



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

Parcours : **Biologie et Développement Cellulaires 'BDC'**

<https://master2bdc.ijm.fr/>

Fiche de Projet de Stage de M2, 2025-2026

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

### **Titre du projet : Muscle fibers and motoneuron interplay**

#### **Résumé du Projet de Stage:**

Muscle tissue accounts for approximately 40% of body mass. It is made up of several types of cells, including fibroblasts, tenocytes, endothelial cells, Schwann cells, muscle stem cells, motoneuron extensions and muscle fibers, which ensure contraction thanks to a specific contractile system. The muscle fiber is a giant cell that can measure several centimeters in length. The myofiber is a syncytium that can contain several hundred nuclei that are added as the fiber grows during embryonic and postnatal development. There are three main types of nuclei in the fiber, those present at myotendinous junctions (MTJs), those present at neuromuscular junctions (NMJs) and 97% of the other myonuclei present along the myofiber in a stereotyped manner, each nucleus controlling a defined cytoplasmic domain. The myofiber is innervated at its center by motoneurons, which control its contraction rate by releasing acetylcholine at defined frequencies. The motoneurons also release various neurokines, such as agrin and neuregulin, which contribute to the differentiation and diversity of the myofibers. Conversely, the myofiber instructs the motoneuron by releasing myokines such as Neurturin or BDNF, which enable a dialogue with the motoneuron.

Using snRNAseq approaches in motoneurons and myofibers, we will characterize novel myokines and neurokines involved in the **motoneuron-myofiber dialogue** and characterize signaling pathways downstream of motoneuron stimulation that may be involved in the specialization and coordination of nuclei along the fiber. Using primary cultures of motoneurons and myogenic cells, we will investigate the properties of several identified **myokines and neurokines**. We will mainly use cell culture experiments, RTqPCR, STORM immunocytochemistry on muscle slices, RNAscope and immunocytochemistry on isolated myofibers. These approaches should allow us to characterize the signaling pathways and their effectors that are involved in the dialogue between motoneuron and myofiber and that are required for the harmonious **specialization of muscle fibers and motoneurons and the synchronization of myonuclei** during the development.

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

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](https://doi.org/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](https://doi.org/10.1038/s41467-020-18789-8)