

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 : UMR CNRS 8264, NeuroParisSeine	Responsable du Stage : Isabelle Caillé
Intitulé Equipe : Equipe développement des réseaux neuronaux	Contacts Adresse : IBPS, 9 quai Saint Bernard, BatB 6eme étage, 75005 Paris
ED d'appartenance : ED3C	Email : isabelle.caille@upmc.fr
Responsables de l'Equipe : Alain Trembleau/Isabelle Dusart	Tel : 0623715461

Titre du projet :

Understanding how the primary cilium beats the tempo of neuronal migration

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

Neuronal migration is essential to the formation of functional neural circuits with defective migration leading to severe brain malformations and involved in psychiatric disorders.

We have recently discovered an entirely new mode of regulation of neuronal migration (<https://doi.org/10.1101/765925>). The **primary cilium** is a small antenna-like organelle assembled by the **centrosome** and protruding from the surface of most eukaryotic cells, including neurons. By **FRET-two photon imaging of a cAMP-specific biosensor** in live brain slices, we unexpectedly observed a periodic cAMP hotspot at the centrosome of embryonic, postnatal and adult migrating neurons. We show that the primary cilium cyclically produces cAMP, which diffuses to the underlying centrosome and locally activates centrosomal Protein Kinase A, thereby regulating cytoskeletal dynamics.

We now want to extend these findings by:

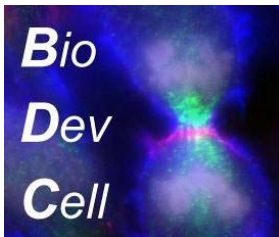
- analyzing the extracellular signals regulating cAMP production in the primary cilium
- understanding how centrosomal PKA acts on the cytoskeleton to regulate migration
- analyzing the presence and functionality of a similar cAMP centrosomal hotspot in other polarized cells like proliferating radial glia and differentiating neurons in mouse **embryoid bodies** and **human brain organoids**
- analyzing the defects of cAMP dynamics in animal models of psychiatric syndromes like **Fragile X Syndrome**, leading cause of autism spectrum disorder.

In this project, the student will learn state of the art **live imaging and super-resolution** techniques to unravel the mysteries of a unique primary cilium driven cAMP subcellular compartmentalization in health and disease.

Publications de l'équipe relatives au projet de stage

Stoufflet, J., Chaulet, M., Doulazmi, M., Fouquet, C., Dubacq, C., Métin, C., Trembleau, A., Vincent, P., **Caillé, I** (2019) Primary cilium dependent cAMP/PKA signaling at the centrosome regulates neuronal migration. *Science Advances* <https://doi.org/10.1101/765925> (2020)

Daroles, L., Gribaudo, S., Doulazmi, M., Scotto-Lomassese, S., Dubacq, C., Mandairon, N., Greer, C.A., Didier, A., Trembleau, A. & **Caillé, I.** (2016) Fragile X Mental Retardation Protein and Dendritic Local Translation of the Alpha Subunit of the Calcium/Calmodulin-Dependent Kinase II Messenger RNA Are Required for the Structural Plasticity Underlying Olfactory Learning. *Biol Psychiatry*, 80, 149-159.



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