Internship offer
M2 Musculo-Skeletal system, Locomotion, Exercise (MuSkLE)

Title of the Internship: Deciphering lysine methylation signaling in regulating muscle stem cell division

Laboratory (name, n°, website): Institute for Advanced Biosciences (IAB), CNRS UMR5309, INSERM U1209, University of Grenoble Alpes,

https://iab-grenoble.fr/en

Research team (name, website): Protein Methylation dynamics in cancer

https://iab-grenoble.fr/en/recherche/equipes/dynamique-de-la-methylation-des-proteines-dans-le-cancer

Supervisor to contact (name, email address): Isabella Scionti, isabella.scionti@inserm.fr

Project description: Post-translational modifications (PTMs) are covalent chemical changes that occur on proteins after their synthesis and play essential roles in regulating cellular functions. Among these, lysine methylation is one of the most functionally diverse and dynamic PTMs. It consists in the transfer of one or more methyl groups to lysine residues of proteins and is tightly controlled by two enzyme families: lysine methyltransferases (KMTs), which catalyze methylation, and lysine demethylases (KDMs), which remove methyl groups.

Although initially studied in the context of histones and chromatin regulation, lysine methylation is now recognized as a broader regulatory mechanism that also targets non-histone proteins. Through crosstalk with other PTMs such as acetylation and ubiquitination, lysine methylation influences protein stability, activity, and subcellular localization without necessarily altering protein structure. Consequently, KMTs and KDMs are emerging as key regulators of diverse biological processes and promising therapeutic targets.

Despite this importance, lysine methylation signaling remains largely unexplored in the context of stem cell fate decisions [1,2]. In skeletal muscle, muscle stem cells (MuSCs) are essential for tissue homeostasis and regeneration, and their behavior is tightly regulated by intrinsic and extrinsic cues. However, the role of lysine methylation in controlling MuSC fate remains poorly understood.

In this context, the student will focus his/her study on the lysine demethylase LSD1 (KDM1A), a key epigenetic regulator involved in chromatin and non-histone protein regulation.

We have demonstrated that the LSD1/β-catenin complex promotes asymmetric division (ACD) of MuSCs at the expense of symmetric division (SCD)[3]. Interestingly, as muscle tissue ages, studies have shown an increase in canonical Wnt signaling activity, which contributes to an alteration in MuSC fate. Rather than generating new muscle fibers, these aged MuSC are more likely to contribute to fibrosis or fat infiltration within the muscle.

Since LSD1 fine-tunes Wnt/β-catenin signaling, the aim of this internship is to investigate how LSD1-mediated lysine methylation signaling regulates MuSC fate during activation and aging.

Methods / approach

- The student will use FACS-isolated MuSCs from control and LSD1 conditional knockout mice. Cell fate outcomes will be analyzed during early divisions in vitro and in vivo.
- CUT&RUN sequencing will be performed to map LSD1, β-catenin, and key histone marks associated with active and repressive chromatin states.
- Candidate genes identified through multi-omics integration will be validated using gain and loss of function assays and pharmacological approaches in primary MuSC cultures.
- Finally, MuSC function (proliferation, differentiation, fusion) will be assessed in young and aged conditions, including co-culture with niche cells such as fibro-adipogenic progenitors and macrophages.

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References:

1. Cicciarello D, Schaeffer L, Scionti I. Epigenetic Control of Muscle Stem Cells: Focus on Histone Lysine Demethylases. Front Cell Dev Biol. 2022;10:917771. doi:ryal PubMed PMID: 35669509; PubMed Central PMCID: PMC9166302.
2. Cicciarello D, Scionti I. [Protein lysine demethylation regulates metabolic reprogramming during muscle stem cells fate]. Med Sci (Paris). nov 2025;41 Hors série n° 2:43-7. doi:10.1051/medsci/2025178 PubMed PMID: 41313060.
3. Mouradian S, Cicciarello D, Lacoste N, Risson V, Berretta F, Le Grand F, Rose N, Simonet T, Schaeffer L, Scionti I. LSD1 controls a nuclear checkpoint in Wnt/β-Catenin signaling to regulate muscle stem cell self-renewal. Nucleic Acids Res. 7 févr 2024;gkae060. doi:10.1093/nar/gkae060 PubMed PMID: 38321961.

Skills required : The candidate should have hands-on experience with core laboratory techniques, including cell culture, histological methods such as tissue sectioning and immunostaining, as well as molecular biology assays including PCR, Real Time PCR for gene expression analysis, and Western blotting for protein detection. Proficiency in standard software tools (e.g., Word and Excel) is also required. Knowledge of mouse genetics would be considered an asset.
The ideal candidate is precise, well-organized, and able to work effectively both independently and as part of a collaborative research team.