M2 internship proposal

Organization: Laboratoire de Biologie du Développement (UMR 7622), Institut de Biologie Paris Seine, Sorbonne Université
Address: 7-9 Quai Saint Bernard, 75005 Paris, FRANCE

Title: Development of a vascularized liver spheroid−on−chip model to study mechanical cues in regeneration mechanisms
Start/End Dates: 02/2025 - 07/2025 (flexible)

Team: Dynamic and multiscale process of auto-organisation in tissue morphogenesis
Team leader
Prof. Mathieu Hautefeuille
Supervisor
Dr Wenjin Xiao

Summary of lab's interests:
To design biological architectures *in vitro* that restore native conditions for biomedical applications, the team focuses on identifying the impact of critical mechanical and biochemical cues on cells and tissues in culture. To this end, the team develops microfluidic platforms of multicellular models that integrate mechanical control of substrate stiffness, vessel luminal pressure, and fluid shear stress.

Project summary:
Liver regeneration after partial hepatectomy (PHx) involves intricate signaling pathways, yet understanding the priming factors is pivotal. Rapid hemodynamic changes in hepatic sinusoids post PHx suggest that mechanical cues may provide initiating signals for liver regeneration, while the underlying mechanisms remain elusive. Developing a biomimetic vascularized *in vitro* human liver model is imperative to address these questions. Microfluidic organ−on−chip technology represents a groundbreaking advancement in biomedical research, which enables modeling of complex physiological processes by precise control over various critical parameters in the microenvironment. Thus, this project aims to investigate the underlying roles of flow−dependent mechanical stimuli in liver regeneration by developing a vascularized−on−chip model that closely replicates the *in vivo* microenvironment. The main tasks of the project are to: 1. fabricate the microfluidic chips that have been designed in the team; 2. develop a vascularized liver spheroid-on-chip model by co-culturing primary human hepatocytes with endothelial cells in extracellular matrix on chip; 3. investigate cell behaviour in response to mechanical cues (i.e. flow) using a diverse array of characterization techniques, including live imaging, immunochemistry and functional assays.

This project combines biofabrication, microfluidics, tissue engineering, cellular and molecular biology for cutting-edge biomedical research.

Keywords:
liver regeneration, organ-on-chip, vasculature, spheroid, mechanical cues

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