Ecole Doctorale Sciences de la Vie et de la Santé - Call for proposals thesis 2019/2020

Laboratory title : [Laboratory title]

Supervisor

Name : [Name]

Thesis title : Functional analysis of two planar polarity genes in establishing neuronal polarity

Keywords : Cell Polarity, Neuron, Protein interactions, High resolution microscopy

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Abstract

DESCRIPTION:
The establishment of cell polarity in mammalian brain is crucial for the function of neurons. Disruption of neuronal polarity (its establishment or its maintenance) leads to many serious brain development disorders and can lead to pathologies (autism, epilepsy ...). It is therefore essential to determine the molecular factors controlling this polarity, which depend on rearrangements of the actin cytoskeleton and microtubules (MT). Our laboratory is working on an intracellular signaling pathway called planar cell polarity pathway (PCP), yet little studied in mammals and is devoted to the modulation of the cytoskeleton (Montcouquiol M et al Annu Rev Neurosci 2006; Mr. Moreau et al. J Neurosci 2010; Ezan J Cell Biol al. Nat and 2013;)

We have recently observed that some molecules of the PCP are localized within specific sub-domains in neurons, which leads us to hypothesize that they play a role in the polarity of the neuron.

OBJECTIVES:
The project aims to study the PCP pathway proteins function in the establishment and maintenance of neuronal polarity. The use of cellular biology techniques (invalidation by using shRNA) and Biochemistry (Yeast-two-hybrid, immunoprecipitation, pull-down, etc.) will allow us to highlight the role of these proteins in regulating cytoskeletal at the axon. Confocal imaging approaches and high-resolution (dSTORM) then let us assess their impact on the cytoskeleton of actin and microtubules in axons in vitro (culture) and in vivo (conditional mutants).

METHODOLOGY:
Molecular Biology, Biochemistry (Double - Hybrid, immunoprecipitation, Western blots, etc ...), cell biology (cell line, primary neuronal cultures, transfection), confocal imaging and high-resolution (STORM)

Qualification required

Strong motivation for combined approaches (imaging, cell biology and biochemistry).