

### Research

The Academic Renal Unit in Bristol undertakes an active programme of renal cell biological research, and is a vibrant mix of clinician-scientists (both adult and paediatric, in roughly equal numbers) and basic scientists at various levels. In particular it is a recognized training environment for scientists and clinicians to study for PhD or MD higher degrees, with a strong track record of training adult and paediatric nephrologists aiming for academic career pathways. Currently training in paediatric nephrology we have an academic F2 in post, an Academic Clinical Fellow and an Academic Clinical Lecturer

The Paediatric programme is led by Dr Moin Saleem (Reader in Paediatric Nephrology) and Dr Richard Coward (MRC Senior Lecturer), and the Adult programme is led by Professor Peter Mathieson.

### RESEARCH SUMMARY

The glomerulus is the elemental unit of kidney filtration, and the glomerular podocyte is a central component of this filtration barrier, disruption of which is the key feature of a multitude of kidney diseases.

One of the main focuses of the Academic Renal Unit is the study of podocyte biology, with a team of clinical paediatric and adult nephrologists at various levels of training, working side by side with basic scientists.

The resources we use are unique in the world, comprising human conditionally immortalised podocyte cell lines from normal kidneys and from patients with congenital mutations in key podocyte genes, as well as the more recent development of human conditionally immortalised endothelial cell lines, the other key cell of the filtration barrier.

Current projects fall into four basic areas:

1. The role of plasma factors in the pathogenesis of nephrotic syndromes. This utilises the resource of patients' plasma and its effect on the cell lines, concentrating on the slit diaphragm proteins, actin cytoskeleton and the signalling pathways that connect them.
2. The role of the podocyte in early diabetic nephropathy. This arena of work builds on our observation that the podocyte is a novel insulin sensitive cell, and addresses the biological basis of this clinical renal disease which is by far the biggest cause of end-stage renal failure worldwide, and whose incidence is rapidly rising.
3. Influences on podocyte differentiation – we are investigating the roles of genes, cytokines, endothelial cells, matrix etc. as components of the podocyte environment that influence mature differentiation. This includes work that has revealed that mature podocytes display key features of smooth muscle cells.
4. Co-culture of glomerular endothelial cells and podocytes, to engineer the properties of the intact filtration barrier.

In addition there are strong links with the Departments of Physiology (study of the glomerular microcirculation) and of Biochemistry, within the University of Bristol.

## **Selected Recent Publications-Original papers**

### **A proteomic investigation of glomerular podocytes from a Denys-Drash Syndrome patient with a mutation in the Wilms tumour suppressor gene *WT1***

Rebecca Viney, Avril Morrison, David Patton, van den Heuvel LP Lan Ni, Peter W Mathieson, Moin A Saleem and Michael Ladomery. Proteomics – in press

### **Nephrin is critical for the action of insulin on human glomerular podocytes**

Richard JM Coward, Gavin I Welsh, Ania Koziell, Sagair Hussain, Rachel Lennon, Lan Ni, Jeremy Tavaré, Peter W Mathieson, Moin A Saleem. Diabetes-In press

### **Prospective Study Of Childhood Nephritis In South Western Uganda**

Walker A, Ellis J, Irama M, Axton J, Coward R, Peat D, Bode H, Mathieson P  
Kidney International-in Press

### **Direct Effects Of Dexamethasone On Human Podocytes.**

Xing CY, Saleem MA, Coward RJM, Ni L, Witherden IR, Mathieson PW.  
Kidney International. September 2006 1038-45.

### **Conditionally Immortalised Human Glomerular Endothelial Cells Expressing Fenestrations In Response To VEGF.**

Simon C Satchell, Candida Tasman, Anurag Singh, Lan Ni, Thea J van der Velden, Jessica Turnbull, Chris J von Ruhland, Michael J O'Hare, Moin A Saleem, Lambert P van den Heuvel, Peter W Mathieson. Kidney International – 2006 May;69(9):1633-40

### **The Human Glomerular Podocyte is a Novel Target for Insulin Action**

Richard JM Coward, Gavin I Welsh, Jing Yang, Candida Tasman, Ania Koziell, Simon Satchell, Geoffrey D Holman, Donscho Kerjaschki, Jeremy M Tavaré, Peter W Mathieson, Moin A Saleem. Diabetes 2005 Nov; 54(11) 3095-102

### **Nephrotic Plasma Alters Slit Diaphragm dependent Signalling, and Translocates Nephrin, Podocin and CD2AP in the Human Podocyte.**

Coward RJ, Foster RR, Patton D, Ni L, Lennon R, Bates DO, Harper SJ, Mathieson PW, Saleem MA. J Am Soc Nephrol. 2005 Mar;16(3):629-37

## **Selected Recent Grants**

2006 Medical Research Council – Clinician Scientist Fellowship (Dr Richard Coward) - £705,000

2005 Medical Research Council - Programme Grant – ‘The cellular basis of Albuminuria’ – £680,000

2004 Wellcome Trust – Wellcome Research Training Fellowship (Rachel Lennon, 3 years) - £192,000

## **Charity**

The charity NeST (Nephrotic Syndrome Trust) was launched in June 2005 by the New Zealand rugby legend Jonah Lomu, who is our ambassador. The charity is also sponsored by Brita Waters Filters. The proceeds all go towards ongoing research in Bristol, and further details can be found on [http://www.brita.net/uk/brita\\_charity.html](http://www.brita.net/uk/brita_charity.html)