**University of Leicester**

British Heart Foundation Centre of Research Excellence

PhD studentship

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| **Additional Supervisor** | Dr David McVey |

**Section 2 – *Project Information***

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| **Project Title** | Engineering 3D Vascular Models for Functional Genomics and Systems Genetics of Cardiovascular Disease. |
| **Project Summary** | |
| Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide1, placing a major burden on both patients and healthcare systems. Improving outcomes requires a better understanding of the biological mechanisms and risk factors that drive disease development, particularly the molecular pathways linking genetic risk variants to cellular dysfunction.  Genetic variation is an important contributor to CVD risk. Genome-wide association studies have shown specific risk regions across the genome for specific vascular diseases, but this is not enough. What is really needed is an understanding of the molecular mechanisms linking genetic variation to vascular disease.  Omic technologies such as transcriptomics, proteomics, and epigenomics are poweful tools for exploring these mechanisms in vascular cells. We have developed a unique, well-characterised biobank of primary human vascular cells2,3 that enables systematic, large-scale analysis of gene regulation and function. However, traditional 2D cell culture models fall short of capturing the complexity of the in vivo vascular environment, where cells experience dynamic flow and interact within layered three-dimensional structures.  This interdisciplinary PhD project aims to develop and apply next-generation, tissue-engineered vascular models that combine biomaterials, co-culture of multiple vascular cell types, and physiologically relevant flow conditions. These models will better mimic native vessel architecture and mechanical forces, enabling more accurate investigation of how genetic variation and flow affect key regulatory pathways.  The student will gain broad expertise in biomaterials engineering, advanced 3D cell culture, flow-based systems, imaging, and genomics. The project offers an exciting opportunity to generate biologically meaningful insights into the genetic regulation of vascular function and disease. | |
| **References** | |
| 1. McAloon, C.J., Boylan, L.M., Hamborg, T. et al. 2016. The Changing Face of Cardiovascular Disease 2000-2012: An Analysis of the World Health Organisation Global Health Estimates Data. International Journal of Cardiology 224, 256-264. 2. Solomon, C.U., McVey, D.G., Andreadi, C. et al. 2022. Effects of Coronary Artery Disease-Associated Variants on Vascular Smooth Muscle Cells. Circulation 146(12), 917-929. 3. McVey, D.G., Andreadi, C., Gong, P. et al. 2024. Genetic Influence on Vascular Smooth Muscle Cell Apoptosis. Cell Death and Disease 15(6):40 | |
| **Specific entry requirements**  UK 2:1 in relevant subject or overseas equivalent (biology, engineering, materials science, chemistry, physics, medicine or clinical sciences). Candidates with experience of cell culture, tissue engineering and/or biomaterials are particularly encouraged to apply.  Standard University of Leicester English language requirements | |