**University of Leicester**

**Department of Respiratory Sciences**

**Funding Source:** There is no funding available for this project. Self-funded applications can be considered.

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| **Eligibility:** International applicants **Fees:** £34,000 (2022/2023 entry) or £35,350 (2023/2024 entry) |

**Supervisors:** Prof Andrea Cooper and Manish Pareek

**Project Title: Stratification of TB risk by immunophenotyping and expression of key diagnostic markers**

**Project Description**

Tuberculosis (TB) is a worldwide disease characterized by dramatic differences in individual outcomes. Many infected with the etiological agent never see any signs of disease while others succumb to rapid fulminant infection in the lung. In between these extremes, there is a range of outcomes. To manage TB effectively we need to understand who of the 2-3 billion people in the world infected with the etiological agent is most likely to develop significant disease. In this studentship – the cellular and humoral responses of human subjects who have been clinically characterized for disease phenotype will be investigated. The hypothesis is that specific signals are associated with progression to active disease. Immunological, metabolomic and bioinformatic techniques will be brought together to test this hypothesis. Some samples and tools are in place so the studentship will balance sample collection with immediate data generation.

Tuberculosis (TB) is a significant public health issue and remains a cause for concern in the UK. Migrants arriving from high TB burden settings undergo routine screening for latent infection (LTBI) in primary care with an interferon gamma release assay (IGRA). The IGRA does not differentiate between individuals with TB and LTBI. Previous work (Cooper) shows that expression of an alternative splice variant of the IL12RB1 (IL12Rb1ΔTM) is high in active TB and low in LTBI, expression also drops during effective drug therapy[1]. The power of this expression is that it harnesses the host’s sensitivity to the pathogen rather than direct detection of the pathogen, which is in low abundance. We are currently collecting samples from the clinic under ethical approval to assess the role of IL12Rb1ΔTM in TB.

**Aim**: To determine whether expression of IL12Rb1ΔTM correlates with the clinical and immunological phenotype in IGRA positive individuals.

**Hypothesis**: IL12Rb1ΔTM expression and antigen-specific T cell phenotype correlate with the severity of disease defined by clinical parameters.

**Methods:**

Subjects from secondary TB care clinics in Leicester – (Pareek/Haldar).

RNA analysis and q-PCR

PBMC stimulated with Mtb-antigen pools and T cell flow

Analysis of humoral samples for metabolic markers

**Data analysis**: All parameters will be normalized and unsupervised clustering performed to test the null hypothesis. If we find correlation between any one or group of symptoms or clinical outcome and the level of the IL-12Rb1ΔTM and T cell phenotype our hypothesis will be supported. This is a pilot study and so numbers of samples required to test the hypothesis are not yet determined. We will collect at least 40 samples from the LTBI clinic.

**References:**

1. Das, M.K., et al., *Differential expression of an alternative splice variant of IL-12Rβ1 impacts early dissemination in the mouse and associates with disease outcome in both mouse and humans exposed to tuberculosis.* bioRxiv, 2018.

**Entry requirements:**

Applicants are required to hold/or expect to obtain a UK Bachelor Degree 2:1 or better in a relevant subject or overseas equivalent.

The University of Leicester [English language](https://le.ac.uk/study/research-degrees/entry-reqs/eng-lang-reqs/ielts-65) requirements apply

**Application advice:**

To apply please use the application link at the bottom of the web page <https://le.ac.uk/study/research-degrees/research-subjects/respiratory-sciences>

With your application, please include:

* CV
* Personal statement explaining your interest in the project, any relevant research experience and why we should consider you
* Degree Certificates and Transcripts of study already completed or a transcript to the current date of study currently being undertaken
* Evidence of English language proficiency if applicable
* In the reference section please enter the contact details of your two academic referees in the boxes provided or upload letters of reference if already available.

In the funding section please specify how you are able to fund your study.

In the proposal section please provide the name of the supervisors and project title (a research proposal is not required)

**Project / Funding Enquiries:** **RespSci-PGR@le.ac.uk**

**Application enquiries to** **pgradmissions@le.ac.uk**

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