

M2 internship offer

Organization: Développement, Adaptation et Vieillessement (Dev2A), UMR8263-U1345, Institut de Biologie Paris Seine (IBPS), Sorbonne Université

Address: 9 Quai Saint Bernard, Bâtiment C, 75005 Paris, France

Title: Effect of mechanical cues on the differentiation of liver-specific endothelial cells from human iPSCs

Start/End Dates: January/February 2027 – June/July 2027

Host team: Dynamic and multiscale process of auto-organisation in tissue morphogenesis (PAOTiM)

Team leader: Dr. Wenjin Xiao (CNRS, CR) & Prof. Mathieu Hautefeuille (SU, Pr)

Internship supervisor: Dr. Wenjin Xiao, wenjin.xiao@sorbonne-universite.fr

Project summary:

The liver is a central metabolic organ, where cells are organized into hepatic lobules around a central vein, forming hepatocyte cords that are vascularized by specialised capillaries called sinusoids. These sinusoids are highly permeable and display a metabolic gradient known as zonation, which allows efficient nutrient and waste exchange. However, studying these vessels is complex due to the difficulty of replicating their natural environment *in vitro*, including paracrine signaling from other hepatic cells, extracellular matrix composition, and mechanics such as flow-dependent shear stress. To address this challenge, the project aims to use human induced pluripotent stem cells (hiPSCs) and apply defined mechanical and chemical signals to guide the specification of endothelial cells toward liver sinusoidal endothelial cells (LSECs). The goal is to generate LSECs with a more mature phenotype than those obtained by traditional differentiation protocols relying solely on growth factors and small molecules. By drawing on principles of developmental biology, this strategy seeks to establish a physiologically relevant model for advancing liver biology and disease research.

The main tasks of the project are to:

1. Culture human iPSCs and direct their differentiation into endothelial cells.
2. Fabricate the microfluidic chips that the team has designed.
3. Assess the impact of mechanical stimuli (e.g., flow, matrix stiffness) and paracrine signals on the specification of endothelial cells to LSECs.
4. Characterize endothelial function using diverse characterization techniques, including imaging, immunochemistry, and RT-qPCR, and functional assays.

Keywords: hiPSCs, LSECs, organ-on-chip, mechanical cues

Interdisciplinary aspect of the project: This project combines microfluidics, biophysics, stem cell biology, and molecular biology.

Contact: Dr. Wenjin Xiao, wenjin.xiao@sorbonne-universite.fr

Supervisor publications (5 of the most significant publications in recent years)

1. How to prevent endothelial cells from losing their edge: a simple patterning of development-like matrix guides a microvessel morphogenetic process by self-organization

A. X. Monroy-Romero, B. Nieto-Rivera, W. Xiao, M. Hautefeuille#

ACS Materials Science and Engineering, 2024, 10:7054-7072.

DOI: 10.1021/acsbiomaterials.4c00939.

2. Intratumor heterogeneity and cell secretome promote chemotherapy resistance and progression of colorectal cancer

J. Kallberg, A. Harrison, S. Berzina, V. March, I. Nemazanyy, O. Kepp, G. Kroemer, S. Mouillet-Richard, P. Laurent-Puig, V. Taly#, W. Xiao#

Cell Death & Disease, 2023, 14:306.

DOI: 10.1038/s41419-023-05806-z.

3. Scalable formation of highly viable and functional hepatocellular carcinoma spheroids in an oxygen-permeable microwell device for anti-tumor drug evaluation.

J. He, C. Zhou, X. Xu, Z. Zhou, M. Danoy, M. Shinohara, W. Xiao, D. Zhu, X. Zhao, X. Feng, Y. Mao, W. Sun, Y. Sakai, H. Yang#, Y. Pang#

Advanced Healthcare Materials, 2022, 11:e2200863.

DOI: 10.1002/adhm.202200863.

4. An artificial membrane binding protein-polymer surfactant nanocomplex facilitates stem cell adhesion to the cartilage extracellular matrix.

R. Cuahtecntzi-Delint, G. J. Day, W. Kafienah, W. Xiao#, A. W. Perriman#

Biomaterials, 2021, 276:120096.

DOI: 10.1016/j.biomaterials.2021.120996.

5. Designer artificial membrane binding proteins to direct stem cells to the myocardium.

W. Xiao*, T. Green*, X. Liang*, R. Cuahtecntzi-Delint, G. Perry, H. Wang, R. Barker, M. S. Roberts, P. R. Race, A. W. Perriman#

Chemical Science, 2019,10:7610-7618.

DOI: 10.1039/c9sc02650a.