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) : **UMR9199. Neurodegenerative disease laboratory**
Research Unit Director : **Dr. E. Brouillet**
Research Team Director : **Dr. C. Escartin**
Team name : ***Molecular complexity of reactive astrocytes in neurodegenerative disease***

Address : **MIRCen. 18 route du Panorama**
92260 Fontenau-aux-Roses

Supervisor of the Research Intern for this project : **Dr. C. Escartin**

Telephone : **01-46-54-72-33**
E-mail : carole.escartin@cea.fr

2. Internship project title:

Heterogeneity of reactive astrocytes in Alzheimer disease

3. Internship Description :

Astrocytes are key partners to neurons in the brain. They perform important supportive functions for neurons and actively regulate synaptic transmission. In brain diseases, such as Alzheimer's disease (AD), astrocytes change at the morphological and molecular levels and become "reactive" (Ben Haim et al. *Front. Cell. Neuro*. 2015). We recently showed that reactive astrocytes have mostly deleterious effects in AD, as their inhibition improves disease outcomes (Ceyzeriat et al. *Acta Neuropathol. Com.,* 2018). However, recent studies suggest that astrocytes are heterogeneous cells, and astrocytes could form distinct sub-populations when becoming reactive, with variable effects on neurons. Indeed, our own data show that reactive astrocytes have beneficial effects in models of Huntington disease (Ben Haim*, J Neuro*, 2015). This calls for a refined understanding of the heterogeneity of reactive astrocytes, as different molecular and functional classes of reactive astrocytes could influence disease progression differently. Hence, the specific inhibition of only deleterious classes of reactive astrocytes could produce even stronger therapeutic effects.

How are such different classes of reactive astrocytes generated? Our hypothesis is that a combination of signaling cascades in an environment unique to each astrocyte conditions the acquisition of a specific reactive profile, which will be beneficial or deleterious for neighboring neurons during AD. **Identifying the cascades that control these classes of reactive astrocytes will allow the development of specific therapeutic approaches to promote the acquisition of a neuroprotective astrocytic phenotype during diseases.**

The M2 student will use multidisciplinary approaches such as viral gene transfer, cytometry, molecular biology and histology on relevant mouse models of AD to characterize the signaling cascades activated in reactive astrocytes and the associated molecular profile of sub-populations of reactive astrocytes.

This project will be carried out in MIRCen (Molecular Imaging Research Center) at the UMR9199, on the CEA campus in Fontenay-aux-Roses, which offers state-of-the-art facilities. We are looking for a strongly motivated, reliable student ready to work in a multidisciplinary environment and join our young team focused on reactive astrocytes.