3 Year PhD Studentship available for September 2019

Department: Cardiovascular Sciences

Supervisors: Prof Gavin Murphy, gjm19@le.ac.uk
Dr Syabira Yusoff, ny70@le.ac.uk
Dr Marcin Woźniak, mw299@le.ac.uk

Eligibility: UK/EU applicants only

Project Title: The role of FOXO1 in obesity-driven protection in cardiac surgery

Project Description:

The PhD student will work as part of the BHF funded Cardiac Surgery Research Group, the largest cardiac surgery research group in the UK. Our research aims to reduce deaths attributable to multiple organ failure.

Organ injury is common and often life-threatening complication following cardiac surgery [1, 2]. One of the independent factors in the development of cardiovascular diseases is obesity; however, overweight patients have better survival chances when undergoing cardiac surgery [3]. Analysis of transcriptome from obese animals points towards mild mitochondrial dysfunction as a potential mechanism. Heart energy supplies rely on mitochondrial ATP production, and interference with the mitochondrial function associates with cardiac dysfunction and diseases [4]. However, it also triggers mechanisms that enable management of stress associated with surgery or ischaemia-reperfusion (IR) [5]. These mechanisms involve mito-nuclear retrograde signalling, central to which are sirtuins and FOXO1, known to activate genes involved in mitochondrial biogenesis and oxidative stress response [6]. SIRT1 and FOXO1 expression levels are significantly higher in animals fed high-fat chow. Increasing SIRT1/FOXO1 expression by obesity or a pharmacological intervention like treatment with valproic acid (also known to reduce organ injury after IR [9]) could be particularly beneficial to underweight patients with underlying diseases and severely obese, who are at highest risk when undergoing cardiac surgery [3].

This project will test the hypothesis that moderate mitochondrial stress leads to increased expression levels of genes that confer organ protection after cardiac surgery, which is orchestrated by moderately increased FOXO1 expression. The project will be paired with randomised clinical trials that test how changes in metabolic status affect patient outcomes after cardiac surgery.

The student will gain skills in statistics, bioinformatics and machine learning to analyse high throughput data such as transcriptomics, proteomics and chromatin condensation profiling, as well as, experience with molecular and cell biology techniques such as expression construct generation,
transfection, tissue culture, fluorescent microscopy, CRISPR/Cas9 technology, IR models, ex vivo heart reperfusion and organ injury diagnostics.

This project will suit an enthusiastic and dynamic student with a background in Biological Sciences, Molecular Genetics or medical students who have an interest in multidisciplinary research. The project will be performed in collaboration with our partners across the University of Leicester and the UK.

References:


Funding details:

The College of Life Sciences studentship will provide a stipend at RCUK rates and UK/EU fees for 3 years.

Entry requirements:

Applicants are required to hold/or expect to obtain a UK Bachelor Degree 2:1 or better in a relevant subject. The University of Leicester English language requirements apply where applicable.

How to apply:

You should submit your application using our online application system.

Apply for a PhD in Cardiovascular Sciences

In the funding section of the application please indicate you wish to be considered for a CLS CVS studentship.

In the proposal section please provide the name of the supervisor and project you want to be considered for.

Project / Funding Enquiries: cvspgr@le.ac.uk

Application enquiries to pgradmissions@le.ac.uk