# MASTER 2 BMC
# PARCOURS GENOPATH
# ANNÉE 2023-2024

**Titre du sujet de stage :** Role of PHF2 lysine demethylase in the regulation Muscle stem cell fate.

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

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**Sujet de stage:**
Muscle stem cells (MuSCs) are tissue resident stem cells essentials for muscle growth and regeneration. In adult healthy muscle, MuSCs are quiescent and, in response to different stimuli, such as muscle growth or injury, activate to repair the damaged area guarantying at the same time the repopulation of muscle stem cell pool. Although considerable progress have been made in elucidating the molecular regulation of MuSCs biology, the molecular mechanisms regulating muscle stem cells fate decision still needs to be addressed. Thus, understanding how stem cell fate is orchestrated is critical for the identification of novel tools with high impact in regenerative medicine and clinical applications.
Recently, a key role of metabolism in regulating muscle stem cell fate choice has emerged. In particular, current evidences have proposed that MuSC fate choice is finely controlled by lipid droplets abundance. Indeed, the dynamic changes of lipid droplets in MuSCs might correlate with distinct metabolic demands among different MuSC fate states. However, which are the upstream factors coordinating lipid droplet dynamics with MuSC fates are poorly investigated. Among these factors, epigenetic modifications, in particular lysines methylation of histone proteins, could play an important role. PHF2 is a demethylase able to demethylate histone and non-histone proteins. PHF2 has key role in several cell lineage progression, but there are no evidences on its involvement in MuSC fate choice. Here, we show that specific PHF2 ablation in MuSCs leads to skeletal muscle regeneration impairment upon injury. Unexpectedly, some MuSCs depleted of PHF2 accumulate lipid droplets, impairing their regenerative capacity and self-renewal potential. Our results support the hypothesis that PHF2 might be crucial in regulating MuSCs fate, modulating the lipid droplet dynamics.

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

**Technologies utilisées :** FACS-sorting, Primary muscle stem cell culture, molecular biology, histology, immunofluorescence, imaging, single muscle stem cell RNA-seq and proteomics.

**Mots clés :** Epigenetics –protein methylation– transcription – lipid metabolism – 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

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