



Lab: TaRGeT UMR 1089

Team: Rétine et Chemicals

Name and position of the supervisor: Allwyn Pereira, PhD (Ingénieur de recherche) et Mathieu Mével, PhD (Chercheur)

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Candidate (if internship filled):

Title of the internship: Bio-MICRO-BBB: **BIO**conjugation Strategies for **MICRO**glia to Cross the Blood-Brain Barrier in Neurodegenerative Diseases.

Summary of the internship proposal:

Our project aims to use chemical bioconjugation to enhance the targeting of iPSC-derived microglia-like cells (iMGLs) for therapeutic applications. By conjugating biologics, such as peptides and nanobodies, to the microglial cell surface, our goal is to improve recruitment across the blood-brain barrier (BBB) following intravenous administration.

To this end, the hCMEC/D3 cell line will be employed as an *in vitro* model to mimic the BBB and screen the ability of bioconjugated iMGLs to cross this cellular layer. The hCMEC/D3 cell line has been shown to stably express endothelial markers such as CD34, CD31 and VE-cadherin. A monolayer of hCMEC/D3 cells will be cultured on the microporous surface of a transwell insert. The impermeability of the cellular layer will be validated by incubating the cells with fluorescently labelled 70kDa dextran for a period of 48 hours. The impermeability of the cells will be assessed by collecting the medium from the lower compartment of the transwell at 12, 24 and 48 hours, and measuring fluorescence using a Tecan microplate reader. Once the impermeability is confirmed, the first screening test will involve the incubation of bioconjugated iMGLs with the hCMEC/D3 cells in the transwell insert for 48 hours. The transmigration of the bioconjugated iMGLs will be performed by collecting the medium from the lower compartment at 12, 24 and 48 hours, and analyzing it *via* flow cytometry for the iMGL surface markers such as P2RY12. This will allow us to identify biologics that enhance the transmigration capacity of the iMGLs.

The candidate will be trained to employ cell and molecular biology techniques, image analysis and flow cytometry. The candidate will also be integrated in lab meetings and journal clubs. The project offers the candidate an opportunity to work in an interdisciplinary environment at the interface of biochemical engineering and cellular biology.

Profile(s) linked to the project:

- ☒ Experimental Biology (*Recherche expérimentale*)
- ☐ Clinical Research (*Recherche clinique*)
- ☐ Research in data analysis (*Recherche en analyse de données*)