementation may present a way of improving this.

Dr Fábio Nery presented completed research demonstrating arterial spin labelling (a magnetic resonance imaging [MRI] technique that can measure kidney blood flow non-invasively). This showed measurements in children with severe kidney disease are robust and repeatable when using optimised acquisition and data processing methods making the technique more suitable for clinical applications.

Kidney failure, kidney injury, and fibrosis

Kidney scarring or fibrosis is the primary cause of kidney disease. Abigail Dear's research showed that a protein called CCN3 is an anti-scarring factor made by kidney cells; if it detaches from the cells it stops protecting them. This factor could contribute to scarring (fibrosis) and if it could be stabilised at the cell's surface, it could be antifibrotic.

Raiyyan Aftab's research indicated that, by blocking a molecule αvβ6, the kidney cells developed less scarring despite being oxygen deficient representing an opportunity to protect kidneys from damage and improve patient outcomes.

Dr Katharine Mylonas presented research indicating that senescence (the process by which cells stop dividing and enter a state of permanent growth arrest without undergoing cell death), can be reversed using the novel drug ABT-263. In doing so, this treatment also protected kidneys from scarring after subsequent kidney injury.

Dr Agnieszka Bierzynska's research focused on idiopathic nephrotic syndrome (INS), a rare condition that causes kidneys to leak huge amounts of protein into the urine leading to chronic illness and potential kidney failure. Her research will combine the clinical and biological data from the UK NURTuRE-NephroS cohort of INS patients with bioinformatic approaches to identify new ways of early diagnosis, predicting the course of the disease and best treatment options.

Transplantation and regenerative medicine

Transplantation is the most effective treatment for end-stage kidney failure; however, organ rejection remains a major risk and organ acceptance is currently achieved using immunosuppression treatment which may lead to serious side effects. Dr Joanna Hester's research investigates the mechanisms of regulatory cells' action and their potential to remove the need for immunosuppressive drugs.

Dr Rhys Evans' research demonstrated that salt increased the activation of cells that cause kidney inflammation and transplant rejection. A low salt diet, or being born with a condition which causes chronic salt depletion, reduces these cell responses. He is currently investigating if salt restriction may be a potentially beneficial treatment in immune-mediated kidney disease.

Amir Parsa Salahi presented research that has used human stem cells to create vascularised mini kidneys. This research is a step towards making more realistic mini kidneys for use in regenerative medicine.

Inherited diseases

Determining mechanisms in the condition can be important in informing the development of pharmacologic therapies. Dr Neil Roberts presented his research on urofacial syndrome (whereby affected individuals are unable to properly empty their bladders and also cannot smile normally). Examination of mice bladders with urination defects showed increased nerve growth, and loss of nerves in the outflow that allow urine to be released from the bladder. This indicates the potential to target nerves for future therapies.

Research from Sebastian Wild used different techniques to investigate one of the faulty proteins known to cause cystinuria (an inherited disease that causes patients to develop kidney stones). Results suggest that when the proteins are faulty they do not stick together properly which can cause the disease. Dr Ragada El-Damanawi also presented on a common inherited condition, polycystic kidney disease (see page 4).

2018 Patient speaker

What is Joubert Syndrome?

Joubert Syndrome is an inherited disorder. Most people carry different faulty genes but the parents of children with JS, though healthy themselves, carry the same faulty genes, and risk passing them on to their children. It is estimated that around 1 in 100,000 babies are born with the condition. Children affected by the illness have a range of problems including learning difficulties, movement problems, loss of eyesight and life-threatening cystic kidney disease, often leading to total kidney failure by the age of 13. A child with JS can expect to spend up to 12 hours a day on dialysis.

Profile: Leanne Buckley

The patient keynote speech this year was given by Leanne Buckley. Leanne is the mother of two children – Emma (aged 10 years) and Benjamin (aged 7 years). Both have been diagnosed via genetics with JS and have a range of medical issues. Both young children are blind, unable to walk or talk and Emma was also on dialysis until she recently received a kidney transplant.

Leanne gave an inspirational talk. She spoke frankly of her experience and shared photographs of precious moments with Emma and Benjamin. Both children have complex needs and the resultant burden of care is substantial and particularly challenging. Social media has enabled her to establish links with other families of children with JS which through shared experience proves a valuable support. Despite the many challenges in caring for her children, they bring Leanne lots of joy.

Leanne is pleased to help Professor Sayer in his research and would encourage others to participate in research if they have the opportunity. JS (or related syndromes) is affecting more families; the more people talk about these rare conditions the more known they become.

Dr Ragada El-Damanawi

Winner of the 2018 Trevor Cook Award

Clinical Training Fellow, University of Cambridge

(Training Fellowship funded by Kidney Research UK)

The Fellows Day Conference is a time for delegates to collaborate, sharing information and experiences. It is the patients who drive and inspire the charity's research, making this award so relevant. The Trevor Cook Award honours and celebrates the life and contribution of Trevor Cook, a former chair of Kidney Research UK's Lay Advisory Committee (LAC). The award was presented by Patricia Gooden, vice chair of the LAC. The judges congratulated Dr Ragada El-Damanawi on explaining concepts of her research in an accessible and creative way.

Ragada presented results from the DRINK (Determining feasibility of Randomisation to high versus ad libitum water INtake in polycystic Kidney disease) trial which assessed key design and feasibility questions required to deliver a successful water intake trial.

Autosomal dominant polycystic kidney disease (ADPKD) is a common inherited condition where cysts grow rapidly inside kidneys causing early-onset kidney failure. Vasopressin is a brain signal that drives cyst growth. Drinking enough water stops the brain from making vasopressin and may work just as well as medications. Participants were randomised to high water intake or normal water intake drinking groups. Results indicated that the high-water intake cohort were able to drink plenty safely maintaining dilute urine throughout the 8-week trial and demonstrated that a large-scale water intake trial in ADPKD is feasible.

Dr Nicholas Medjeral-Thomas

Winner of the Best Oral Presentation prize

Clinical Training Fellow, Imperial College London

(Training Fellowship funded by Kidney Research UK)

In his research, Nick has investigated the role of complement in IgA nephropathy (IgAN) something he has found "… challenging, enjoyable and rewarding."

IgA nephropathy (IgAN) is a common cause of CKD and end-stage renal failure, especially in young people. The mechanisms leading to renal impairment in IgAN are not well understood. Published evidence suggests a role for the complement factor H related proteins (FHR) 1 and 5 in IgAN. FHR1 and FHR5 interfere with complement regulation by factor H. Nick developed novel tests and used them on blood and stored kidney samples from IgAN patients.

Nick found circulating FHR1 and FHR5 levels were higher in IgAN patients compared with healthy controls, and were higher in patients with severe compared to stable IgAN. Glomerular deposition of FHR5, but not FHR1, was also associated with IgAN disease severity.

His research indicates that the complement family protein FHR5 contributes to kidney damage in IgAN. This finding improves our understanding of IgAN and may lead to the development of improved diagnostic techniques and new treatments for IgAN patients.

News from Kidney Research UK

Sandra Currie presented the charity's increased research funding, and stressed the need to continue to raise significantly more funds for kidney research.

The benefits of partnerships and collaboration are many – expanded reach, increased revenue, and shared resources. Through continued partnership with the Medical Research Council (MRC) Kidney Research UK is in a position to ensure additional renal research projects are funded. A further three years of funding for the Stoneygate Research grants round has also been secured.

The development of partnerships with a wide variety of stakeholders is ongoing and the charity continue to seek out other opportunities to leverage investment in research. By maintaining and developing partnerships with industry and with patients, we maximise opportunities for innovation and help to realise meaningful benefits for patients.

"Prevention" and "protection" have been explored as research priorities for the organisation, and the next steps will be to agree and establish the focus of these priorities in the context of short-, medium- and long-term impact and outcomes.

Continued engagement of all stakeholders is encouraged to raise the profile of kidney disease and influence investment in renal research.

Ruth Nightingale

Winner of the Best Poster Presentation prize

PhD student, Great Ormond Street Hospital, London/University of Leeds

Allied Health Professional Fellowship funded by Kidney Research UK

Developing independence can be challenging for young people, particularly if they have a long-term condition such as CKD.

Ruth Nightingale presented results from a systematic review to find out how children with long-term conditions assume responsibility from their parents for self-management of their condition and what influences the parent-to-child transfer of this responsibility. Twenty-nine papers were identified in the review, the majority of which focused on children with diabetes. Assuming self-management responsibility was viewed as part of normal development. Children and parents adopted strategies to help the transfer but there was limited evidence around the role of the healthcare professional. Available evidence suggests that the process is complex. Ruth aims to build on this research by working with teenagers with CKD, their parents and healthcare professionals to 1) find out how young people take control of their health care, and 2) develop a resource to help families with the handover of responsibility for CKD from parents to their child.

Making collaboration work for you

Industry keynote speaker Dr Sandra Wächter (Global Medical Lead Anaemia Therapy in Nephrology, Vifor Fresenius Medical Care Renal Pharma) talked about models for collaboration.

Collaborative models can expedite the availability of innovative technologies. Partnership models allow the sharing of expertise and resources. Collaborative use of compounds and technology can also help to drive innovation; innovation centres sponsored by industry allow the progression of new technologies and/or drugs in research and development networks, which are guided by joint steering committees. Innovations are then normally filed in the name of both partners with the industry partner typically having a preferred right to obtain a licence for pre-clinical, clinical development and commercialisation. Pre-commercial activities typically focus on areas including: development of biomarkers, collection of preclinical safety data, development of methods or validation of outcomes. Crowdsourcing is an evolving model and refers to the outsourcing of a particular task to a wide range of people to get a job done more efficiently. Two examples where crowdsourcing has been used in the pharmaceutical industry are InnoCentive® (Eli Lilly and Company) and Your Encore® (Procter & Gamble and Eli Lilly).

Collaboration can also support the clinical development pathway. Advice from clinicians can be beneficial in the development of trial protocols with clinically meaningful endpoints while advice from regulatory authorities can help to understand requirements for drug approval. Multi-stakeholder engagement can also support market access activities or patient engagement. In addition, investigator-initiated studies can serve as a means of closing the knowledge gap for a product or of enhancing the understanding of a disease.

Dr Wächter spoke of the benefits of the collaboration between Kidney Research UK and Vifor Fresenius Medical Care Renal Pharma Ltd via the PIVOTAL study (EudraCT number 2013-002267-25). Kidney Research UK is helping to deliver and drive the PIVOTAL trial, supported by an unrestricted grant of just under £3.5 million from Vifor Fresenius Medical Care Renal Pharma Ltd. The company is also providing all the iron treatment for the study, free of charge in line with standard clinical trial protocols.

Sandra Wächter's advice for successful collaboration:

- Align goals
- Formulate expectations
- Address challenges and discord
- Build trust and promote communication
- Retain full transparency
- Regular progress review

It is important to remain open to any possibility for collaboration in order to overcome challenges in the long road to new medicines

Closing comments

Both John Sayer and John Feehally conveyed thanks to the Kidney Research UK team, keynote speakers, and industry supporters for helping to make Fellows Day 2018 such a success. The event was a great opportunity to hear progress but also to feel the commitment to the longer-term projects. Researchers should continue to ask the right questions, in the right settings, and using the right techniques.

Researchers are encouraged to take the opportunity to communicate research to different audiences. to raise awareness of kidney disease, influence policy, and ultimately realise patient benefit.

Thinking of attending next year?

Don't miss Professor John Feehally's top tips for developing your presentation skills

- Prepare
- Consider your audience
- Keep it simple – concentrate on your core message
- Have a clear structure (introduction to what you intend to say); body (the presentation itself); conclusions (what you have said)
- Make eye contact with your audience
- Preparation of slides (make sure they are legible from a distance)
- Practise (do a dry-run with a friend or colleague who can give you feedback, or record yourself and listen back)
- Delivery (aim for appearing confident and relaxed, take deep breaths; vary your intonation)
- Questions (answer simply and directly. If you don't know the answer, say so, nobody has all the answers all of the time!)

Save the date

Join us for Fellows Day 2019
Thursday 12 and Friday 13 September 2019
University of Leicester.

Kidney Research UK
Funding research to save lives

0300 303 1100
www.kidneyresearchuk.org

Kidney Research UK, Nene Hall, Lynch Wood Park, Peterborough PE2 6FZ

Registered company no. 905963. Registered charity no. 252892. Registered Scottish charity no. SC039245.

November 2018