



Project: The predisposition to infection in patients with cirrhosis: rationale for drug design based on novel functional and structural studies of the albumin.

"Winning the Falk/Core Student Bursary is a huge honour, and I cannot thank Core and Dr Falk Pharma enough for this award! It provides recognition for taking time off medicine to explore medical research and also further bolsters my aspirations to one day contribute to the field of gastroenterology."

Zhi-Yang Low is currently completing an integrated BSc in Clinical Sciences at University College London.

'Liver cirrhosis, a chronic disease of the liver strongly associated with alcohol, has become a leading cause of death worldwide, with a considerable proportion of deaths occurring due to infections, explains Mr Low. 'It has been suggested that increased levels of the hormone prostaglandin E2 (PGE \rightarrow 2) may be the cause of heightened infection rates in cirrhotic patients. There is evidence that the high levels of PGE \rightarrow 2 might be due to serum albumin not being able to effectively clear PGE2 from the circulation due to qualitative changes in its ligand binding activities.'

'I chose this project partly because albumin is such an interesting protein. It is one of those proteins you start hearing about when you're really young, and as I go through medical school the importance of albumin has only become even more apparent. My personal interest in hepatology also spurred me on to take up a project pertaining to liver cirrhosis - a condition which has become so rampant in the UK in recent decades. When I was first introduced to the project and found that immunosuppression in liver cirrhosis may be due to a dysfunction in albumin binding activities, I felt that this project was perfect for me and it really has been wonderful to work on something I have grown very passionate about.'

'This project aims to determine what defects are causing this decreased activity of albumin in the blood of these patients with liver cirrhosis.'

Using functional studies to analyse binding activity in albumin samples from healthy volunteers and patients with liver cirrhosis, we have thus far succeeded in demonstrating a complete loss of activity in one of albumin's two major binding sites. Further studies are currently being undertaken to elucidate the exact nature of the defect, so as to facilitate future treatment approaches.

'Structural studies, using X-ray crystallography, are also being undertaken to study the binding of PGE2 in normal albumin, in order to better understand the potential defects causing the ineffective binding observed in liver cirrhosis. This will also facilitate future work on possible treatment approaches which will hopefully enable cirrhotic patients to respond effectively to infective threats.'

Mr Low's supervisor Dr Alun R Coker states:

'Zhi-Yang is a talented individual who has displayed great enthusiasm for this project. The background literature for the project is voluminous but Zhi-Yang has shown a great aptitude for tracking down key papers overlooked by others. His detailed understanding of the literature is impressive. He has also shown himself to be a competent experimentalist quickly mastering techniques he is shown and pushing the work forward at a good pace.'

'Zhi-Yang is a cheerful and engaging individual with excellent interpersonal skills. He is popular and well regarded amongst other members of the research group. I have no hesitation in endorsing his application.'