LABORATORY OF TISSUE BIOLOGY AND THERAPEUTIC ENGINEERING
CNRS-UMR5305

M2- CANDIDATE starting IN 2024/2025

CONTROL OF THE DEGENERATIVE CARTILAGE THROUGH THE HISTONE MODIFYING ENZYME LSD-1

Name, address of the Host Unit:
Tissue Biology and Therapeutic Engineering Laboratory (LBTI), CNRS UMR 5305, 7 passage du Vercors 69367, Lyon cedex 07 and Université Claude Bernard Lyon1
Name, address of the host team/Name of the team leader:
Team ROAD: OsteoArticular and Dental Research (team leader: Frédéric Mallein-Gerin)
https://lbti.ibcp.fr/?page_id=1908
Supervisor: Jérôme Lafont (assistant professor, cell biology)
Jerome.lafont@univ-lyon1.fr

Keywords: articular cartilage, transcriptional regulation, epigenetic signaling, extracellular matrix, osteoarthritis, inflammation and metabolism.

Research objective:
Our project aims at deciphering the epigenetic signaling exerted by the histone modifying enzyme Lsd-1 in articular cartilage. The interplay with inflammatory pathway and metabolism will be analysed in the context of degenerative joint disease such as osteoarthritis (OA).

Project:
Epigenetic modifications have emerged as crucial in many pathophysiological processes. Although some epigenetic enzymes have been described in cartilage homeostasis, their precise role is still unclear. To explore the role of one histone modifying enzyme (Lsd-1) in cartilage, we invalidated *Lsd-1* specially in chondrocytes (Col2a1-CreERT: Lsd-1fl/fl). Using a murine model of cartilage disease, we demonstrated that Lsd-1 promotes cartilage catabolism, potentially through molecular interplay with inflammatory signaling (manuscript submitted). Considering Lsd-1 is a transcriptional co-regulator, we suspect it could also impact the chondrocyte metabolism.
The project will aim at examining the metabolic pathways and the molecular interplay with inflammation, which are both modulated by Lsd-1 in several tissues. We will use animal models of genetically modified mice (conditional KO). These mice will experience a surgically-induced osteoarthritis and compared with spontaneous OA. Joint integrity will be characterised with histomorphometric and spatial-omics approaches. Primary culture of chondrocytes will be used to investigate the transcriptional targets and regulatory mechanisms exerted by Lsd-1 to control the metabolic activity (Seahorse) with regard to inflammation.

References

1. Hunter DJ, Bierma-Zeinstra S. *Lancet* 2019;393:1745–1759. **doi**: 10.1016/S0140-6736(19)30417-9.
2. **Lafont** J, et al. Frontiers in Physiology 14, 1070241. **doi**: 10.3389/fphys.2023.1070241
3. Monteagudo S, et al. *Nat Commun* 2017;8:15889. **doi**: 10.1038/ncomms15889
4. **Durand** AL, et al. Int. J. of Mol. Sc. 2020 Aug 31;21(17):6322. **doi**: 10.3390/ijms21176322
5. Mansouri FE El, et al. *Arthritis Res Ther* 2014. **doi**: 10.1186/ar4564