Master Biologie Moléculaire et Cellulaire 'BMC',
Université de Paris - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
http://www.master2bdc.fr/
Fiche de Projet de Stage M2, Année 2021-2022

Unité INSERM ou CNRS ou Université : **U1024, IBENS** **Intitulé Equipe :** **Cilia biology and neurogenesis** **ED d'appartenance :** **ED3C** **Responsable de l'Equipe :** **Nathalie Spassky**	**Responsable du Stage :** **Nathalie Delgehyr** **Contacts** Adresse : 46 rue d'Ulm 75005 Paris Email : delgehyr@biologie.ens.fr Tel :01 44 32 37 15

Titre du projet :

Ependymal fate choice: Role of mechanical stress on the nucleus

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

During development, cells are submitted to significant **mechanical forces**. Accumulating evidences suggest that the forces are directly transmitted to the nucleus through the cytoskeleton and regulate processes such as gene expression. Thus, it is possible **that tension applied on the nucleus via the cytoskeleton** directly drives **cell fate**.

How radial glial cells, precursor of many cells in the brain including neural stem cells, neurons and ependymal cells, are specify remains unclear. **Multiciliated ependymal cells** (ECs) are located along ventricles of mammalian brain, forming a protective barrier. Their cilia beating ensures the cerebrospinal fluid flow that regulates signalling pathways. Impairment of this flow correlates with age-related dementia, schizophrenia and hydrocephalus. While the cells do their last division at embryonic stages, they stay quiescent and differentiate only after birth. Interestingly, staining of differentiating ECs showed that during differentiation, nuclear morphology and localisation are subjected to major changes. Impairment of the actin cytoskeleton or of the link between the actin cytoskeleton and the nuclear envelope leads to ependymal differentiation defects. Thus, **mechanical pressure** exerted by **the actin cytoskeleton** on the **nucleus** may drive the **ependymal fate choice.**

To test this hypothesis, we will study how cytoskeletal rearrangements trigger nuclear morphology rearrangement and the consequences of this deformation on the ependymal cell fate. Notably, we will modify the cytoskeleton or the nuclear morphology **in vivo in mouse models**, using depletion or overexpression of relevant proteins, and assess the consequences of these modifications on the differentiation process. These in vivo approaches will be complemented **in vitro** by mechanically inducing nuclear deformation on cells in culture or purified nuclei and directly assessing the consequences of these deformations on gene expression.
This project will be performed at the IBENS in the laboratory of "Cilia biology and neurogenesis" under the direct supervision of a permanent researcher: Nathalie Delgehyr.

Publications de l'équipe relatives au projet de stage (max 5)

- Ortiz-Álvarez G *et al.* Adult Neural Stem Cells and Multiciliated Ependymal Cells Share a Common Lineage Regulated by the Geminin Family Members. Neuron. 2019 Apr 3;102(1):159-172.e7.
- Mercey O *et al.* Massive centriole production can occur in the absence of deuterosomes in multiciliated cells. Nat Cell Biol. 2019 Dec;21(12):1544-1552.
- Mahuzier A *et al*. Ependymal cilia beating induces an actin network to protect centrioles against shear stress. Nat Commun. 2018 Jun 11;9(1):2279.
- Jord AA *et al*. Centriole amplification by mother and daughter centrioles differs in multiciliated cells. Nature. 2014 Dec 4;516(7529):104-7