Postdoctoral fellow - Emergence 2023 CNRS-INC project

Project

ASTER
Ana**ST**omosis in **E**ngineered netwo**R**ks

Location

PASTEUR laboratory, Ecole normale Supérieure
Chemistry Department, 24 rue Lhomond, 75005 Paris
CIRB, Collège de France
11 place Marcelin Berthelot, 75005 Paris

Contract

18-month postdoctoral contract
Starting April 1st 2023

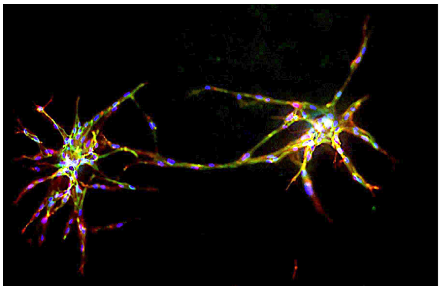
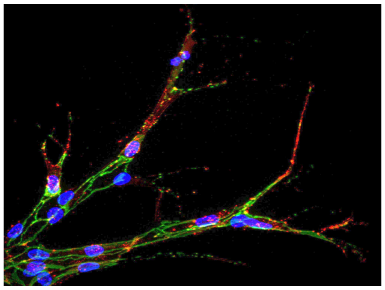
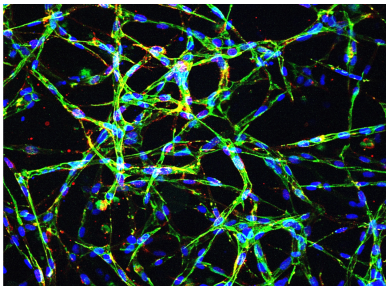
Summary

There is an extensive medical and societal need for the development of ***vascularized*** tissue models for regenerative medicine and replacement of animal models. Biomimetic models based on microfluidics are a promising avenue. This project aims at **developing a vascularized tissue model with microfabricated 3D devices and collagen hydrogels co-seeded with endothelial cells and mesenchymal stem cells.**

Since the first reports of skin model on a chip [1], skin equivalents have been interfaced with vascular endothelial models. Typically, endothelial cells were seeded to grow as monolayers either on porous membranes [2,3] or microfabricated channels [4] but not allowed to generate microvascular structures. Connecting fabricated channels to self-assembled endothelial microvessels is a major challenge. The **ASTER** project aims at creating such relevant and functional perfused microvascular models. To this aim, we microfabricate porous supports, which exhibit a controlled and patterned number of pores. On the bottom side of the support, a monolayer of endothelial cells is grown, while the top side hosts a collagen hydrogel loaded with stem cells. Preliminary results have shown that endothelial cells invade the hydrogel through the pores and form *de novo* vascular structures having an aster shape. This process called sprouting results in the formation of actual lumenized microvessels. The vascular, aster-like structures, can then fuse *via* anastomosis thus forming a luminized vascular network that we have already characterized[5].

Such generation of microvascular network from an endothelial monolayer is a unique model, in a very active area of research. Tuning the dimensions and distribution of the pores in this unique setup will provide control of the hierarchical structure of vascular networks. As such, **ASTER** will provide a key platform to address fundamental questions in biology about the drivers of sprouting and anastomosis. In addition, the integration of this vascularized model in a microfluidic chip will open doors for setting up therapeutic assays.

[1] Abaci et al. LabChip 2015 15, 882; [2] Wufuer et al. SciRep 2016 6, 37471; [3] Kwak et al. BiotechnolBioeng 2020 117, 1853; [4] Lee et al. BiomedMicrodevices 2017 19, 22. [5] Atlas et al, Biomaterials 2021 268, 120594.

Missions and main activities
The postdoctoral fellow will have five main missions: (1) Microfabrication of porous supports (2) Optimization of co-culture conditions including endothelial cells, mesenchymal stem cells and fibroblasts (3) 3D characterization of vascular networks (cross-section area, capillary length, branching) (4) Perfusion of the vascularized networks (5) Investigation of the impact of shear stress on the maturation of vascular networks
Supervision
The postdoctoral fellow will work under the supervision of Carole Aimé (PASTEUR Lab) in collaboration with Laurent Muller (CIRB).
General context
The research activity will be carried out on a full-time work week, within the PASTEUR and CIRB laboratories, 800 m apart. The postdoctoral fellow will have an office and lab space to work in both laboratories.
Knowledge and skills required for the position
The postdoctoral fellow will work on the development of microfabricated platforms and microfluidic devices for exploring the formation and hierarchical organization of vascular structures – sprouting and anastomosis. She/he will then implement the perfusion of the resulting vascular network. A good candidate would have skills in biomaterials engineering and cell biology. A strong interest or background in (bio)microfluidics will also be appreciated.
Main expected results
(1) Control of the hierarchical organization of vascular structures: correlation of the dimensions of the porous support with the formation and morphology of vascular structures; (2) Investigation of cell-mediated anastomosis: impact of the pre-anastomosis architecture controlled by varying the microfabricated pattern; (3) Functionality of the vascular network and development of applied tools: connection of the vascularized hydrogel after anastomosis with the microfluidic chip.
How to apply
Applications should be sent to Carole Aimé (carole.aime@ens.psl.eu) and Laurent Muller (laurent.muller@college-de-france.fr) by January 31st, 2023. The files should include a CV, a summary of doctoral thesis, a letter of motivation and a list of publications.