

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: Brahim Nait Oumesmar
Team name: Myelin Plasticity and Regeneration
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2. Internship project title: Function of PAK1 in Myelin Plasticity

3. Internship Description:

Myelin, produced by oligodendrocytes in the central nervous system (CNS), has been thought for a long time as a static structure. Recent studies demonstrated that myelin is dynamic: myelination increases upon sensitive stimulations and decreases after sensory deprivation. It has also been shown that the fine-tuning of actin cytoskeleton remodeling in OL plays a critical role in myelination. Our preliminary *in vitro* data identified the p21 activated kinase 1 (PAK1) as a major regulator of OL differentiation and maturation, through the modulation of actin cytoskeleton dynamics. Based on these findings, we aim at deciphering the functional role of PAK1 during oligodendrocyte development and myelination processes. We generated a conditional knockout mouse of *Pak1* in oligodendroglial cells (*Pak1* cKO), and several molecular tools to study the function of PAK1 in oligodendrocyte development and myelination, *in vitro* and *in vivo*. We will also modulate the activity of this protein in oligodendrocytes *in vitro* and determine the effects on the dynamic of oligodendrocyte membranes by live imaging. Myelination will be also studied in cerebellar slices transplanted with OPCs transduced with different forms of PAK1.

This project will provide a better understanding of the regulation of actin cytoskeleton dynamics and PAK1 function in oligodendrocyte development and myelination. The perspective of this project is to determine how the dynamics of actin cytoskeleton might affect myelin plasticity and repair in the adult CNS.