**University of Leicester**

British Heart Foundation Centre of Research Excellence

PhD studentship

|  |  |
| --- | --- |
| **First Supervisor** | Prof David Adlam |
| **School/Department** | Cardiovascular Sciences |
| **Email**  | da134@le.ac.uk |

|  |  |
| --- | --- |
| **Second Supervisor** | Prof Leong Ng |
| **School/Department** | Cardiovascular Sciences |
| **Email**  | lln1@leicester.ac.uk |

|  |  |
| --- | --- |
| **Additional Supervisor** | Dr Tom Webb (tw126@leicester.ac.uk) and Dr Furqan Aziz (fa311@leicester.ac.uk) |

**Section 2 – *Project Information***

|  |  |
| --- | --- |
| **Project Title** | Machine-learning directed plasma proteomics to develop a novel blood test for the diagnosis of spontaneous coronary artery dissection (SCAD) |
| **Project Summary**  |
| SCAD is an increasingly recognised cause of non-atherosclerotic AMI, predominantly afflicting young women with few conventional atherosclerotic risk factors. In this multidisciplinary cardiovascular sciences studentship, we propose to use machine learning tools in collaboration with the school of computing and mathematical sciences, to conduct a hypothesis independent approach to the identification of a diagnostic biomarker panel for SCAD, derived from a deep exploration of the human plasma proteome data from the University Van Geest multiomics facility at the Hodgkin building. For this biomarker-development phase we will use existing biobanked cohorts of SCAD, age-gender matched healthy volunteers and non-SCAD ACS (UK SCAD, *Swiss SCAD and InterSCAD SPUM-ACS*). We will using high-definition mass spec instruments with ion mobility   e.g.  Waters G2S, Bruker timsTOF and thermo Orbitraps which give up to 6000 proteins per run, using different matrices which are non-overlapping. These can identify half the known proteome quite easily (not including post translational modifications). These will be analysed with state-of-the art machine learning strategies. Candidate biomarker(s) identified using these omics strategies will be taken forward for prospective validation in patients recruited to the APT-SCAD clinical trial and relevant controls. The student will develop interdisciplinary skills in laboratory science, clinical science and machine learning.The student will benefit from support from existing funds (BeatSCAD) to support additional proteomics consumables above the standard available studentship funds and from support from our BHF Special Project Grant funded academic partnership (Adlam, Webb, Nelson, Ng) and associated funded post-doctoral ECR scientists with relevant experience (McVey, Saxby, Solomon).Our research will continue to be conducted in close partnership with our patients both in the UK (<http://beatscad.org.uk/>) and Europe (https://www.rareconnect.org/en/community/spontaneous-coronary-artery-dissection). |
| **References** |
| 1. Adlam D, Alfonso F, Maas A, Vrints C, Writing C. European Society of Cardiology, acute cardiovascular care association, SCAD study group: a position paper on spontaneous coronary artery dissection. *Eur Heart J* 2018;**39**:3353-3368. doi: 10.1093/eurheartj/ehy0802. Hayes SN, Kim ESH, Saw J*, et al.* Spontaneous Coronary Artery Dissection: Current State of the Science: A Scientific Statement From the American Heart Association. *Circulation* 2018;**137**:e523-e557. doi: 10.1161/CIR.00000000000005643. Hayes SN, Tweet MS, Adlam D*, et al.* Spontaneous Coronary Artery Dissection: JACC State-of-the-Art Review. *J Am Coll Cardiol* 2020;**76**:961-984. doi: 10.1016/j.jacc.2020.05.0844. Adlam D, Tweet MS, Gulati R*, et al.* Spontaneous Coronary Artery Dissection: Pitfalls of Angiographic Diagnosis and an Approach to Ambiguous Cases. *JACC Cardiovasc Interv* 2021;**14**:1743-1756. doi: 10.1016/j.jcin.2021.06.0275. Kotecha D, Garcia-Guimaraes M, Premawardhana D*, et al.* Risks and benefits of percutaneous coronary intervention in spontaneous coronary artery dissection. *Heart* 2021;**107**:1398-1406. doi: 10.1136/heartjnl-2020-3189146. Chan N, Premawardhana D, Al-Hussaini A*, et al.* Pregnancy and Spontaneous Coronary Artery Dissection: Lessons From Survivors and Nonsurvivors. *Circulation* 2022;**146**:69-72. doi: 10.1161/CIRCULATIONAHA.122.0596357. Saw J, Starovoytov A, Humphries K*, et al.* Canadian spontaneous coronary artery dissection cohort study: in-hospital and 30-day outcomes. *Eur Heart J* 2019;**40**:1188-1197. doi: 10.1093/eurheartj/ehz0078. Vasilopoulou CG, Sulek K, Brunner AD*, et al.* Trapped ion mobility spectrometry and PASEF enable in-depth lipidomics from minimal sample amounts. *Nat Commun* 2020;**11**:331. doi: 10.1038/s41467-019-14044-x9. Ding J, Blencowe M, Nghiem T*, et al.* Mergeomics 2.0: a web server for multi-omics data integration to elucidate disease networks and predict therapeutics. *Nucleic Acids Res* 2021;**49**:W375-W387. doi: 10.1093/nar/gkab40510. Cao TH, Jones DJL, Voors AA*, et al.* Plasma proteomic approach in patients with heart failure: insights into pathogenesis of disease progression and potential novel treatment targets. *Eur J Heart Fail* 2020;**22**:70-80. doi: 10.1002/ejhf.160811. Emmens JE, Jones DJL, Cao TH*, et al.* Proteomic diversity of high-density lipoprotein explains its association with clinical outcome in patients with heart failure. *Eur J Heart Fail* 2018;**20**:260-267. doi: 10.1002/ejhf.110112. Su X, Junior GPO, Marie AL*, et al.* Enhanced proteomic profiling of human plasma-derived extracellular vesicles through charge-based fractionation to advance biomarker discovery potential. *J Extracell Vesicles* 2024;**13**:e70024. doi: 10.1002/jev2.7002413. Wu CC, Tsantilas KA, Park J*, et al.* Mag-Net: Rapid enrichment of membrane-bound particles enables high coverage quantitative analysis of the plasma proteome. *bioRxiv* 2024. doi: 10.1101/2023.06.10.544439 |