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) : INSERM UMR-S1270, Institut du Fer à Moulin 17 rue du Fer à Moulin 75005 Paris
Research Unit Director : Jean-Antoine GIRAULT
Research Team Director : Luc MAROTEAUX, Anne ROUMIER
Team name : Serotonin, microglia, plasticity and pathology
Address : INSERM UMR-S1270, Institut du Fer à Moulin17 rue du Fer à Moulin 75005 Paris
Supervisor of the Research Intern for this project : Luc MAROTEAUX, Anne ROUMIER
Telephone : 0145876123
E-mail : luc.maroteaux@inserm.fr; anne.roumier@inserm.fr

2. Internship project title:

Interaction between serotoninergic and immune systems: effects on neuronal plasticity regulating behavior?

3. Internship Description :

Serotonin is a neuromodulator involved in many physiological functions (sleep, food intake, thermoregulation...). In addition, many psychiatric disorders (depression, anxiety, schizophrenia) have been associated with dysfunctions of the serotonergic system, and are improved by substances that modulate serotonin levels, such as antidepressants of the SSRI family (eg Prozac). It has recently been suggested that the positive action of this type of antidepressants is due to an increase, induced by the elevation of serotonin level, of neuronal and behavioral plasticity, and therefore of adaptability to new situations. However, the precise roles of serotonin, its targets and the receptors involved in these different functions, and the associated pathologies, are still poorly understood - there are indeed more than a dozen different receptors for this neuromodulator.

Our team is mainly interested in serotonin receptors of the 5-HT_{2B} subtype. Mutations reducing the expression of this receptor are associated with impulsive / suicidal behavior in humans, and we have shown that mice lacking the *Htr2b* gene, which codes for this receptor, are impulsive and do not respond to SSRI antidepressants. Moreover, in the absence of 5-HT_{2B} receptor, the mice exhibit an exacerbated response to peripheral inflammation or chronic stress, defects in social interaction and behavioral flexibility, and memory and sleep disorders. We have demonstrated that 5-HT_{2B} receptors are expressed by neurons that secrete serotonin and by microglia, that is, resident macrophages of the brain. Via this receptor, serotonin, on the one hand, increases the activity of serotonergic neurons, and on the other hand, induces an oriented growth of microglial processes towards the source of serotonin. Current and future projects aim to understand the cellular and molecular effects of serotonin on serotonergic neurons and microglial cells, and why the absence of this receptor in either cell type induces the above-mentioned phenotypes. Uraveling these mechanisms will lead to a better understanding of how serotonin facilitates an organism's ability to adapt flexibly to dynamic environments by controlling neuronal plasticity and ultimately our behaviors.

For this purpose, we combine genetic approaches (transgenic mice), and behavioral approaches (memory, sociability ...), biphotonic imaging and optogenetic techniques (on brain slices), cell culture (primary cultures of microglia and neurons), molecular biology (quantitative PCR), immunohistochemistry and biochemistry (ELISA, WB, signaling).

The candidate will develop one aspect of the projects according to their progress at the time of application, as well as his/her interest and skills.