

Internship Proposal Academic Year 2019-2020

1. Host team :

Research Unit (e.g. Department or Institute) : Institut de la Vision UMR S968
Research Unit Director : Pr José-Alain Sahel
Research Team Director : Dr Xavier Nicol
Team name : Mechanisms of sensory map development

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2. Internship project title:

Deciphering the role of Fidgetin-like 1 in the microtubule/actin crosstalk required for directed axon outgrowth

3. Internship Description :

A crucial step in the assembly of neuronal circuits and thereby in the execution of complex behaviours relies on the accurate navigation of developing axons towards their correct neuronal targets. Imprecise or ectopic connections during development can lead to major and long-lasting disorders. At the tip of developing axons, the growth cone critically depends on the close relationship between the microtubule (MT) and actin (F-actin) networks to drive directed axon migration. However, although critical for growth cone steering behaviour, the numerous players that connect MTs and F-actin as well as their precise roles and regulation by guidance cues remain poorly characterised. This Master 2 project aims at deciphering molecular mechanisms linking MT/F-actin remodelling to guidance signals during neuronal circuit assembly. This project will focus on the functional analysis of Fidgetin-like 1 (Fignl1), a key MT-bound ATPase in axon navigation that we recently positioned at the crossroads between MTs, actin and guidance signals based on cellular and proteomic data. The project will use an original combination of biological systems (*in vitro* cell-free systems, primary cell cultures, *in vivo* analysis in zebrafish embryos) and cutting-edge imaging technologies to address the following issues: (i) exploring how Fignl1 influence F-actin organisation, dynamics and crosstalk with MTs in migrating growth cones and (ii) identifying guidance signalling events that regulate its activity during this developmental process.

This project will unravel critical interactions and novel key players in the MT/actin crosstalk underlying neuronal connectivity, which should ultimately shed new light into the aetiology of some neurodevelopmental and neurodegenerative disorders.