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

Internship Proposal
Academic Year 2018-2019

1. Host team :

Research Unit (e.g. Department or Institute) : Myology Institute UMPC-INSERM-AIM UMRS974

Research Unit Director : G. Butler-Brown
Research Team Director : L. Strochlic and B. Fontaine
Team name : Neuromuscular connectivity in health and diseases

Address : Faculté de Médecine de la Pitié Salpétriere
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Supervisor of the Research Intern for this project : L. Strochlic and J. Messéant
E-mail : laure.strochlic@inserm.fr/ julien.messeant@inserm.fr

2. Internship project title:

Function of Wnt signaling in neuromuscular connectivity

3. Internship Description :

Neuromuscular connectivity requires a temporally fine-tuned balance of distinct signaling activities initiated from muscle or motoneuronal-secreted molecules. Any disruption of these signaling activities drastically affects neuromuscular junction (NMJ) formation and maintenance and may lead to neuromuscular diseases. Therefore, it remains critical to understand the molecular and cellular mechanisms orchestrating the formation and maintenance of the neuromuscular connectivity during embryonic development and in adulthood in order to develop therapies based on new molecular targets. How do signals arising from the muscle and the nerve orchestrate the formation and maintenance of the neuromuscular connectivity? How does the disruption of the brain and skeletal muscle communication cause neuromuscular disorders? These are key questions regarding neuromuscular development and maintenance remaining to be investigated. Recently our team provided in vivo evidence that the secreted Wnt cues are critical regulators of mammalian NMJ formation and maintenance (Messéant et al., 2015 *J. Neurosci*; Messéant et al., 2017 *Development*). We generated a transgenic mouse bearing the deletion of the Wnt binding domain (CRD) of the tyrosine kinase receptor called MuSK, a central player in NMJ formation. MuSK CRD deletion causes significant defects of innervation and leads to a pathogenic phenotype in adult mice (Messéant et al., 2015). Based on these findings, the aim of this research project is (1) to cartography the Wnt-derived signals that regulate the formation and stabilize the neuromuscular

synapse and (2) to dissect the underlying pathways and cross talk between nerve and muscle. To realize this project, the student will use biochemistry and cell biology approaches both in vitro (muscle cell culture) and in vivo (transgenic mice lines). He will be supervised by a chargé de recherche INSERM, holding an HDR.

We are looking for a highly self-motivated M2 candidate with a background in molecular and cellular biology and with interest in the neuromuscular system. Applicants should have good interpersonal and communication skills.

Applications containing a CV and a brief letter of motivation should be sent by e-mail to laure.strochlic@inserm.fr and julien.messeant@icm-institute.org and selected candidates will get an interview.