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Dr Falk/Guts UK Awards 2021

MEDICAL STUDENT ESSAY PRIZE WINNER: Niraj Doshi

PROJECT:

A Genome-Wide Association Study of Non-Alcoholic Fatty Liver Disease in Trivandrum, India.



Mr Niraj Doshi undertook this research at the Institute for Liver & Digestive Health and Molecular Psychiatry Laboratory at University College London, whilst intercalating in an Integrated BSc Medical Sciences with Clinical Sciences. He is currently in his fifth year at University College London Medical School.

Mr Doshi explains:

'Although non-alcoholic fatty liver disease (NAFLD) is fast becoming a public health emergency, there is currently little public awareness about the condition. Certain populations (such as those in South Asia) appear to be more susceptible to NAFLD and its associated complications, with the burden of liver disease increasing by 46% between 1980 and 2010, in low and middle-income countries such as India, Pakistan, and Bangladesh. At the same time, there is a paucity of high-quality research into the genetics of diseases in ethnic minority populations compared to Europeans/Caucasians.'

'I am passionate about redressing this balance; doing so is imperative for ensuring health equality and reducing disparities in our understanding of disease risk in different populations. Additionally, being from a South Asian background, I feel privileged to have undertaken the first genome-wide association study (GWAS) in liver disease in this ethnic group. Having had no prior experience in the fields of hepatology, genetics, and bioinformatics, the learning curve was extremely steep. However, I managed to carry out all stages of this genome-wide association study (GWAS) with a great amount of independence.'

'The Trivandrum NAFLD cohort comprises 2222 adults were recruited from across Kerala in South India. Cases were defined as participants with evidence of fatty infiltration of the liver on ultrasound scanning. Controls were defined as participants with no evidence of fatty infiltration using the same technique. Extensive historical, dietary, anthropometric, and biochemical measures were available from all included participants. Genomic DNA was available from 1118 participants and was extracted in Trivandrum, before genotyping in London, with rigorous quality control applied to all data.'

'Findings from the study showed that genetic risk loci robustly associated with the development and progression of NAFLD in European/East Asian populations are not associated with disease susceptibility in South Asians. This, coupled with additional findings concerning lack of associations in loci previously associated with serum enzyme activities, suggests there may be divergence in the genetic risk profile for developing NAFLD in the South Asian population, compared with others. These findings may have significant implications for identifying individuals at risk of the condition and for potential therapeutic targeting. Overcoming the technical and conceptual challenges that I faced, and using analytical techniques not previously used by my research group to solve issues, was extremely rewarding. I feel confident that these skills and experiences will stand me in good stead for continuing computational research in this field.'

Mr Doshi's Project Supervisor, Andrew McQuillin, Professor of Molecular Psychiatry, comments:

'Despite having no experience of statistical computing and bioinformatics, Niraj fully threw himself into the deep end from the start of this project. He successfully overcome the technical and conceptual challenges that he faced, going on to learn a tremendous amount about the analysis of genetic data and independently developing skills such as genotype imputation and statistical manipulation in R. He has carried out all stages of the GWAS with a great amount of independence and a huge amount of enthusiasm and has been a pleasure to have in my research group. Niraj's research project was outstanding and of publishable quality; his ambition is constantly reflected in the quality of work he produces. His findings of possible divergence in the genetic risk profile for developing NAFLD between populations may have significant implications for identifying individuals at risk of the condition and for potential therapeutic targeting. I look forward to working with Niraj as he furthers his analysis.'

Mr Doshi states:

'I am extremely grateful to Guts UK and Dr Falk for their generosity in awarding me this prize and helping to raise awareness of the need for research into metabolic liver disease. The results of this study will help to improve our understanding of the processes underlying the development of NAFLD, and facilitate further research into how this disease may be detected at an earlier stage. It will also shed light on targets for new drugs, many of which are being developed to target specific genetic pathways.' 'Being recognised for my contribution to this work has inspired me to continue research in this field, and I will now be working to replicate my findings in other cohorts of South Asian ancestry. I would also like to thank my supervisors,

for allowing me to work on this project and always offering me their unwavering support.'



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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

Company Registration Number: 2307698