Falk Foundation/Guts UK Awards 2025

MEDICAL STUDENT PRIZE WINNER:
Nikhil Mistry

Investigating the Role of Regulatory T cells (Tregs) in Perianal Fistulising Crohn's Disease

Mr Mistry undertook this project whilst intercalating for an iBSc in Medical Sciences with Gastroenterology and Hepatology at Imperial College London. Mr Mistry will return to the fifth year of his medical degree in August at the University of Birmingham School of Medicine.

Mr Mistry explains:

'Perianal fistulas are a severe and debilitating complication of Crohn's Disease (CD). Patients have a poor quality of life and typically suffer with pain, bleeding, infection and faecal incontinence. On a personal level, I have had a long-standing interest in Gastroenterology and specifically Crohn's Disease stemming from my own personal struggle with disease.

'There is an unmet need to better characterize the immunopathology of perianal fistulising Crohn's disease (pCD). The role of regulatory T cells (Tregs) has been well researched within the context of luminal CD, with the adoptive transfer of Tregs already being investigated as a potential therapy in this cohort of patients. However, the role of Tregs in the development of perianal fistulas in Crohn's Disease is not yet understood.

'Previous work at this lab showed that unsupervised clustering analysis of single cell RNA sequencing data identified two distinct Treg populations in pCD and cryptoglandular fistula (CGF) patients. These populations differentially expressed IKZF2 (Helios), a transcription factor thought to be important in Treg stability and function. Differential gene expression analysis of $IKZF2^{low}$ Tregs indicated that this subpopulation expressed more pro-inflammatory transcripts than their $IKZF2^{high}$ counterparts at gene level.

'Building on these findings, the aim of my project was to understand the potential role of Tregs in the development of perianal fistulas in Crohn's Disease. To do so we assess the phenotypic profile of Tregs within perianal fistula tissue of both Crohn's Disease patients and non-IBD (cryptoglandular fistula) patients at protein level using flow cytometry studies. In doing so, this work highlights a potential role of Tregs in the development of perianal fistulas in Crohn's Disease.

'This study established that Tregs are preferentially enriched within fistula tissue compared to peripheral blood and contain a higher proportion of cytokine-producing Tregs, namely IL17A. We also demonstrated that a significantly higher proportion of IL17A producing Tregs were found to have low levels of IKZF2 expression in fistula tissue, compared to Tregs with high levels of IKZF2 expression, suggesting potential pro-inflammatory plasticity. Despite our limited sample size due to time constraints, these findings offer preliminary evidence for the presence of pro-inflammatory Tregs at protein level within the fistula environment that warrant further investigation.

'This project will deepen our understanding of Treg phenotypes within the perianal fistula microenvironment, shedding light on their role in pCD pathology. Identifying pro-inflammatory subpopulations of Tregs in pCD could be key in the development of novel therapeutic strategies with the potential to have a significant impact on the quality of life for CD patients.

'During my time at the Powell lab, I have developed a keen interest in immunology, particularly in its relation to the pathogenesis of Crohn's Disease. I look forward to my return to University of Birmingham and will endeavour to get involved in research projects there.'

Mr Mistry's Project Supervisor, Dr. Laura Constable, Research Associate, Department of Metabolism, Digestion and Reproduction, Imperial College London comments:

'From the outset, I've been incredibly impressed with Nikhil's focus, his enthusiasm for research, his willingness to learn and his ability to seamlessly integrate into a busy translational science lab. Despite being early in his scientific career, he's helped to make valuable and novel contributions to our understanding of the immunopathology of perianal fistulising Crohn's disease (pCD), an important yet under-researched and difficult-to-treat complication of Crohn's disease. Nikhil has displayed great academic potential and, hopefully, this project has provided him with some helpful insights into academic research and has encouraged him to consider a career in academic clinical research in the future.'

Mr Mistry states:

'It is a tremendous honour to be recognised with this award for my research. Through experiencing the ups and downs of research, I have gained a deep appreciation for the process and receiving this prestigious award serves to reaffirm my commitment to pursuing research in this discipline. While I am still in the early stages, I am eager to grow further as both a scientist and clinician as I work towards a career as an academic clinician.'

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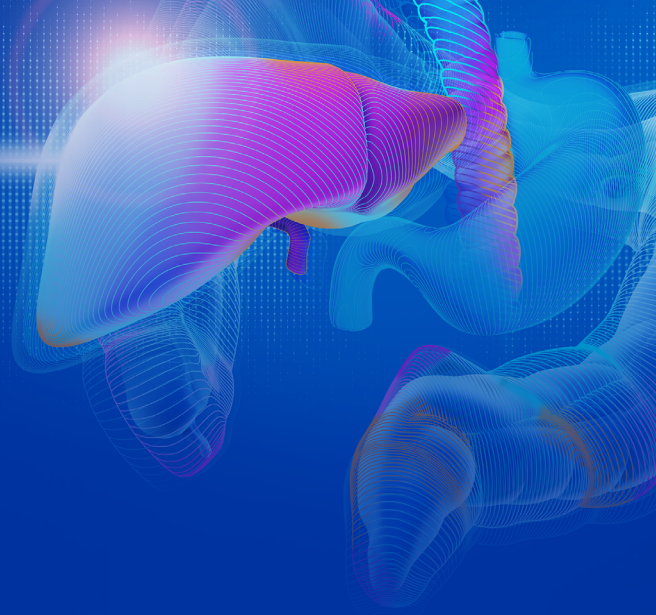

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