SEMS: RESEARCH PROJECT DESCRIPTION

1. Project Background and Description

An artery-on-a-chip model to study vascular smooth muscle cell mechanosensing

Vascular smooth muscle cells (VSMCs) play a central role in the onset and progression of many cardiovascular diseases, from atherosclerosis to vascular injury. While normally exhibiting a contractile phenotype that is required to set the tone in the vessel wall, VSMC can switch to a migratory phenotype that leads to a degradation of the vascular extracellular matrix. This switch is significantly enabled by the formation of podosomes. Podosomes are adhesive, mechanically protrusive structures at the basal interface that enable degradation of the underlying extracellular matrix. Or previous work has identified that arterial vascular smooth muscle cells respond to mechanical stimuli by changing their behaviour, when cultured on 2D environments; i.e. they switch the phenotype in environments mimicking the ageing artery or when mimicking hypertension. It is however still unclear how this is regulated in a 3D environment mimicking the situation in vivo. Here we want to test the mechanosensitivity in a tissue engineered artery-on-a-chip.

2. Project Scope

The specific objectives for this project are:

A) Construction of an artery-on-a-chip microfluidic device for vascular smooth muscle and endothelial cell co-culture using the RegenHu 3D printer at the Queen Mary Create facility.

B) Investigate the change in vascular smooth muscle cell behaviour and phenotype after mechanical stimulation through changing flow condition and using a new state-of-the-art 3D super-resolution spinning disc microscope

C) Investigate the molecular mechanism of vascular smooth muscle cell mechanical sensing. Using phospho-proteomics analysis in 2D cultures we will identify signalling cascades after mechanical stimulation, which we will then validate in the artery-on-a-chip using immunostaining as well as knockdown or CRISPR knockout cell lines

3. Desired Skills from the Student

The ideal candidate will have a good level of experience with cell and tissue culture, microscopy, as well as interest in 3D bioprinting. Further she/he will have experience with image analysis and statistical analysis skills and should have basic understanding and interest in biophysics, molecular biology and cardiovascular biology

4. Supervisory Team

Primary: Dr Thomas Iskratsch, Senior Lecturer for Bioengineering, SEMS

Secondary: Prof Julien Gautrot, Professor in Biomaterials and Biointerfaces, SEMS