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) : CNRS UMR8197, INSERMU1024, IBENS
Research Unit Director : Antoine Triller
Research Team Director : Nathalie Spassky
Team name : Cilia in brain development and Pathology
Address : Institut de biologie de l'Ecole Normale Supérieure, 46 rue d'Ulm 75005 Paris

Supervisor of the Research Intern for this project : Alice Meunier
Telephone : 01 44 32 37 27
E-mail : alice.meunier@ens.fr

2. Internship project title: Making motile cilia for brain fluid propulsion

3. Internship Description :

Centrosomes organize cilia and microtubule networks in animal cells. Their semi-conservative duplication in cycling cells gives rise to centrosomes composed of one mother and one daughter centriole. This symmetric duplication of centrioles is crucial for cell division homeostasis. By contrast, brain multiciliated cells (MCC) eschew this archetypal duplication program to form, instead, hundred centrioles that are required for the growth of motile cilia and the propelling of cerebrospinal fluid. Until recently, the origin of these new centrioles was unknown. They were postulated to arise *de novo*, that is, independently from the centrosome, around electron-dense structures called deuterosomes. Defects in MCC centriole amplification are associated with hydrocephalus, altered neurogenesis and may affect other brain functions since cilium-driven cerebrospinal fluid circulation represents a cell-extrinsic route regulating brain communication (1).
To assess the mechanism of centriole amplification in brain MCC, we have developed a primary cell culture assay and combined it with single cell high resolutive imaging techniques. We have shown that the deuterosomes are nucleated from the pre-existing progenitor cell centrosome and strikingly from the single immature daughter centriole (2,3). We also revealed that this deuterosome-mediated centriole amplification is controlled by a calibrated version of the mitotic oscillator showing that this clock-like regulatory circuit can be repurposed in differentiating cells (4).
The aim of the M2/PhD project is to characterize with sub-micrometer precision and in three dimensions the cradle of centriole production, using state of the art imaging techniques (3D-super-resolution microscopy, correlative live imaging and focused ion beamed-scanning electron microscopy). In parallel, a functional approach will be run to identify how the mitotic oscillator can be calibrated to control centriole amplification in differentiating MCC without triggering unscheduled divisions in the brain. Beyond the importance of deciphering the mechanisms underlying motile cilia formation in brain ventricles, understanding how centrioles

are amplified is of particular relevance in the context of cancer biology. The student will benefit from an interdisciplinary environment with expertise in cell biology, neurodevelopmental biology and imaging, and will have access to leading edge equipment.

1. Spassky N, Meunier A. The development and functions of multiciliated epithelia. Nat. Rev. Mol. Cell Biol. 2017; http://dx.doi.org/10.1038/nrm.2017.21
2. Al Jord A, Lemaître A-I, Delgehyr N, Faucourt M, Spassky N, Meunier A. Centriole amplification by mother and daughter centrioles differs in multiciliated cells. Nature. 2014 516(7529):104–7.
3. Al Jord A, Spassky N, Meunier A. Centriole amplification : #DaughterCentriole. Médecine Sci. 2015;31(3):250–3.
4. Al Jord A, Shihavuddin A, D'Aout RS, Faucourt M, Genovesio A, Karaiskou A, Sobsczak-Thépot J., Spassky N., Meunier A. Calibrated mitotic oscillator drives motile ciliogenesis. Science. 2017;358:803–806.