« PROPOSITION DE STAGE»

Laboratoire : **Ecole Normale Supérieure, Département de Chimie, PASTEUR**
Adresse : **24 rue Lhomond, 75005 Paris**
Directeur du laboratoire : **Rodolphe Vuilleumier**
Équipe de recherche (si pertinent) : **Microfluidic group, Pôle NanoBiosciences & MicroSystems**
Responsable de l'équipe **: Yong Chen**
Responsable de stage : **Carole Aimé**
Adresse électronique : **carole.aime@ens.fr**
Collaborateur : **Laurent Muller, (CIRB), Collège de France**
Adresse électronique : **laurent.muller@college-de-france.fr**
N° et intitulé de l'Ecole Doctorale de rattachement : **ED388**
Profil recherché : **Biophysicien**
Possibilité de poursuite en thèse : **OUI**
Si oui financement envisagé : **ANR, bourse de l'école doctorale**

Titre du stage : **Microfluidic chip for perfusion of microvascularized tissues**

Keywords: microfluidics, microfabrication, microvascularization, angiogenesis, stem cells
Tools: cell culture, microscopy, micro-fabrication

In vitro generation of micro-tissues is becoming the standard alternative to animal testing and for assessment of pathologies and treatments in personal medicine. Such models require perfused microvascularization in order to mimic tissue physiology and to allow delivery of drugs and collection of the secreted products. Our project aims at **combining cell self-assembly with microfabrication in order to generate micro-tissues equipped with a perfused capillary network**.

We will thus develop innovative 3D microfluidic devices that consist in two layers connected with fluidics and assembled with magnetic bonding. Both layers will contain channels coated with matrix proteins and seeded with cells. The central area of the bottom layer will contain a circular central area to host a 3D collagen hydrogel cellularized with endothelial cells co-cultured with stem cells under conditions that promote formation of a capillary network. Microfabricated channels lined with endothelium and self-assembled microvascular network in hydrogels will be connected through anastomosis resulting from promotion of angiogenesis by mesenchymal stem cells. This project will provide a tool for generation of vascularized and perfused 3D micro-tissues.

In the long term, it will be adapted to a tissue engineered model of vascularized skin substitute. It will thus impact future development in a wide range of applications from basic research to disease modelling and pharmacological testing.

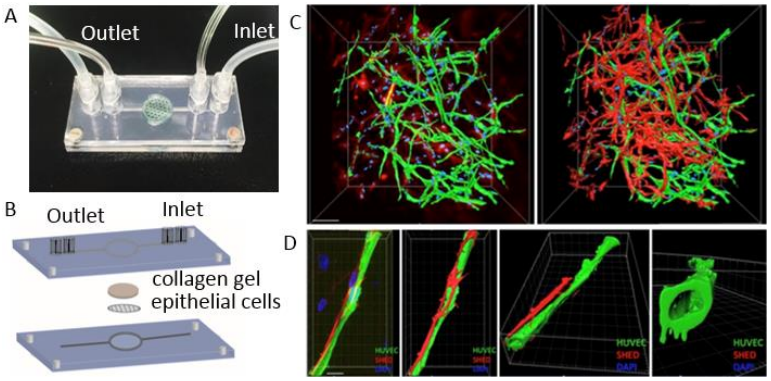

Fig.: **A** and **B**: Photograph and scheme of the microfluidic chip prototype. **C** and **D**: 3D reconstruction of a microvascular network displaying capillaries with lumen formation and perivascular recruitment.

Publications of the team related to the project:

Bignon M*, Pichol-Thievend C*, Muller L & Germain S. (2011). Lysyl oxidase-like protein-2 regulates sprouting angiogenesis and type IV collagen assembly in the endothelial basement membrane. Blood. 118: 3979-3989

Gorin C, Rochefort G, Muller L, Chaussain C, Germain S. (2016). Priming Dental pulp stem cells with FGF-2 increases angiogenesis of implanted tissue engineered constructs through HGF and VEGF secretion. Stem Cells Translational Medicine. 5: 392-404

Liu L, Kamei KI, Yoshioka M, Nakajima M, Li J, Fujimoto N, Terada S, Tokunaga Y, Koyama Y, Sato H, Hasegawa K, Nakatsuji N, Chen Y. (2017) Nano-on-micro fibrous extracellular matrices for scalable expansion of human ES/iPS cells. Biomaterials. 124:47-54.