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) : Neurosciences Paris Seine UMR CNRS 8246
Research Unit Director : Hervé Chneiweiss
Research Team Director : Alain Trembleau
Team name : Développement et Plasticité des Réseaux Neuronaux

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2. Internship project title:

Dynamics of cAMP signaling in newly-produced neurons of the adult and postnatal brain and alterations in the Fragile X Syndrome

3. Internship Description :

Fragile X syndrome (FXS) is the most common cause of inherited intellectual disability and leading cause of autism spectrum disorder. It is due to the silencing of the *FMR1* gene and resulting absence of FMRP (Fragile X Mental Retardation Protein), an RNA binding protein that regulates translation. The **cAMP signaling** is altered in cells from patients with FXS as well as brain from *Fmr1*-null mice, mouse model of the disease.
We use the continuous **adult neurogenesis** from the sub-ventricular zone to the olfactory bulb to analyze at the cellular and sub-cellular levels the defects in cAMP signaling induced by the absence of FMRP in developing or integrated neurons. To this end, we analyze cAMP dynamics in migrating or differentiating adult-born neurons of wild-type and *Fmr1*-null mice, by FRET-two photon imaging of a **cAMP-specific biosensor** on live brain slices.
Interestingly, migrating wild-type neurons display a a cAMP-rich small dynamic zone surrounding its moving centrosome whereas *Fmr1*-null neurons display multiple, dysregulated cAMP rich zones correlated with an accelerated migration. We now want to molecularly understand this defect in order to try and rescue it. We also want to extend these results to further steps of differentiation and integration of the newly formed neurons.
This project will help to characterize the defects of cAMP signaling that might participate in defective brain development and adult functioning of FXS patients.