



## Project: Characterisation of neutrophil and regulatory T-cell/effector T-cell interactions in alcohol-related liver disease

*'I aspire to a career working in hepatology both as a clinical doctor and an academic researcher. I currently work as an Academic Foundation Year 2 Doctor with an academic attachment within the Liver Unit at Kings College Hospital.'*

*'Winning the Dr Falk Core bursary has allowed me to fully pursue lab based research in an area I find extremely interesting and worthwhile while gaining valuable experience in research, such as new methodologies and experimental design, which will greatly benefit my future career.'*

*Dr Middleton is currently undergoing his Academic Foundation Year 2 at Kings College Hospital, London. His research was carried out at the Institute of Liver Studies and Liver Transplantation, Kings College Hospital, London.*

'Liver disease is the fifth most common cause of death in the UK and unlike other major causes of death, which have benefited from improving mortality over the last 30 years, liver disease mortality has increased 4 fold over this time.'

'Patients with cirrhosis, the end-stage of chronic liver disease, have long been recognised as having an increased susceptibility to infections. Indeed infections represent a major cause of hospital admissions, deterioration and death in patients with cirrhosis.'

'Previous studies have identified significant changes in the immune system of patients with cirrhosis which may explain this increased risk of infection. Immune cells in patients with cirrhosis are found to simultaneously be over-activated while having impaired ability to fight infection. Over-activation of immune cells leads to collateral damage to the body and may promote further deterioration in liver function. As liver function deteriorates the immune system becomes exhausted and its ability to fight infection further deteriorates leading to overwhelming infection and death.'

'As the prevalence of chronic liver disease is increasing so is the concern of antibiotic resistance and multi-drug resistant infections. This makes gaining a deeper understanding of cirrhosis associated immunodeficiency and developing treatments to prevent or reverse these changes to the immune system an important goal for hepatology research.'

'This project aims to further understand these immune changes by examining the function and interaction of two main immune cell groups, neutrophils and T-cells, from healthy volunteers and patients with cirrhosis secondary to alcohol related liver disease. By characterising how these cells behave and interact in patients with cirrhosis we may be able to contribute to identifying targets for managing this condition.'

### *Dr Middleton's supervisor Dr Debbie Shawcross states:*

'Academic Foundation Year doctors as gifted as Paul do not come along very often in my experience and we have been extremely lucky to have Paul working with us. Throughout his medical training he has received a number of prizes for academic excellence which complements his solid knowledge base and good clinical skills. Despite incredibly intensive jobs he has had 3 high impact abstracts published. Furthermore he co-wrote a chapter for the Oxford Textbook of Medicine on Hepatic Encephalopathy with me last year.'