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) : Institute of Psychiatry and Neuroscience of Paris (IPNP)

   Research Unit Director : Thierry Galli
   Research Team Director : Maria Cecilia Angulo
   Team name : Interactions between neurons and oligodendroglia in myelination and myelin repair

   Address : 102, rue de la Santé, 75014 Paris

   Supervisor of the Research Intern for this project : Maria Cecilia Angulo
   Telephone : 0140789243
   E-mail : maria-cecilia.angulo@parisdescartes.fr

2. **Internship project title:** Role of lineage-related GABAergic interneurons and oligodendrocyte precursor cells (OPCs) in cortical circuit assembly

3. **Internship Description :**

GABAergic interneurons are inhibitory neurons that play a critical role in neural network activity and behavior. During development of the cerebral cortex, GABAergic interneurons are mainly born from the medial ganglionic eminence (MGE) that produces around 60% of cortical interneurons in mice. The caudal ganglionic eminence (CGE) is the second source producing approximatively 30% of interneurons, and the embryonic preoptic area (POA) is a third source contributing with approximately 10%. Interestingly, as for 70% of the interneurons, the first wave of oligodendrocyte precursor cells ($_{first}$OPCs) is generated from the MGE and POA. Therefore, all $_{first}$OPCs and 70% of cortical interneurons are born from the same embryonic origins. The convergence in the development of $_{first}$OPCs and interneurons suggest possible interactions between these two cell types that might participate to cortical circuit construction and maturation.

A major characteristic of OPCs is that they are the only glial cell type receiving *bona fide* functional synapses from neurons in the CNS. We previously demonstrated that GABAergic interneurons constitute the major synaptic input of OPCs in the mouse somatosensory cortex *(Vélez-Fort et al., 2010, J Neurosci; Balia et al., 2015, Cereb Cortex; Orduz et al., 2015, eLife; Balia et al., 2017, Glia)*. This neuron-glia synaptic innervation is highly regulated in time and space and reaches a peak of connectivity at postnatal day 10 *(Orduz et al., 2015, eLife)*. Interestingly, $_{first}$OPCs are supposed to disappear by programmed cell death at this developmental stage and thus, it is considered that this specific OPC population does not play a role at postnatal stages. However, our unpublished data show that not all $_{first}$OPCs dye and that the surviving population preferentially interacts with GABAergic interneurons sharing a common

embryonic origin. These results reveal an exquisite postnatal relationship between interneurons and firstOPCs favored by a the same origin and uncover an unprecedented lineage-related cell interaction during a critical postnatal period for circuit formation and myelination in the cortex. In this project, we hypothesize that the interactions between firstOPCs and their lineage-related interneurons contribute to the correct assembly and myelination of cortical neuronal networks. To test this hypothesis, we have already generated different mouse models of OPC survival. The aim of this M2 training will be to analyze the impact of firstOPC survival on cortical circuit development and myelination, with a special focus on inhibitory circuits, using these models. The student will have the opportunity to perform electrophysiological (patch-clamp) experiments to analyze cortical circuit dysfunction, immunostainings to examine oligodendroglia and myelination defects and 3D confocal reconstructions of single cells to assess abnormal axon integrity. This study has potential implications in pathological conditions such as psychiatric neurodevelopmental disorders.