Understanding cellular interactions in a 3D bioprinted model of the glomerulus

Supervisory team:
Main supervisor: Dr James Armstrong (University of Bristol)
Second supervisor: Prof Gavin Welsh (University of Bristol)
Dr Liliang Ouyang (Tsinghua University, China), Dr Julia Sero (University of Bath)

Host institution: University of Bristol

Project description:
Kidneys filter circulating blood through a complex structure known as the glomerulus. This contains three interconnected biological barriers: a collagen-rich basement membrane sandwiched between podocyte and endothelial cells (https://doi.org/10.1038/s41573-021-00242-0). The importance of the glomerulus in kidney health and disease has led to widespread research into bioengineering methods that can replicate this cell structure in the laboratory (https://doi.org/10.1038/s41581-021-00528-x). For example, it is well known that podocytes and endothelial cells can self-assemble into simple cell structures that can subsequently lay down a basement membrane. Recently, Prof. Welsh (secondary supervisor on this project) showed that different biomaterials can be used to guide this self-assembly process (doi.org/10.1002/adhm.201900698). We wish to build upon this work by incorporating a new 3D bioprinting approach known as in situ endothelialisation (doi.org/10.1002/adfm.201908349). This method, co-developed by Dr Ouyang (co-supervisor) and Dr Armstrong (primary supervisor), allows us to 3D print biomaterials containing small channels that are lined with endothelial cells. This system can then be connected to syringe pumps and microfluidics to continuously perfuse these "blood vessels" with liquid media.

In this project, the PhD student will combine these methods to 3D print a perfusable cell model of the glomerulus. These cell organization within these printed glomeruli will be visualized as they are perfused and matured using confocal fluorescence microscopy and immunostaining. Finally, the barrier transport of fluorescent molecules and drugs will be studied in glomeruli printed with podocytes carrying disease mutations. This is a highly interdisciplinary project that draws on major advances in polymer chemistry, biomaterials science, kidney biology, and biological characterization. The student will benefit from the diversity of experience of the supervisory team and will be fully trained across all these techniques. The work will be largely conducted in the laboratories of the primary supervisor, who has broad expertise in biomaterials, 3D printing, microfluidics, and tissue engineering. These labs are based within the Dorothy Hodgkin Building (DHB), a state-of-the-art research environment providing unrestricted access to onsite core facilities (e.g., cell culture, bioimaging, histology, molecular biology).

The secondary supervisor (Prof. Gavin Welsh) is part of Bristol Renal, which is also based at the DHB, and will support the student in all aspects of kidney biology. The project is co-supervised by experts in polymer synthesis and 3D printing (Dr Liliang Ouyang, Tsinghua University) and advanced bioimaging and image analysis (Dr Sero, University of Bath).

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.