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

Parcours : **Biologie et Développement Cellulaires 'BDC'**
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Fiche de Projet de Stage M2, Année 2020-2021

Unité INSERM ou CNRS ou Université : Institut Cochin INSERM U1016 **Intitulé Equipe :** Développement neuromusculaire, Génétique et Physiopathologie **ED d'appartenance : BioSPC** **Responsable de l'Equipe : Pascal Maire et Athanassia Sotiropoulos**	**Responsable du Stage : Pascal Maire et Athanassia Sotiropoulos** **Contacts** Adresse : Adresse : Institut Cochin 24 rue du Fbg Saint Jacques, 75014 Paris Email :pascal.maire@inserm.fr Tel : +33 1 44 41 24 13

Titre du projet : Single nucleus transcriptomic profiling of skeletal muscle atrophy

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

Adult skeletal muscle tissue can atrophy upon disuse observed during ageing or denervation and upon caloric restriction. The modulation of muscle mass is mainly achieved by the re-programming of gene expression and by the modification of protein turnover in myofibers. At the cellular level, many aspects of muscle plasticity such as muscle atrophy rely on the interplay between different cell types present in the muscle tissue. Skeletal muscle consists mainly of multinucleated post-mitotic myofibers, of resident muscle stem cells (MuSC), tenocytes, fibroblasts, endothelial cells and immune cells. However the contribution of the muscle resident cells other than MuSC and myofibers to muscle atrophy has not been studied so far.

Our general goal is to understand **how muscle plasticity, and in particular muscle mass, is controlled** and to decipher on the involvement of cell-cell communication. To achieve this goal we will perform trancriptomic analysis at the level of single nucleus in three different situations in adult muscle : basal state, acute denervation-induced atrophy and denervated atrophy observed in muscles of mutant mice that have never been innervated. This approach allows not only a single cell cartography of muscle cell populations but also has the advantage to render possible the study of transcription of the individual myonuclei (nuclei of the myofibers) and possibly unravel their heterogeneity during muscle atrophy.

In the team we have already conducted this analysis (**single nucleus sequencing**, 10X genomics) at basal state. We were able to discriminate all cell types present in the muscle tissue, and the differential transcriptional regulation of the myonuclei (M. dos Santos et al, 2020). We would like to complete this study with atrophic conditions by comparing the transcriptional profiles of nuclei in innervated and non-innervated muscles.

This approach will allow to finely analyze the **transcriptional modulations occurring in myofibers and in other cell types upon disuse**, the receptors, ligands and the signaling pathways involved.

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

Dos Santos,M., Backer,S., Saintpierre,B., Relaix,F., Sotiropoulos,A., Maire,P. Single-nucleus RNA-seq and FISH reveal coordinated transcriptional activity in mammalian myofibers. 2020. Submitted. https://biorxiv.org/cgi/content/short/2020.04.16.043620v1

Randrianarison-Huetz V et al. Srf controls satellite cell fusion through the maintenance of actin architecture. *J Cell Biol. 2018,* 217(2):685-700.

Santolini M et al. MyoD reprogramming requires Six1 and Six4 homeoproteins: genome-wide cis-regulatory module analysis. *Nucleic Acids Res.* 2016; 44(18):8621-8640.

Sakakibara,I., Santolini,M., Ferry,A., Hakim,V., Maire,P. 2014. Six homeoproteins and a linc-RNA cooperate at the fast MYH locus to lock terminal fast myofibre phenotype. PLoS Genet. 10 (5) : e1004386