Le Grand Team
fabien.le-grand@cnrs.fr
https://pgnm.inmg.fr/le-grand/

*Internship project: Joint gene expression and open chromatin profiling from the same nuclei during muscle fusion*

Skeletal muscles are composed of myofibers; giant cells containing hundreds of nuclei. Myofibers are formed through the fusion of muscle progenitor cells during development and postnatal growth. Our lab is investigating the molecular regulation of the fusion process using adult muscle stem cells which can fuse to generate multinucleated myotubes. We recently performed "multiomic" ATAC* + Gene Expression analysis on single nuclei extracted from cultures of fusing cells. (*: **A**ssay for **T**ransposase-**A**ccessible **C**hromatin with highthroughput sequencing)

The student will process and analyze the single nuclei data, through peak calling for ATAC-seq and mapping of transcripts for RNA-seq. He/She will then preform Principal component analysis for Gene expression and Latent Semantic Analysis for Chromatin accessibility. Clustering of single nuclei data, for joint profiling of ATAC and RNA will next identify transitory states between mononucleated cells, and multinucleated, terminally differentiated myotubes. To this aim, the student will use packages such as Seurat (https://satijalab.org/seurat/) and scMVP (https://github.com/bm2-lab/scMVP).

The bioinformatics student will define, in interaction with the biologist students in the team, the analysis plan and interpretation of the data. The goal is to characterize nuclei states during the fusion process, and uncover gene regulatory programs controlling the repair of adult myofibers. The long-term goal of this research project, extending beyond the master internship into a PhD project, is to define novel aspects of the machinery regulating MuSC fusion.

**Publications of interest:**

1: Giordani L, He GJ, Negroni E, Sakai H, Law JYC, Siu MM, Wan R, Corneau A, Tajbakhsh S, Cheung TH, Le Grand F. High-Dimensional Single-Cell Cartography Reveals Novel Skeletal Muscle-Resident Cell Populations. Molecular Cell. 2019 May 2;74(3):609-621.e6. doi: 10.1016/j.molcel.2019.02.026. PMID: 30922843

2: Girardi F, Taleb A, Ebrahimi M, Datye A, Gamage DG, Peccate C, Giordani L, Millay DP, Gilbert PM, Cadot B, Le Grand F. TGFβ signaling curbs cell fusion and muscle regeneration. Nature Communications. 2021 Feb 2;12(1):750. doi: 10.1038/s41467-020-20289-8. PMID: 33531466