**Clinical – supervisor Professor David Wheeler**

*Occurrence of hyperkalaemia in incident dialysis patients and its importance as a factor determining initiation of dialysis, and its incidence in the UK haemodialysis population*

Clinical trials have not convincingly demonstrated that an early start to dialysis in patients with stage 4/5 chronic kidney disease (CKD) improves long-term outcomes. Therefore, the decision to commence dialysis is based on a number of clinical parameters including biochemical profile and patient well-being. Hyperkalaemia is a problem in this population, due to reduced renal potassium excretion and may cause life-threatening cardiac arrythmias. The extent to which high blood potassium levels precipitate initiation of dialysis has not been systematically studied. Furthermore, once on dialysis, patients may experience intermittent hyperkalaemia potentially affecting outcomes, particularly sudden death, which accounts for approximately 25% of mortality in the haemodialysis population, but is still unexplained. Using existing local and national databases, this clinical project will suit an enthusiastic student and aims to systemically study the serum potassium levels at haemodialysis initiation and the prevalence of high potassium levels in the chronic haemodialysis population. These data will be of value in defining the need to treat or prevent hyperkalaemia and the potential scope of new oral potassium binding agents.

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**Basic – supervisors Professor Jill Norman and Professor Fred Tam**

*The role of the macrophage and P2 X7 receptor in vascular calcification*

Initial findings have suggested that the P2X7 receptor, when activated, may promote vascular calcification, and that inhibition may be protective, but that this might depend on local macrophage activity. Using a model of rat vascular (aortic) ring calcification *in vitro* when exposed to a high phosphate concentration, and the transwell cell culture system, it is possible to separate bone-derived (BMD) macrophages in culture from the vascular ring, and thereby test factors secreted by macrophages, which can be exposed to high phosphate or stimulated in other ways. Preliminary data suggest that BMD macrophages when exposed to high phosphate may actually reduce vascular calcification, an unexpected finding. However, the phenotype and secretory characteristics of these macrophages needs to be defined, as well as the effect of pro-inflammatory stimuli, and the role of the P2X7 receptor in this setting. We have access to vascular tissue samples and BMD macrophages from a unique P2X7 knockout rat model, and propose to use these to define the role of P2X7 expression and BMD macrophages in the pathogenesis of vascular calcification. This project will provide an able and motivated student with training in the relevant *in vitro* techniques as part of a translational project that has a clear set of goals and can be completed within 6-12 months.

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**Basic Science-Supervisors: Dr Stephen Walsh and Professor Alan Salama**

*An Investigation of T-Cell and Macrophage Membrane Sodium Transport Physiology*

The western diet is high in sodium, and this sodium load is implicated a high burden of cardiovascular disease. However, there is increasing evidence linking a high-salt diet to inflammatory autoimmune diseases (e.g. rheumatoid arthritis and multiple sclerosis). Recently, two papers in *Nature* demonstrated that a raised extracellular sodium concentration causes naïve T-helper cells to differentiate into pathogenic Th17 cells. Sodium has a similar pro-inflammatory polarising effect on macrophages preventing M2 and propagating M1 phenotype switch. Intriguingly, neither the way that sodium enters the cell, nor the mechanism of cell polarisation have yet been elucidated. We will investigate the effect of a high sodium environment on T-cell and macrophage polarisation on cellular phenotype. We will use pharmacology and electrophysiology to identify membrane transporters of sodium in T-cells and macrophages and transcriptomics to examine events around this polarisation. The project uses well defined *in vitro* techniques using cells from a unique IL-17 tracker mouse and is ideal for an enthusiastic student who is interested in a basic science project that is an interface between immunology and physiology with a direct applicability to clinical medicine. The goals are well defined and deliverable within 6-12 months.

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