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Host laboratory:

BioSanté, MAB2 team
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Title of the M2 research internship:

Study of PROKs and BMP9 effects on the permeability on a 3D blood brain barrier model organ on chip

Project summary:

The M2 internship will be dedicated to investigate a collaborative project of two BCI teams (from Biosanté) initiated in september 2021, the MAB2 team (Mechanisms of Angiogenesis in Biological Barriers) and the BAL team (BMP Family in Angiogenesis and Lymphangiogenesis).

The objective of the internship is to evaluate the impact of cytokines such as PROK 1 and 2 (pro-angiogenic and pro-inflammatory factors), BMP9 (a factor that is responsible for the development of the blood-brain barrier (BBB)) on a 3D microchip model of the BBB, in relation with hemodynamic parameters (pressure, shear). To do so, we will use commercial microfluidic chips, composed of a central chamber to host a mini brain cell model with astrocytes/pericytes/neuron grow on matrigel, and two lateral channels to develop endothelial vessels. Thin microfluidic channels allow astrocytes to interact with endothelial cells mimicking in vivo interactions. Each of these channels or chambers is independently powered, allowing for stimulation by cytokines or other therapeutic molecules.

Currently, a co-cultured BBB model (brain endothelial cells and astrocytes) is already implemented in the MAB2 team in vitro, on transwell inserts, in a static model. This model has already allowed to demonstrate an effect of prokineticins on permeability and trans-endothelial electrical resistance (TEER). It is known that it is possible to increase the resistance of this blood-brain barrier in dynamic to reach TEER values closer to those in vivo.

The M2 internship will be dedicated to study the signaling pathways of these factors on the BBB using the iP1 activity assay, the cellular response to these cytokines based on the cellular reactivity and secretion measurements of the mini-brain cells. In addition, amyloid fibers will be searched and imaged by NIR imaging.

Keywords:

blood brain barrier on Chip, inflammatory response, cell signaling

Relevant publications of the team:

Reynaud, et al. Evidence-Based View of Safety and Effectiveness of Prokineticin Receptors Antagonists during Pregnancy. *Biomedicines* 2021, 9, 309. <https://doi.org/10.3390/biomedicines9030309>

Agnès Desroches-Castan, Emmanuelle Tillet, Claire Bouvard, Sabine Bailly. BMP9 and BMP10: Two close vascular quiescence partners that stand out. 2021 <https://doi.org/10.1002/dvdy.395>