MASTER 2 BMC
PARCOURS GENOPATH
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Titre du sujet de stage : Role of LSD1 lysine demethylase in modulating Muscle stem cell plasticity.

Nom, adresse de l'Unité d'accueil / Nom du responsable de l'unité :

Institut NeuroMyoGène-Pathophysiology and genetics of Neuron and Muscle (INMG-PGNM), Faculté de Médecine, 8 Avenue Rockefeller, 69008 Lyon. Director: Laurent Schaeffer

Nom, adresse de l'Equipe d'accueil / Nom du responsable d'équipe :

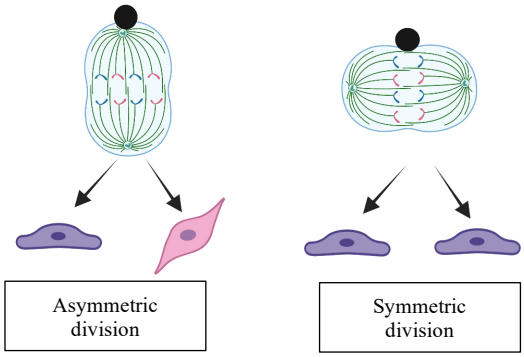
Equipe : Nerve-muscle interactions/L. Schaeffer

Nom, tel, adresse e-mail de l'encadrant de stage :

Scionti Isabella, isabella.scionti@inserm.fr, 04 26 68 82 64

Sujet de stage:

Skeletal muscle constitutes the largest organ of the human body. It contains two types of muscle cells: multinucleated innervated muscle fibers that confer muscle contractility and resident quiescent muscle stem cells (MuSCs) that repair injured muscle fibers. These cells have unique plasticity skills, which are governed by a constant adjustment of metabolic demand and gene expression programs, to allow adaptation to their environment. In chronic diseases such as dystrophies and in aging, muscle plastic abilities are challenged and fail to prevent deleterious muscle atrophy, leading to compromised muscle function. The recognition of epigenetics as a significant contributor to both normal development and diseases has opened an expanding new era for drug discovery and therapeutics. Thus, unveiling the physiological role of epigenetic modifiers in regulating muscle cell plasticity is crucial to designing novel therapeutic strategies. Consistently, the most important challenge in epigenetic therapy is defining which epigenetic variations are causing the disease and which ones occur as a consequence of the disease.



We have previously shown that Lysine-specific demethylase 1 (LSD1) plays a key role in the timely activation of *MyoD* expression during the commitment of embryonic muscle progenitors, via the activation of the Core Enhancer region (CER). Interestingly, upon muscle injury *in vivo,* LSD1 Knock out (KO) MuSCs undergo more symmetric divisions as compared to the control. While, it is widely recognized that MuSC symmetric and asymmetric divisions function in maintaining the balance between MuSC commitment and self-renewal, the mechanism for the determination of either asymmetric or symmetric division needs more investigations. Our preliminary data bring the exciting hypothesis that LSD1 can orient MuSC decision towards asymmetric division *vs* symmetric division by regulating other genomic regions than the CER and/or via other proteins than β-catenin.

The internship has the objective to investigate LSD1 molecular mechanisms which triggers MuSCs fate decision towards asymmetric decision (at transcription level and/or at post translational level).

This subject is of particular interest for candidates that would like to apply to doctoral school.

Techniques: FACS-sorting, Primary muscle stem cell culture, molecular biology, histology, immunofluorescence, imaging, CUT&RUN, ATAC-seq, single muscle stem cell RNA-seq and proteomic approaches.

Mots clés : Epigenetics –protein methylation– transcription – muscle regeneration – single cell.

Publications d'intérêt :

- Sandrine Mouradian, Delia Cicciarello, Nicolas Lacoste, Francesca Berretta, Fabien Le Grand, Nicolas Rose, Laurent Schaeffer, **Isabella Scionti** "LSD1 controls a nuclear checkpoint in Wnt/β-Catenin signaling to regulate muscle stem cell self renewal" doi: https://doi.org/10.1101/2022.06.10.495614

- Delia Cicciarello, Laurent Schaeffer, **Isabella Scionti.** "Epigenetic Control of Muscle Stem Cells: Focus on Histone Lysine Demethylases". Front Cell Dev Biol. 2022 May 20;10:917771. doi: 10.3389/fcell.2022.917771. eCollection 2022.

- **Isabella Scionti**, et al "LSD1 controls timely *MyoD* expression via MyoD Core Enhancer transcription". Cell Rep. (2017) 21;18(8):1996-2006.