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) : UMR8256
Research Unit Director : Bertrand Friguet
Research Team Director : Pierre Vincent
Team name : Cellular Integration of Neuromodulatory Processes

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2. Internship project title:

Type 2 phosphodiesterase in the striatum: a novel therapeutic target for psychiatric diseases ?

3. Internship Description :

Psychiatric diseases such as schizophrenia is a major public health concern, and the current treatments only partially correct the deficits of the disease. All antipsychotic drugs share the property of inhibiting dopamine D2-like receptors, and, in the context of the dopamine hypothesis of schizophrenia, it is commonly accepted that therapeutic efficacy is related to a remediation of imbalances in cAMP signaling.

We use biosensor imaging to monitor in real time the cAMP/PKA response to dopamine in striatal brain slices. Using this approach, we characterized the response to dopamine in the D1 and D2 types of striatal medium-sized spiny neurons (Yapo et al, J Physiol, 2017). Such protocols also showed that type 2 phosphodiesterase (PDE2) plays a critical role in the regulation of high cAMP levels in D2 neurons.

In this project, we will use biosensor imaging on striatal brain slices as a cellular readout to analyze PDE2 action, comparing the effect of PDE2 inhibitors with those of antipsychotic drugs. Animal models of the disease will be analyzed using this approach, while checking in parallel for changes in PDE2 levels. Finally, we see if brain penetrant PDE2 inhibitors affect behavioral readouts of the disease.