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) : ICM
Research Unit Director : Alexis Brice
Research Team Director : Catherine Lubetzki and Bruno Stankoff
Team name : Mechanisms of myelination and remyelination in the CNS

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2. Internship project title:

Functional analysis of a newly-discovered contact between axon initial segments and microglial cells in the mouse

3. Internship Description :

The axon initial segment (AIS) fulfills two fundamental functions: i) it forms a barrier between the somato-dendritic and axonal compartments, and as such maintains the neuron's polarity, allowing information to be propagated from cell to cell in the nervous system; ii) it is the site where action potentials are generated, and as such allows neurons to inform their target cells. The AIS is also a plastic domain, where subtle molecular and morphological changes enable neurons to adapt their spiking properties to a changing environment (Rasband, Nature Rev. Neurosci. 2010). Evidence is accumulating that the AIS is also very vulnerable. AIS alterations are found in several neurological diseases and could thus be involved in their pathophysiology: in Alzheimer's disease, several autistic or epileptic syndromes, and our preliminary results point to AIS defects in multiple sclerosis. Yet, the mechanisms of these physiological or pathological AIS changes remain largely unknown.

A novel physical contact has been very recently discovered between AISs and microglial cells, the resident immune cells of the central nervous system (Baalman et al., J. Neurosci. 2015), suggesting a direct crosstalk between these actors. Given the importance of microglial cells in both healthy and pathological conditions as surveying cells playing both protective and disruptive roles, depending on their activation status and the inflammatory context, their interaction with AISs raises many new questions. It may play a key role in sensing the spiking properties of neurons or in controlling AIS function and stability and could thus be responsible for AIS alterations found in many neurological diseases.

The aims of the current project are the following:

To gain insight into the role of the AIS-microglia interaction, we plan to further characterize how microglia interact with neurons: whether they interact with specific subtypes of neurons, what are the molecular and morphological signatures of the interacting microglial cells (pro or anti-inflammatory), how stable is the interaction (given the highly motile nature of microglial cells constantly sensing their environment), does the AIS-contacting microglial process display calcium waves (which could reflect signaling events occurring between the AIS and the microglia), and, in order to address a potential involvement of the contact in AIS alterations, do the above-mentioned AIS-microglia contact characteristics change upon pathological or inflammatory conditions?

We plan to address these questions mostly by immunohistochemistry and in vivo two photon microscopy using transgenic reporter mouse lines and stereotaxically-injected viruses or in utero electroporation followed by image analyses.