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, IBPS
Research Unit Director : Hervé Chneiweiss
Research Team Director : François Tronche
Team name : Gene Regulation and Adaptive Behaviors

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## 2. Internship project title:

Molecular dissection of SWI/SNF chromatin remodeling complexes role in stress related behaviors

## 3. Internship Description :

Glucocorticoids (GC) release is a key physiological response to stress exposure enabling the organism to cope with environmental challenges. Beneficial when working, a dysfunction of this adaptive response is associated to multiples pathologies including psychiatric disorders. GC act through the binding to their receptor, GR, a ubiquitously expressed transcription factor. Our team previously showed that GR gene inactivation in dopaminoceptive neurons ($GR^{D1Cre}$ mice) reduces dopamine neurons activity, decreases responses to cocaine and blocks social aversion induced by repeated social defeat (Ambroggi et al. 2009, Barik et al. 2010, Parnaudeau et al. 2014, Barik et al. 2013).

GR can control target genes expression through its interaction with SWI/SNF chromatin remodeling complexes that include either Brahma (Brm) or Brahma-related gene 1 (Brg1). Mutations within these two genes are associated with psychiatric disorders including schizophrenia and autism. We recently showed that the inactivation of Brm gene (Brm-/-) and Brg1 gene in dopaminoceptive neurons ($Brg1^{D1Cre}$ mice) leads to the same behavioral phenotype than the absence of GR in the same cell population, e.g. a marked reduction of behavioral responses to cocaine and of social aversion following repeated defeats. These defects are associated with a deficit of the induction of immediate early genes expression in the dorsal striatum and the nucleus accumbens after a social defeat, in spite of a normal activation of Erk2, suggesting a defect of gene expression plasticity at the transcriptional level (Zayed et al. In preparation).

First, the candidate will deepen the phenotypic characterization of stress-related behaviors of $Brg1^{D1Cre}$ mice. He will study the consequences of BRG1 gene inactivation on PFC-dependent working memory and flexibility in T-maze and operant boxes tasks, some behaviors that we showed to be affected by stress and GR gene inactivation.
Second, the candidate will participate in the identification of the genes under the control of Brg1 by comparative analysis of the transcriptome between mutant and control mice using RNAseq.

Altogether, the results obtained should help to better understand the role of nuclear plasticity and to identify new molecular mechanisms underlying stress-induced maladaptive behaviors.