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| **First Supervisor** | Professor Dave Adlam |
| **School/Department** | Cardiovascular Sciences |
| **Email** | da134@le.ac.uk |

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| **Second Supervisor** | Dr Tom Webb |
| **School/Department** | Cardiovascular Sciences |
| **Email** | tw126@leicester.ac.uk |

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| **Additional Supervisor** | Dr Furqan Aziz |

**Section 2 – *Project Information***

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| **Project Title** | Understanding How Female Hormones and Genetics Drive SCAD, a Major Cause of Heart Attacks in Young Women using clinical, cellular and AI-enhanced OMICs |

**Project Summary**

Heart attacks in young women are uncommon, poorly understood, and often overlooked. One major cause is spontaneous coronary artery dissection (SCAD), a condition where a tear develops in a coronary artery. SCAD overwhelmingly affects women who often have few traditional cardiovascular risk factors, and it is more common during pregnancy, around menopause, and at times of significant hormonal change. Many women experience long-term anxiety about recurrence, but we still lack clear evidence about who is most at risk and how best to personalise care.

Our recent work has uncovered genetic factors that increase vulnerability to SCAD, but genetics alone cannot explain the strong influence of female sex hormones. This PhD tackles one of the most important unanswered questions in women's cardiovascular health: how do hormonal fluctuations interact with genetic susceptibility to trigger SCAD? Understanding this relationship may help identify those at highest risk, improve clinical guidance around hormone therapies, and ultimately support safer, more personalised treatment options for women.

This project offers an interdisciplinary training environment where the student can tailor the balance of epidemiology, laboratory work and data science to their interests. You will work across three connected research themes:

**1. Clinical and epidemiological analysis**
Using data from the SCAD-UK and SCAD-EU registries, you will study how menopausal status, pregnancy history, hormonal contraceptives and HRT relate to SCAD recurrence. This will give population-level insight into hormonal risk factors.
**2. Molecular analysis of coronary arteries**
Working with national and international collaborators, you will examine hormone receptor expression in coronary tissue using immunohistochemistry, spatial transcriptomics and single-cell analysis. This will help reveal how hormone-sensitive pathways change in SCAD.
**3. Cell-based multi-omics and AI approaches**
You will expose vascular cells to hormone conditions mimicking menstrual cycling, pregnancy and menopause. Using transcriptomics, epigenetics and AI-based data integration, you will identify the molecular pathways linking hormonal environments to genetic risk.

This project is ideal for motivated students fascinated by women's cardiovascular health, genomics, molecular biology, or AI in medicine. You will gain high-value interdisciplinary skills at the interface of data science, laboratory science and translational cardiovascular research.

**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/ehy080

2. Adlam D, Berrandou TE, Georges A*, et al.* Genome-wide association meta-analysis of spontaneous coronary artery dissection identifies risk variants and genes related to artery integrity and tissue-mediated coagulation. *Nat Genet* 2023. doi: 10.1038/s41588-023-01410-1
3. Carss KJ, Baranowska AA, Armisen J*, et al.* Spontaneous Coronary Artery Dissection: Insights on Rare Genetic Variation From Genome Sequencing. *Circ Genom Precis Med* 2020;**13**:e003030. doi: 10.1161/CIRCGEN.120.003030