**University of Leicester**

**MRC AIM Studentship Project 2025-6 entry.**

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| **Additional Supervisor** | Prof. Chris Brightling |

**Section 2 – *Project Information***

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| **Project Title** | Understanding the mechanism of action of genomic loci associated with severe asthma for clinical translation |
| **Project Summary**  |
| Up to 10% of individuals with asthma struggle to control their symptoms despite high intensity treatment, leading to increased risk of hospitalisation and death. We recently performed a genome-wide association study of difficult-to-treat asthma in order to identify genetic risk factors for this condition. However, the causal variants, genes and mechanisms underlying these associated genomic regions is not fully understood. In this project, you will use both computational and experimental approaches to identify the key drivers of difficult-to-treat asthma in these genomic regions. The first 18-24 months of the PhD will be spent in the Genetic Epidemiology Group at the University of Leicester, an internationally renowned group with a large, vibrant student community. Here, you will learn state-of-the-art statistical genetics and bioinformatics techniques, including analysis of long-read sequencing and multi-omic datasets. You will then have the opportunity to investigate prioritised asthma-associated regions at the prestigious Biodiscovery Institute at the University of Nottingham using cutting-edge wet-lab techniques such as genome editing in *in vitro* model systems. This project will provide valuable insights into the biology of difficult-to-treat asthma and potentially inform the development of new therapies for these patients. |
| **References** |
| McDowell PJ, McDowell R, Busby J, Eastwood MC, Patel PH, Jackson DJ, Mansur A, Patel M, Burhan H, Doe S, Chaudhuri R, Gore R, Dodd JW, Subramanian D, Brown T, Heaney LG; UK Severe Asthma Registry. Clinical remission in severe asthma with biologic therapy: an analysis from the UK Severe Asthma Registry. Eur Respir J. 2023 Dec 14;62(6):2300819. doi: 10.1183/13993003.00819-2023. PMID: 37857423; PMCID: PMC10719453.Shrine N, Portelli MA, John C, Soler Artigas M, Bennett N, Hall R, Lewis J, Henry AP, Billington CK, Ahmad A, Packer RJ, Shaw D, Pogson ZEK, Fogarty A, McKeever TM, Singapuri A, Heaney LG, Mansur AH, Chaudhuri R, Thomson NC, Holloway JW, Lockett GA, Howarth PH, Djukanovic R, Hankinson J, Niven R, Simpson A, Chung KF, Sterk PJ, Blakey JD, Adcock IM, Hu S, Guo Y, Obeidat M, Sin DD, van den Berge M, Nickle DC, Bossé Y, Tobin MD, Hall IP, Brightling CE, Wain LV, Sayers I. Moderate-to-severe asthma in individuals of European ancestry: a genome-wide association study. Lancet Respir Med. 2019 Jan;7(1):20-34. doi: 10.1016/S2213-2600(18)30389-8. Epub 2018 Dec 11. PMID: 30552067; PMCID: PMC6314966.Nelson, M., Tipney, H., Painter, J. et al. The support of human genetic evidence for approved drug indications. Nat Genet 47, 856–860 (2015). <https://doi.org/10.1038/ng.3314> |