**Department of Respiratory Sciences PhD**

**Self funded Project information**

**Funding Source: Self-Funded**

**Proposed project start date: Sept 2023 or Jan 2024**

**Eligibility: International students only**

**Department/School:** Respiratory Sciences

**Supervisory team:**

**Primary supervisor: Dr. John E. Pearl [****jep38@leicester.ac.uk****]**

**Secondary supervisors: Dr. Chris Holmes [cwh17@leicester.ac.uk] and Dr. Andrew Millard [adm39@leicester.ac.uk]**

**Project Title:** Survey of clinical non-tuberculous mycobacteria isolates for mycobacteriophages: their presence, diversity and potential role in disease.

**Project Description**

This project seeks to advance our understanding of infectious disease by examining the role that bacteriophages might play in the context of clinical diagnostics. We seek to test whether clinical specimens of non-tuberculous mycobacteria [NTM] harbour mycobacteriophages and to determine if their presence is associated with altered phenotypes or modulated responses to chemotherapeutics. From the larger context, this study will provide essential insight into the complex relationship between bacteriophages, their targets and human health. As a recent report of the presence of prophages in a variety of type and clinical strains of *Mycobacterium abscessus* suggests [1], we deem it likely that the multiple species classified as NTM also contain genetic evidence of phage infection. Induction of phages from species that comprise NTM have been reported using UV light or treatment with mitomycin C [2]. Induction of phages from and sensitivity to infection has been proposed for use as a species typing approach for some of the species classified as NTM [3].

This project will experimentally test whether clinical isolates from non-tuberculous mycobacterial infections collected from pulmonary sources, such as those acquired during biopsy or bronchiolar wash, from sputum, or from other sampled tissues contain evidence of bacteriophage(s). Based on Oxford Nanopore sequencing performed in-lab, the student will perform genomic sequence analysis of the clinical isolates for signatures of prophage and will sequence all induced phage. Critically, this informatic analysis will investigate any genetic payload incorporated into the phage as a potential mechanism for horizontal transfer of virulence determinates or disease modulating genes.

Among the techniques available for this project are confocal microscopy and flow cytometry for the determination of bacterial membrane potential, cryo-electron microscopy for visualization of enzymatic complexes, bioreactors of various capacities with a range of features, real-time and quantitative PCR and various methods for extracting RNA and DNA, as well as other intracellular materials from mycobacteria.

We expect the project to generate at least one peer-reviewed publication and to significantly contribute to on-going efforts to combat the emergence of antibiotic resistance and to mitigate clinical chemotherapeutic failure.

**References:**

1. Amarh, E.D., et al., *Unusual prophages in Mycobacterium abscessus genomes and strain variations in phage susceptibilities.* PLOS ONE, 2023. **18**(2): p. e0281769.

2. Timme, T.L. and P.J. Brennan, *Induction of bacteriophage from members of the Mycobacterium avium, Mycobacterium intracellulare, Mycobacterium scrofulaceum serocomplex.* J Gen Microbiol, 1984. **130**(8): p. 2059-66.

3. Crawford, J.T., J.K. Fitzhugh, and J.H. Bates, *Phage typing of the Mycobacterium avium-intracellulare-scrofulaceum complex.* Am Rev Respir Dis, 1981. **124**(5): p. 559-62.

**Tuition Fee details:**

*Full payment of international fees university and experimental bench fees are required*

**Entry requirements:**

Applicants with an MSc within the field of biological sciences or a related discipline are encouraged to apply.

Candidates with a first or upper second honours undergraduate degree (or equivalent) in a biological sciences or related discipline will be considered. Qualifications recognised as equivalent to a British University lower second-class degree (2.2) will also be considered, as will applicants who do not hold a bioscience degree but have significant and relevant industrial, professional medical or veterinary experience. Such applicants will be considered on a case-by-case basis.

Students for whom English is not their first language are required to meet the minimum standard set by the University of Leicester (as specified in Senate Regulation 1: Regulations governing minimum entry qualifications and language requirements for taught programmes of study). This includes an IELTS minimum score of 6.5; a TOEFL iBT, minimum score of 90 or a Pearson Test of English (PTE) minimum score of 61.

**Application advice:**

To apply please refer to <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 state how you will fund your studies

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

**Project Enquiries:** **jep38@leicester.ac.uk**

**Application enquiries to** respsci-pgr@leicester.ac.uk

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