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) : Institut du Cerveau et de la Moelle epiniere
Research Unit Director : Alexis Brice
Research Team Director : Claire Wyart
Team name : Sensory Spinal Signalling

Address : GH Pitié-Salpêtrière - Bâtiment ICM
47 Bld de l'Hôpital
75651 Paris cedex 13

Supervisor of the Research Intern for this project : Pierre-Luc Bardet
Telephone : 01 57 27 41 10
E-mail : pierreluc.bardet@icm-institute.org

2. Internship project title:

Role of the cerebrospinal fluid in axial morphogenesis of zebrafish embryos and in models of juvenile scoliosis

3. Internship Description :

Our team is interested in the role of the CerebroSpinal Fluid (CSF) in spinal cord development and physiology, using zebrafish as a model organism. Present in the CerebroSpinal Fluid from early stages onwards, the Reissner Fiber is an extracellular fibrillar structure that is formed by the aggregation of a secreted glycoprotein named SCO-spondin (Rodriguez et al., 1998). We have recently discovered that the Reissner Fiber plays an important role in embryonic morphogenesis (Cantaut-Belarif et al., Current Biology, 2018). We have shown that ciliary motility is required for the formation of fiber in the CSF. In the absence of a fiber, after mutation of the gene encoding SCO-spondin or when the ciliary functions are altered, zebrafish embryos develop with an abnormally curled-down tail.

The intern will work to characterize the mechanisms by which the Reissner Fiber controls the morphogenesis of the posterior axis in the zebrafish embryo. The nature of the molecular signals responsible for the morphogenesis of the tail and what are their target tissues will be investigated.

For this, the student will participate in an ongoing transcriptomic comparison of straight wild-type embryos or curled-down mutants lacking the Reissner fiber. The analysis of the results will lead to the identification of potential signals involved, and the results will be confirmed by in situ hybridization and / or immunofluorescence on embryos. The most promising ones will be functionally tested using loss (CRISPR / Cas9 method) and gain (mRNA injection) of function to try to modify the tail curvature in mutants without fiber.

In order to better understand the tissues at the origin of the curvature of the posterior axis, the intern will develop new tools for imaging and finely measuring the deformation of the tissues that could cause this curled-down, in particular the notochord and muscles. These measurements will be supplemented by an evaluation of proliferation, apoptosis and cell size in these tissues. Finally, the involvement of the tissues studied in the morphogenesis of the tail will be studied using drugs (paralysis, etc ...) and loss of function (CRISPR/Cas9 method).

Finally, cilia motility has also been implicated at juvenile stage in the appearance of abnormal torsion of the spine in model zebrafish for human idiopathic scoliosis (Grimes et al., 2016). By analogy with our results in the embryo, we envisage that the Reissner fiber plays a role in the axial morphogenesis of the juvenile as well. In collaboration with researchers and orthopedic doctors, the intern will be able to extend the object of his study to the juvenile stages, by testing the role of the signals discovered in the embryo in models of juvenile scoliosis.

The student will join our team of fifteen people with a wide range of profiles : physiology, genetics, biophysics. The intern will work closely with the two people already involved in the project, making the best of the diversity of approaches followed by the rest of the team. The experiments will include zebrafish genetic manipulation, cell and tissue imaging, and quantitative analysis. Knowledge in cellular and molecular biology, genetics and development are required. Prior laboratory experience in these areas will be seen as a plus.

Rodríguez, E. M., et al. (1998). The subcommissural organ. Microscopy Research and Technique, 41(2), 98–123.

Cantaut-Belarif, Y. et al. (2018). The Reissner fiber in the cerebrospinal fluid controls morphogenesis of the body axis. Current Biology, in press

Grimes, D. T. et al. (2016). Zebrafish models of idiopathic scoliosis link cerebrospinal fluid flow defects to spine curvature. Science, 1284(1995), 1281–1284.