Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2019-2020

1. Host team :

Research Unit (e.g. Department or Institute) : Center for Interdisciplinary Research in Biology (CIRB)- Collège de France- UMR 7241- INSERM U1050
Research Unit Director : Marie-Hélène VERLHAC
Research Team Director : Isabelle BRUNET
Team name : Molecular Control of Neuro-vascular Development

Address : Collège de France. 11 Place Marcelin Berthelot 75005 PARIS

Supervisor of the Research Intern for this project : Isabelle Brunet & Sonia Taib
Telephone : 0144271693
E-mail : isabelle.brunet@college-de-france.fr

2. Internship project title:

Investigation of the blood-nerve barrier: role in chemically-induced peripheral neuropathies.

3. Internship Description :

The goal of our team is to study the establishment of neurovascular interactions and their functions in a normal or pathological context. The peripheral nervous system, made up of nerves, is vascularized by the intra-nervous vascular system (INV) to provide the nutrients and oxygen necessary for its proper functioning. Control of the nerve microenvironment is therefore crucial and is ensured by the blood-nerve barrier that regulates the passage of molecules between the blood circulation and nerve tissue.
Using a transcriptomic approach (RNA sequencing), we aim to characterize the molecular composition of this barrier while comparing it to another barrier known to be the least permeable in the body: the blood-brain barrier. This will enable us to obtain the molecular identity card of these barriers and identify changes that occur during the course of the disease.
Peripheral neuropathies are diseases that cause nerve and INV degeneration, causing chronic pain in patients. These diseases can have different origins, but we are interested in chemically-induced neuropathies, which are extremely deleterious side effects of anti-cancer treatments.
The etiology of these illnesses is still poorly understood and there is currently no treatment to directly treat neuropathy.
This project therefore aims to better understand how this disease develops, what is the role of the barrier and what therapeutic approaches can be used to limit nerve damage. To do so, we will use a mouse model of chemotherapy-induced neuropathy by injecting an anti-cancer drug, oxaliplatin. We will determine whether mice develop neuropathy using various behavioural tests by measuring abnormal pain, also known as allodynia, a characteristic symptom of peripheral neuropathy. We will determine the etiology of this neuropathy, with a particular focus on the INV of the sciatic nerve at different stages of disease progression.

A neuropathological analysis will be performed on the sciatic nerves of mice developing neuropathy, using immuno-histochemical labelling, 3-D light sheet microscopy (ultramicroscopy) and molecular analyses (qPCR and western blot).
In a translational research perspective, we are collaborating with the Faculty of Pharmacy in Paris to develop inhibitors that we will test in our system to propose therapeutic approaches for the treatment of chemically-induced peripheral neuropathies.