

Together we *know more*.  
Together we *do more*.



## 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 Ca<sup>2+</sup> 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.'



Together we *know more*.  
Together we *do more*.



**Collaboration.**



**Formulation.**



**Destination.**

At Dr Falk, we do things differently. Our focus is on people. So for every treatment we develop, from gastroenterology to liver disease, we do it our way.

It's a simple formula.  
**We call it the Dr Falk way.**

[www.dralk.co.uk](http://www.dralk.co.uk)

Dr Falk Pharma UK Ltd  
Unit K, Bourne End Business Park  
Cores End Road  
Bourne End SL8 5AS  
Tel: +44 (0) 1628 536 600  
Email: [office@drfalkpharma.co.uk](mailto:office@drfalkpharma.co.uk)

Company Registration Number: 2307698

UK--2100039

Date of preparation: February 2021