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Dr Falk/Guts UK Awards 2020

MEDICAL STUDENT BURSARY WINNER:

Mr Moksh Sharma

PROJECT:

A Genome-wide Association Study of Severe Alcoholic Hepatitis



Mr Moksh Sharma undertook this research at the UCL Institute for Liver & Digestive Health, Division of Medicine, Royal Free Campus, University College London, whilst intercalating in an iBSc in Clinical Sciences. He is currently completing his 4th year at the University College London Medical School.

Mr Sharma explains:

'Alcohol-related liver disease (ALD) is a complex disorder, resulting from the interplay of environmental and genetic factors. Severe alcoholic hepatitis (sAH) is an acute clinical manifestation of ALD, which develops in a minority of patients and has high associated mortality (40-50%). There is an urgent unmet need to develop new therapies to improve the management of patients with this understudied syndrome.

This project aims to perform genome-wide association studies (GWAS) to identify genetic risk loci associated with the development of sAH, in turn, unravelling its pathophysiology and facilitating therapeutic endeavour. Our preliminary GWAS comparing patients with sAH against alcohol dependent people identified an association with PNPLA3 (Patatin-like Phospholipase Domain-containing Protein 3) at genome-wide significance. Other potential risk loci were also identified at suggestive significance, including ATP2C2 (ATPase Secretory Pathway Ca2+ Transporting 2) which is implicated in the regulation of reactive-oxygen species in the gut; PHYH (Phytanoyl-CoA 2-Hydroxylase) which is involved in phytanic acid metabolism (phytanic acid binds to and/or activates the transcription factors PPAR-alpha and retinoid X receptor); and ANGPT1 (Angiopoietin 1) which encodes an angiogenic promoter implicated in liver fibrosis.

I will be continuing with this project and performing GWAS comparing patients with sAH against alternate populations: patients with alcohol-related cirrhosis and healthy controls. Furthermore, I hope to use available clinical data on disease severity measures, complications and outcomes in our sAH cohort to undertake additional GWAS with the aim to develop and test polygenic risk scores.'

Mr Sharma's Project Supervisor, Research Fellow Dr Stephen Atkinson comments:

'Moksh is an extremely bright and enthusiastic medical undergraduate who has been working together with myself and my colleagues to design and undertake a study to examine the genetic basis of severe alcoholic hepatitis. This project will potentially offer valuable insights into the aetiology of a condition which is comparatively poorly understood, has a dearth of available treatments and predominantly affects a marginalised and stigmatised patient population.'

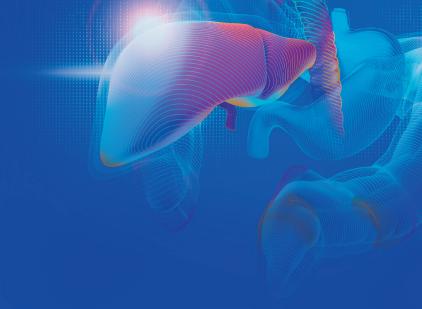
Mr Sharma states:

'I am immensely grateful to Guts UK/Dr Falk for awarding me this prize and enabling us to share our research on a wider platform. I am also very thankful to my supervisors who have continued to provide invaluable guidance and support in these difficult times. Through this project I have gained great insight into academic gastroenterology and hope to continue pursuing my interests in this specialty.'



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