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| Equipe du Dr MARTIN |  |

Encadrant:

**Stéphane MARTIN** 04 93 95 34 61 ; [martin@ipmc.cnrs.fr](mailto:martin@ipmc.cnrs.fr)

Sujet :

**Investigating the metabotropic Glutamate Receptor-dependent regulation of the SUMO machinery in a Fragile X Syndrome context**

**Master 1 ou 2**

Mots-clés : *SUMO, trafficking, synapse, neurons, live cell imaging.*

The synapse is the contact point between neurons where neurotransmission occurs. This highly specific area is a dynamic compartment where all molecular processes are orchestrated both in time and space. Among these is the activity-dependent reorganization of protein composition at synapses, which mainly occurs via modulation of protein-protein interactions and diffusion of signaling molecules in and out of spines. Such reorganization is at the **basis of synaptic plasticity events and learning and memory processes**. This activity-dependent shaping of the synaptic content relies mainly on post-translational modifications (PTMs) including phosphorylation or ubiquitination. In the past years, another protein modification called **SUMOylation** also appeared as an essential regulator of synaptic communication and plasticity **(1-2)**. It consists in the **covalent but reversible** **conjugation** of the Small Ubiquitin-like MOdifier SUMO polypeptide to specific lysine residues of target proteins. **Disruption of the SUMOylation/deSUMOylation balance in neurons leads to early lethality** indicating that the regulation of this process is **central to brain development**.

In the past years, we have demonstrated that the **SUMOylation/deSUMOylation balance is regulated by the activation of type 1 metabotropic glutamate receptors mGluRs (3-5).** The overall aim of the present project is thus to assess **how alterations in the mGluR-signaling pathway impact the SUMOylation/deSUMOylation balance and consequently lead to neuronal communication defects.**

The selected student will use molecular, biochemical and live cell-imaging approaches to investigate the regulatory mechanisms of the SUMOylation and deSUMOylation machinery in living neurons obtained **from genetically-modified mouse models of the Fragile X Syndrome in which, the mGluR signaling pathway is altered.**

Publications relatives au sujet :

* 1- Martin S. et al. (**2007**) **Nature** 447:321.
* 2- Schorova L. & Martin S. **Frontiers in Synaptic Neuroscience** 8:9 (2016).
* 3- Loriol C. et al. **Nature Communications** 5:5113 (2014).
* 4- Schorova L. et al. **Cellular and Molecular Life Sciences** 5:5113 (2019).
* 5- Pronot M. et al. **Cellular and Molecular Life Sciences** 79:378 (2022).