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Dr Falk/Guts UK Awards 2022

MEDICAL STUDENT ESSAY PRIZE WINNER:

Mr Joachim Hanna

PROJECT:

Hedgehog Signalling Controls Th17 Differentiation to Drive Intestinal Inflammation and is a Druggable Target in the Treatment of Inflammatory Bowel Disease



Mr Joachim Hanna undertook this research at the Cancer Research UK Cambridge Institute at the University of Cambridge whilst studying for a PhD in Immunology as part of a MB/PhD Programme. He is currently in his final year at Cambridge University Medical School.

Mr Hanna explains:

'The burden of inflammatory bowel disease (IBD) is enormous and is rapidly rising, with the annual global burden of IBD estimated at over one million years lived with disability. There has been a great push to understand the cellular and molecular features that are specifically dysregulated in IBD, in order to develop novel targeted therapeutics.

'One of the key disease drivers in IBD are CD4+ T cells which differentiate in the intestine to become Th17 cells which are key drivers of gut inflammation. There has been great interest in trying to understand this process of Th17 differentiation and function to try and exploit this to identify new drug targets. The hope is that drugs targeting Th17 cells could reduce intestinal inflammation with minimal off-target effects in other cells.

'My PhD project focussed on the role of an ancient signalling pathway, the Hedgehog pathway, in T cell function. I was particularly interested in this pathway since it is highly druggable, and Hedgehog inhibitors are already in use in the clinic as anti-cancer drugs.

'My work has shown that the Hedgehog signalling pathway is a novel key regulator essential for CD4+ T cells to specifically differentiate into Th17 cells both in vitro and in vivo without affecting the function of other protective immune cell types.

Furthermore, this work shows not only that central Hedgehog signalling components are upregulated in patients with IBD and correlate with Th17 infiltration, but also demonstrates that a clinically approved Hedgehog inhibitor specifically and potently inhibits Th17 differentiation in vivo.

'Thus, this work raises the possibility of repurposing existing Hedgehog inhibitors to provide a novel targeted therapy in the treatment of IBD.'

Mr Hanna's Project Supervisor, Dr Maïke de la Roche, Group Leader at the Cancer Research UK Cambridge Institute comments:

'Joachim has been an excellent student whose outstanding competence and work ethic has led to two excellent pieces of research work with high translational relevance in my laboratory.

'Joachim was the driving force behind his projects and came up with many new ideas, he stayed on top of the literature and readily incorporated new perspectives and methodologies into his research. He worked independently and in addition to his intellectual brilliance, he was a kind and considerate member of the team.'

Mr Hanna states:

'Receiving a Dr Falk/Guts UK Essay Prize is a tremendous honour. I am deeply grateful to both my supervisor and fellow lab colleagues for their continuous support. Working on this project has been such an amazing opportunity and has cemented my goal to combine my research and clinical interests as an academic gastroenterologist.

'As an early career medic, this award is an amazing platform to highlight my work and will allow me to attend international conferences to share my work and gain invaluable insights into the field'



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