HIGH-RESOLUTION HYBRID IMAGING OF ENDOTHELIUM USING ARTIFICIAL MICROVESSELS

Scientific Objective : to explore the Metabolism of Endothelial Cells using Artificial Microvessels and Ultra High Resolution Molecular Imaging

The vascular network is the largest organ of the human body. Endothelial cells (EC) are the first barrier between blood and tissue. In healthy tissue, there is an exquisite balance between the formation (angiogenesis), and senescence and death of endothelial cells. In disease states, EC are at the front line of pathological processes. For instance, in tumor tissues, EC proliferation drives angiogenesis; in diabetes, EC are intoxicated by glucose; in atherosclerosis they are attacked by lipid deposits triggering inflammation. ECs are constantly in direct contact with a myriad of biologically active elements, e.g. oxygen, carbon dioxide, reactive oxygen species, hormones, cytokines, growth factors, pathogens, inflammatory cells, exovesicles derived from normal or sick cells, etc. Accordingly, evolution has made EC extremely well fit to react rapidly to toxic or pathogen exposure, through efficient endothelial remodeling, orchestrated by an exquisite adjustment of metabolic activities coordinating morphogenesis. Changes in the metabolism of EC are early signals of many diseases such as diabetes, sepsis, cancer and obesity. However, very little is known about EC metabolism because *in situ* experiments are extremely difficult. We propose to build an artificial vascular network to measure EC metabolism in a controlled microfluidics environment using Ultrafast Ultrasound Doppler (USD) and ultra-high positron emission tomography (PET)[1].

Approach: to build an artificial vascular network to measure accurately and longitudinally endothelial cell metabolism with ULTRAFAST Ultrasound DOPPLER and ultra high resolution positron imaging

We propose to design an artificial vascular network of live EC amenable to be imaged with customized ultra-high resolution positron imaging (PE) and Fast US Doppler devices. Taking advantage of (i) improved PE resolution and (ii) predefined geometry of the network, we will explore the EC metabolism quantitatively and longitudinally in artificial EC vessel walls. The approach is similar to super-resolution" techniques: here, the limited resolution of PE cannot resolve metabolism from one EC layer but co-registration in a geometrically-designed microfluidics system assigns PE metabolic measurements to that layer. In these controlled microfluidics cell conditions we will screen molecular effectors of EC development. We will measure the effect on EC metabolism of flow, temperature and pressure (physical conditions), and glucose, oxygen and other naturally occurring molecules such as glutamine, lactate, succinate (chemical conditions). We will test drugs targeting EC metabolism and observe, for the first time in an accurate and reproducible way, the metabolic response of ECs to the effectors of their environment.

Workplan

(i) Design, assembly and assessment of the microfluidics system to explore EC metabolism
(ii) Biological, metabolic and acoustical characterization of the EC engraftment
(iii) Live imaging of EC metabolism in response to the effectors of the environment

Required skills

Knowledge in microfluidics, hemodynamics and vascular biology
Skilled in experimental design and setup
Excellent capacity to work in a multidisciplinary environment

[1] Provost J, Garofalakis A, Sourdon J, et al. Simultaneous positron emission tomography and ultrafast ultrasound for hybrid molecular, anatomical and functional imaging. Nature Biomedical Engineering. 2018; 2: 85–94.