3 Year PhD Studentship available for September 2019

Department: Leicester Precision Medicine Institute / Leicester Biomedical Research Centre / Cardiovascular Science

Supervisors:
- Prof Donald Jones - donald.jones@leicester.ac.uk
- Prof Nilesh Samani - njs@leicester.ac.uk
- Prof. Gerry McCann - gpm12@le.ac.uk

Eligibility: UK/EU applicants only

Project Title: Biomarkers of Coronary Artery Disease in multi-ethnic populations

Project Description:
Coronary artery disease (CAD) is a serious and prevalent cardiovascular disease which can present in patients in many ways. Notably, it has a higher prevalence in the South Asian population. Markers found in blood are highly sought after and in particular would allow an investigation into the effectiveness of markers in diagnosing CAD in multi-ethnic populations. Additionally, differentiating the mechanisms of disease between ethnic groups could provide novel therapeutic targets for precision medicine.

We will use state of the art analytical equipment (HPLC and Mass spectrometry) in combination with computational tools to detect and quantify proteins present in blood. Quantitative differences between disease groupings will be used to establish a statistical model for determining the extent of CAD in patients. This will be then extended into a much larger cohort to guide the selection of a novel test for the extent of CAD and investigate the implications of ethnicity.

The studentship will provide comprehensive training in mass spectrometry based proteomics for discovery and targeting of markers, statistics and bioinformatics, which will equip the candidate very well for future research work.

Aims:
- To identify a pattern of proteins accurately measured in the plasma of patients with CAD and healthy matched controls.
- To validate the panel using a LC-MS/MS-SRM multiplex method in the 1000+ cohort of patients.
- To establish the correlation between the panel and the extent of CAD.
Background: Coronary artery disease (CAD) occurs due to the formation and progression of complex atherosclerotic lesions in the coronary arteries which disrupts oxygen delivery to the myocardium. This can manifest as silent ischaemia, angina pectoris, myocardial infarction or even heart failure. CT coronary angiography (coupled with CT calcium score) is currently the gold standard for detecting the presence of CAD, but is expensive and involves radiation exposure. CAD has a higher prevalence in the South Asian population and thus may have slightly different mechanistic etiology. Biomarker discovery has been hampered by the lack of low-cost high-throughput agnostic methods, and natriuretic peptides and troponins have remained the mainstay of cardiology practice. Cardiovascular medicine has benefited from many large-scale endpoint driven trials which have yielded insights into therapy, and many such trials have biobanked plasma samples which have the potential to be mined for patient stratification.

Hypothesis: A panel of proteins will be established and validated to determine the extent of CAD in an ethnically diverse patient population.

Proposed Study:

We will take advantage of our large secondary care population (~2200 rapid access chest pain visits per annum) and our easy access to state-of-the-art cardiac CT (>1000 per annum, ~45% normal) to investigate whether a blood biomarker correlates with the extent of CAD.

Experimental Methods and Research Plan:

- Carry out an agnostic discovery phase using standard operating procedures for LC-IMS-MS/MS (50x50 CAD vs control). Raw data will be processed using proprietary software (Progenesis QI for Proteomics) to provide data amenable to statistical analysis.
- Statistically identify a model of CAD prediction using a panel of proteins.
- Validate this panel of proteins in the 1000 cohort using a multiplex LC-MS/SRM assay with stable isotope labelled internal standards.
- Statistically validate the correlation between the panel of proteins and the extent of CAD.
- Assess the effect of ethnicity on the protein panel.

The student would be situated at the John and Lucille van Geest Biomarker facility, BHF-Cardiovascular Centre at Glenfield Hospital at Leicester. This Research centre is a world leader in biomarker discovery in genetics, proteomics, metabonomics and phenotypes. The laboratory has 4 high resolution mass spectrometers with access to another 5 mass spectrometers which are predominantly triple quadrupole instruments which are more suited to quantitative type experiments. We are in the process of enhancing the analytical capability by buying state of the art instruments that are highly suited for the type of work described herein. The supervisors are experienced in PGR supervision and have jointly supervised 12 students to date.

Outcomes:

- A new test for determining extent of CAD.
- Established phenotypic differences between ethnic groups who present with CAD
- Potential novel targets for CAD therapy which can enable personalised medicine.
**Funding details:**

This project is in competition for a College of Life Sciences (CLS) PhD Studentship. The Studentships are for three years, starting September 2019, and offer tuition fees at UK/EU rates and a Stipend at UK Research Council rates.

**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 LPMI/BRC studentship.

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

You do not need to submit a proposal but please include a personal statement detailing your interest in this project.

**Project / Funding Enquiries:** Prof Donald Jones - donald.jones@leicester.ac.uk

Prof Nilesh Samani - njs@leicester.ac.uk

Application enquiries to [pgradmissions@le.ac.uk](mailto:pgradmissions@le.ac.uk)

Closing date for applications 27th January 2019