CMD InnoCARE (Innovation for CArdiovascular, metabolic and REspiratory diseases)

Master 2 Internship proposal (2026-2027)

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Profile(s) linked to the project:
☒ Experimental Biology *(Recherche expérimentale)*
☐ Research and Omics Data Analysis *(Recherche et analyse de données omiques)*
☐ Clinical Research *(Recherche clinique)*

Lab:	Institut du Thorax
Team:	III, vascular and pulmonary diseases
Name and position of the supervisor:	Dr Anne-Clemence Vion
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Candidate (if known):	---

Title of the internship:

Development of a Human Stem Cell-Based Model of Intracranial Aneurysms

Summary of the internship proposal:

Intracranial aneurysms (IAs) are pathological dilations of cerebral arteries that typically occur at bifurcations of the Circle of Willis and affect approximately 3% of the population. Although often asymptomatic, aneurysm rupture causes subarachnoid hemorrhage, a life-threatening condition associated with high mortality and long-term neurological deficits. Currently, no pharmacological treatment exists to prevent aneurysm formation or progression, and clinical management relies on invasive surgical or endovascular interventions. The mechanisms initiating IA formation remain poorly understood. While hemodynamic stress, vascular wall remodeling, inflammation, and genetic predisposition are known contributors, the sequence of early cellular and molecular events leading to aneurysm development is still unclear. Progress in this field is further limited by the lack of experimental models that accurately reproduce the human disease. Existing animal models do not faithfully replicate the anatomy, cellular composition, or pathophysiology of IAs.

Our team is therefore currently shifting towards in vitro models to better study the development of this pathology, with a specific focus on how mechanical forces contribute to its initiation and progression.

A human in vitro platform that combines stem cell-derived vascular cells with bioengineered vascular structures is a promising alternative. We have successfully developed a protocol for differentiating human embryonic stem cells (hESCs) into endothelial cells (ECs) and neural crest-derived smooth muscle cells (SMCs). The latter represent the embryonic origin of SMCs in intracranial arteries. The internship project will build on this work by first establishing hESC lines with fluorescent reporters for key molecules involved in vascular cell responses to mechanical forces, and then introducing a genetic variant of a known gene involved in human IA using CRISPR-CAS9 technology. Once these cell lines have been established, they will be differentiated into vascular cells (ECs and SMCs), and their responsiveness to mechanical forces will be validated using a 2D model and live microscopy experiments. Depending on the progress of the internship, the next step will be to initiate the construction of a 3D artery-on-chip using needle-based collagen bioprinting.

The goal of the internship is to lay the groundwork for the creation of in vitro human cerebral bifurcations.