MASTER 2 Fundamental and Clinical Neurosciences

Internship proposal 2026-2027

(internship from January to June 2027)

Host laboratory: **Pathophysiology and Genetics of Neurons and Muscle – 8 Avenue Rockefeller, 69008, Lyon**

Host team : *Team Courchet* (https://pgnm.inmg.fr/courchet/)

Internship supervisors : Martijn Kerkhofs (Post-doc/daily supervisor)/ Julien Courchet (DR/Head of the team) Email: martijn.kerkhofs@univ-lyon1.fr

Project title : mRNA isoforms and function in neuronal health and disease

Project summary : The brain produces the largest number of mRNA isoforms in the human body. These mRNA isoforms are shaped by alternative transcription start sites, splicing, polyadenylation and undergo extensive mRNA modifications. The expression of mRNA isoforms is heavily regulated in time and space because they contribute to fundamental properties of neurons such as neuronal identity and function. However, the full extent of mRNA diversity and its significance for neurodevelopment are not clear. In the lab, we are very interested in studying the mRNA lifecycle and its importance in the context of neurodevelopment. Particularly, we want to discover how properties of mRNA molecules such as untranslated regions contribute to the formation of axons in cortical neurons. To do this, we combine classic biochemistry with state-of-the-art gene manipulation techniques and live-imaging in murine cortical neurons *in vitro* and *in vivo*. We use these techniques in healthy mice but also study the contribution of mRNA dysregulation to neurodevelopmental diseases. New insights from this angle may open up therapeutic avenues (including RNA therapies!) for these disorders. If you are excited about the diverse roles of mRNA in axonogenesis, we are happy to welcome you for an internship.

3-5 recent publications :

Courchet, V., Roberts, A.J., Meyer-Dilhet, G., Del Carmine, P., Lewis, T.L., Polleux, F., and Courchet, J. (2018-10-16). Haploinsufficiency of autism spectrum disorder candidate gene NUAK1 impairs cortical development and behavior in mice. Nature Communications 2018 9:1 *9*. 10.1038/s41467-018-06584-5.

Lanfranchi, M., Yandiev, S., Meyer-Dilhet, G., Ellouze, S., Kerkhofs, M., Dos Reis, R., Garcia, A., Blondet, C., Amar, A., Kneppers, A., et al. (2024-03-21). The AMPK-related kinase NUAK1

controls cortical axons branching by locally modulating mitochondrial metabolic functions. Nature Communications 2024 15:1 *15*. 10.1038/s41467-024-46146-6.

Kerkhofs, M., Meyer-Dilhet, G., Polvèche, H., Yandiev, S., Tait-Mulder, J., Lilla, S., Sumpton, D., Murphy, D.J., Ahn, E.-Y.E., Bourgeois, C.F., et al. (2025-10-10). The AMPK-related kinase NUAK1 regulates neuronal morphogenesis through the RNA splicing co-factor SON. bioRxiv. 10.1101/2025.10.10.681550.