Master Biologie Moléculaire et Cellulaire 'BMC',
Université Paris Cité - *UFR Sciences du Vivant*

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage de M2, 2026-2027

Unité INSERM ou CNRS ou Université : **I.Cochin, UPC, INSERM U1016, CNRS UMR 8104.** **Intitulé Equipe : Physiopathology of the neuromuscular system** **ED d'appartenance : BIOSPC** **Responsables de l'Equipe : P.Maire/B.Viollet**	**Responsable du Stage : Pascal Maire** **Contacts** Adresse : 24 rue du Fg St Jacques. 75014 Paris Email : pascal.maire@inserm.fr Tel :

Titre du projet : Mapping Secreted Signaling Proteins at the Neuromuscular Junction in Health and Disease

Résumé du Projet de Stage (en 300 mots maximum, mots clés en gras)

The neuromuscular junction (**NMJ**) is a specialized synapse between motoneurons and skeletal muscle fibers that controls muscle contraction. It relies not only on acetylcholine but also on many secreted signaling molecules (**neurokines** and **myokines**) that regulate muscle fiber identity, synapse stability, and tissue plasticity. Disruption of this molecular dialogue likely contributes to neuromuscular diseases such as amyotrophic lateral sclerosis (**ALS**), where NMJs degenerate early, although many of the exchanged signals remain unknown.

New technologies now allow cell type–specific identification of newly synthesized proteins in complex tissues. One key method is the MetRS metabolic labeling system, which uses a mutant methionyl-tRNA synthetase to incorporate the non-canonical amino acid azidonorleucine (**ANL**) into nascent proteins. These ANL-labeled proteins can then be selectively purified by click-chemistry reactions, enabling precise detection of proteins produced by defined cell types and thus of candidates involved in neuromuscular communication.

This project aims to characterize the molecular dialogue at the NMJ by identifying proteins exchanged between motoneurons and muscle fibers in both healthy mice and ALS models. By combining metabolic labeling, click-chemistry purification, and biochemical analyses, the work will reveal candidate signaling molecules and how their communication pathways change in disease. During the internship, the student will perform metabolic labeling, click reactions, and biochemical analyses of labeled proteins, as well as complementary molecular biology and cell culture techniques such as RT-qPCR and immunocytochemistry. This will help validate candidate signals and deepen understanding of how neuromuscular communication is altered in ALS, while giving the student practical training in molecular biology, protein biochemistry, and proteomics.

Publications de l'équipe relatives au projet de stage (max 5)

Jauliac,E., BackerS., SadakiS., Gondin, J., Escoffier, H., Roullat, M., Di Gallo, M., Vuong V., Dos Santos, M., Ham, A., Levesque, A., Pereira, D., Letourneur,F., Pierre, R., Ruegg, M., Birchmeier, C., Fujita,, R., Sotiropoulos A., Maire, P. c-MAF transduces motor neuron firing to sustain fast-glycolytic myofibers and neuromuscular junctions. 2026. In revision. doi: https://doi.org/10.64898/2026.02.05.703983

Wurmser, M., Madani,R, Chaverot,N., Backer, S., Borok,M., Dos Santos, M., Comai,G., Demignon,J., Relaix, F., Tajbakhsh,S., Santolini, M., Sambasivan,R., Jiang, R., Maire, P. 2023. Overlapping functions of SIX homeoproteins during embryonic myogenesis. PLoS Genet. 19(6):e1010781. doi: 10.1371/journal.pgen.1010781.

Dos Santos,M., Backer,S., Auradé,F., Man-Kin Wong,M., Wurmser,M., Pierre,R., Langa,F., Do Cruzeiro,M., Schmitt,A., Concordet,J-P., Dilworth,F.J., Noordermeer,D., Sotiropoulos,A., Relaix,F., Sakakibara,I., Maire,P. A fast *Myh* super enhancer dictates adult muscle fiber phenotype through competitive interactions with fast *Myh* genes. 2022. *Nat Commun* 13. 1039. DOI: 10.1038/s41467-022-28666-1

Dos Santos,M., Backer,S., Saintpierre,B., Izac,B., Andrieu,M., Letourneur,F., Relaix,F., Sotiropoulos,A., Maire,P. 2020. Single-nucleus RNA-seq and FISH identify coordinated transcriptional activity in mammalian myofibers**.** *Nat Commun* **11,** 5102. DOI: 10.1038/s41467-020-18789-8