MEDICAL STUDENT PRIZE WINNER:

RATNAM GANDHI

PROJECT: The Clearance of Dead Cells by Hepatocytes: Mechanism and Clinical Implications

'Carrying out a research-based intercalation has significantly enriched my understanding, knowledge and appreciation of the impactful advancements in medical treatments; which are possible due to the individuals and teams committed to excellent research. I am deeply grateful to be awarded the Dr. Falk/Core Medical Student Prize. This experience has demonstrated the success which is possible with hard-work combined with a positive, dedicated and inquisitive attitude in research. I have been inspired to pursue a profession which enables me to combine clinical practice, with academic research; allowing further contributions to the field of gastroenterology.'

Ratnam Gandhi has just completed an intercalated BMedSci in Clinical Science at the Centre for Liver Research at the University of Birmingham. She will return to take up her 4th year medical studies at Birmingham University in September.

'Whilst on clinical placement, my exposure to liver disease allowed me to appreciate the profound impact it can have on patients and their families. I further learnt that the rapidly increasing rates of liver disease alongside the current limited therapeutic options means it is essential to understand how to limit inflammation and promote liver regeneration. There is a growing demand for research in this field and it was this need, together with my keen interest in liver immunology, which made this an ideal project for my intercalation.

'The homeostatic function of efferocytosis refers to the phagocytic engulfment of dead or dying (necrotic) cells following liver injury. If necrotic liver cells are not cleared, subsequent pro-inflammatory signalling and recruitment of immune cells can promote inflammation, drive the fibrotic process and increase the risk of autoimmunity. It may also compromise liver regeneration.

'Despite hepatocytes being effective efferocytes (comprising 80% of the liver mass), the molecular mechanism that governs hepatocyte efferocytosis has not previously been understood.

Previous research has documented the involvement of specific surface receptors in efferocytosis, therefore I sought to investigate the contribution of these receptors, specifically Intracellular Adhesion Molecule-1 (ICAM-1) and Asialoglycoprotein receptor 1 (ASGR1), in the capture and internalisation of necrotic cells. This was by using the Huh-7 and Jurkat cell lines to model hepatocytes and necrotic T cells in-vitro.

'Using techniques including flow cytometry and confocal microscopy, we developed an efferocytosis-insufficient Huh-7 cell line, which showed a reduction of ASGR1 compared to the original cell line. In addition, both ICAM-1 and ASGR1 had surrounded the phagocytic cup of the Huh-7 cell which contained the engulfed necrotic cell.

'This reseatch shows that surface receptors provide a potential target for the modulation of efferocytosis in liver diseases which are impacted by necrotic cell death. These discoveries are hoped to contribute to the development of pharmacological therapies in this field of medicine.'

Ms Gandhi's Supervisor Dr Zania Stamataki comments:

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