SORBONNE UNIVERSITÉ

CHINA SCHOLARSHIP COUNCIL

Appel à projets
Campagne 2022
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Title of the research project :

Microfluidic glomerular filtration barrier-on-chip with integrated sensors (ICIS)

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Research Unit

Name : Laboratoire de réactivité des surfaces LRS

Code *(ex. UMR xxxx)* : UMR 7197

Doctorate School

Thesis supervisor's doctorate school (candidate's futur doctoral school) : ED388, Chimie physique et chimie analytique de Paris Centre

PhD student currently supervised by the thesis supervisor (number, year of the first inscription) : 1 en 2018

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Research Unit

Name : CoRaKiD, Common and Rare Kidney Diseases

Code *(ex. UMR xxxx)* : UMRS 1155

École doctorale

Joint supervisor's doctorate school : ED 394, P2T Or, if non SU :

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Research Unit

Name : GeePs, Laboratoire de génie électrique et électronique de Paris

Code *(ex. UMR xxxx)* : UMR8507

École doctorale

Joint supervisor's doctorate school : ED391, SMAER Or, if non SU :

PhD student currently supervised by the joint supervisor (number, year of the first inscription) : 0

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Description of the research project (*ENGLISH*)*:*

Ce texte sera diffusé en ligne : il ne doit pas excéder 3 pages et est écrit en interligne simple.
Ce texte est à l'adresse d'étudiantes et étudiants chinois, il doit donc être rédigé en anglais.

Détailler le contexte, l'objectif scientifique, la justification de l'approche scientifique ainsi que l'adéquation à l'initiative/l'Institut.

Le cas échéant, préciser le rôle de chaque encadrant ainsi que les compétences scientifiques apportées. Indiquer les publications/productions des encadrants en lien avec le projet.
Préciser le profil d'étudiant(e) recherché.

Merci d'enregistrer votre fichier au format PDF et de le nommer :
«CSC_22_Projet NOM Porteur.euse projet »

MIcrofluidic glomerular filtration barrIer-on-Chip with Integrated Sensors (ICIS)

Context:

The prevalence increase of Chronic Kidney Diseases (CKD) is becoming a worldwide public health issue because the only treatments of end-stage kidney failure are not only costly but also rely on heavy treatment such as dialysis or kidney transplantation. Since the renal glomerulus is the first structure to perform the blood filtration, it is the main target in the case of kidney injury. In order to understand the physiology and physiopathology of the glomerulus, there is a need for a new generation of *in vitro* models. Indeed, current *in vitro* models do not reproduce accurately the *in vivo* physiology of the glomerulus and the animal models do not only reproduce poorly human physiology but also suffer of ethical issues. New *in vitro* systems, called MicroPhysiological Systems (MPS) or Organs-on-Chip have been introduced, 10 years ago, by Huh *et al.* [1]. If MPS represent a very promising technology to enhance the physiological relevance of *in vitro* models thanks to the microfluidic technologies [2], they still lack of two majors *in vivo* physiological features: (i) mature cells expressing the specific markers of interest and (ii) basement membrane, an extracellular matrix membrane playing an important role in the glomerular filtration [3]. Further enhancement of MPS should also allow to get real-time readouts, thanks to integrated sensors, in order to monitor the *in vitro* model and the dynamic effects. Up to now, MPS mimicking the glomerulus, do not implement all these three aspects [4,5] or focus on the use of cells that express a better phenotype than glomerular cell lines [6,7]. The development of a new glomerular filtration barrier-on-chip integrating these different aspects will not only help to perform permeability assays but also to model and understand glomerulopathies. This project is based on an existing collaboration between the laboratories CoRaKiD, LRS and GeePs, that has received the support from the department (UFR) of engineering.

Objectives and description of the proposal:

The main aim of this PhD thesis proposal is to develop a sensor-integrated microfluidic platform reproducing the glomerular filtration barrier. This proposal is composed of 3 objectives (O):

- O1: Optimisation of the microfluidic platform and permeability characterization

Based on the work currently undertaken by a postdoctoral researcher and the supervisors, the microfluidic reservoir and the electrode network of the device will be optimized using COMSOL in order to study the effect of the fluid nature and fluid recirculation on the impedance spectroscopy signal. The device will be then fabricated using 3D printing or clean-room facilities. A membrane mimicking the glomerular basement membrane will be placed within the microfluidic reservoir. A first set of characterisation of the device will be performed in order to get the filtration properties of the device without glomerular cells and to optimise the electrochemical sensor setup. Different solutions will be perfused in the microfluidic channels to generate both hydrodynamic and osmotic pressure. The filtration properties of the membranes will be assessed by impedance spectroscopy using the electrochemical sensor.

- O2: iPSC differentiation into glomerular cells under perfusion

As the established conditionally immortalized glomerular cell lines (endothelial cells and epithelial cells called podocytes) [10,11] do not differentiate and mature well in classical 2D, they will be seeded on each side of a physiologically relevant membrane within the microfluidic platform . Cells will be matured under perfusion culture in order to form a physiologically relevant glomerular filtration barrier. Its permeability property will be assessed thanks to: (i) optical methods with fluorescent labelled-proteins and (ii) impedance spectroscopy methods with the electrodes [12] (CoRaKiD and LRS). Cellular phenotype will be assessed by immunofluorescence. Further improvement of the cell phenotype will rely on the induced pluripotent stem cell (iPSC) differentiation into glomerular cells

(preliminary work currently on going at CoRaKiD). Differentiated iPSCs into podocytes and glomerular endothelial cells will be seeded respectively on each side of the membrane. The permeability property will be assessed using the methods described above. The PhD student will carry out these experiments in CoRaKiD in close collaboration with LRS for the impedance spectroscopy methods and with GeePs for the tissue engineering with microfluidic device.

- O3: Reproduction of a glomerulopathy with the glomerular filtration barrier-on-chip

Based on the established expertise of CoRaKid in the pathophysiology of glomerular diseases [13–15], particularly, membranous nephropathy where increase permeability of the glomerular filtration barrier is induced by antibodies to podocytes (the external cell layer of the barrier), the PhD student will leverage this platform to model the glomerular events of the disease using the serum (or purified Immunoglobulins) from the patients with membranous nephropathy of from healthy controls or patients with a different mechanism of disease (IgA nephropathy). The aim, here, is to understand the combined effects of the permeability factors (antibodies) and the glomerular microenvironment. The dynamic of these effects will be monitored in real-time with impedance spectroscopy.

Candidate:

We are looking for a candidate with a Master degree in bioengineering, cellular biology or biochemistry. Able to work in an interdisciplinary environment. Experiences in cell culture with induced pluripotent stem cells, RT-PCR, qPCR and immunofluorescence appreciated.

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