Master de Sciences et Technologies
Mention Biologie Intégrative et Physiologie
Parcours : Neurosciences
Responsable : Professeur Régis Lambert

Internship Proposal
Academic Year 2019-2020

1. Host team :

Research Unit (e.g. Department or Institute) : ESPCI, Brain Plasticity Unit
Research Unit Director : Thomas Préat
Research Team Director : Thomas Préat and Pierre-Yves Plaçais
Team name : Genes and Dynamics of Memory systems

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2. Internship project title:

Mitochondria dynamics and Memory formation in Drosophila.

3. Internship Description :

The human brain only represents 2% of total body weight, yet it consumes 20% of all blood glucose and oxygen resources. As a central regulator of energy homeostasis, the brain prioritizes its own supply over peripheral organs as illustrated by the 'selfish-brain' model. This suggests that the brain's energy needs dictate the consumption by the rest of the organism. On the other hand, several human conditions link energy metabolism perturbations with cognitive defects suggesting that energy metabolism may be a key factor that governs proper brain functioning. How the brain adapts its physiology to the level of available energy, and in particular, how energy metabolism influences neural plasticity are critical questions that our group are trying to address.

Importantly we have recently shown that long-term memory formation in the model organism Drosophila has a significant metabolic cost, relative to the whole organism's consumption (Plaçais and Préat, 2013). Indeed, despite having a much simpler brain, with only 100,000 neurons, Drosophila can feature elaborate associative memory processes involving defined and well-described neuronal networks (Bouzaiane et al., 2015). Most importantly, the neurotransmitters and molecular pathways supporting memory formation and storage are largely conserved from flies to mammals. Working on Drosophila has three main advantages. First, this genetically tractable model offers a wealth of very powerful genetic tools that enable single-cell targeting and temporal control of cellular activity including targeted gene expression; second, the time scale of Drosophila genetics is days or weeks, versus months or years for similar manipulation in rodents; third this 'toolbox' affords us an integrated approach from single-cell in vivo imaging to behavior experiments in our studies of memory processes.

Using this model, we have been working on the mechanisms that control long-term memory formation for years both at the neuronal network level and at the cellular and molecular levels (Plaçais et al., 2012, Pavlowsky et al., 2018; Scheunemann et al. 2018). Recently using a combination of genetic tools, behavior experiments and in-vivo brain imaging, we have shown that, in the drosophila associative olfactory

memory center, the mushroom bodies, pyruvate flux into neuronal mitochondria is critical for long-term memory formation (Plaçais et al 2017).

A second type of consolidated memory, albeit less persistent than long-term memory (LTM), exist in Drosophila. Interestingly, this memory, named ARM for Anesthesia-Resistant Memory, does not require this pyruvate mitochondrial influx (Plaçais et al 2017). Intriguingly, ARM is also increased in starved flies whereas LTM cannot be form (Plaçais and Préat, Science, 2013). These differences between these two types of persistent associative memory suggest that they are not supported by the same energy pathway. Nevertheless, preliminary experiments show that in both case functional mitochondria are required to form persistent associative memories.

Mitochondria are dynamics organelles that continuously move, fuse and divide. In mammalian neurons, depending on their sub-cellular localization, mitochondria shape varies from granular, round mitochondria to tubular, elongated network. This diversity of shapes reflects the heterogeneity of the demands mitochondria need to face depending on the sub-cellular compartment. Mitochondria shape has been shown to influence its energy production, its buffering calcium capacities as well as its motility. Therefore mitochondria shape can impact ts intracellular distribution and its ability to be present at sites of high ATP consumption and Ca2+ buffering needs. A first part of the project will aim at characterizing the different mitochondria populations depending on their sub-cellular localization in the mushroom bodies neurons. In particular, imaging of mitochondria on ex-vivo brain preparation will be used to characterize their motility depending on their neuronal sub-cellular localization. A second aspect of the project is to understand how mitochondria dynamics and specifically their motility is required during memory formation. By genetically targeting the pathways involved in mitochondria motility, we will first describe the consequence on mitochondria sub-cellular distribution using immunostaining and confocal microscopy and correlate these results with behavioral characterization of the two types of persistent memory in the mutants.

We are looking for a candidate student for an M2 internship – and potentially for a consecutive doctoral thesis– to carry on that project. Candidates should be motivated by experimental research, willing to develop careful experimental skills in various fields including imaging, molecular biology and behavior. The selected candidate will work in an international and multidisciplinary environment of about 12 to 14 people gathering geneticists, neurophysiologists and physicists. In addition, she/he will benefit from the three team's own microscopes, the high-throughput behavioral setup and guaranteed funding from the team's ERC grant to perform its research project.