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Internship project: Single-cell/nuclei functional analysis of skeletal muscle regeneration

Adult skeletal muscle is a complex structure endowed with remarkable regenerative potential. This ability relies on the orchestrated interplay between muscle stem cells, called satellite cells (MuSCs), and the multiple muscle resident populations. We previously used a combination of single-cell RNA-sequencing (scRNA-seq) and mass cytometry (CyTOF) to define the blueprint of muscle tissue organization at the single-cell resolution (10.1016/j.molcel.2019.02.026). We now intent to elucidate the framework of the cellular events underlying the different steps of skeletal muscle tissue repair at the single-cell level.

To this aim the master student will first analyze different single cell (sc)RNA-seq and single-nuclei (sn)RNA-seq datasets we recently generated using uninjured, regenerating, and ageing muscle tissue. He/She will use dedicated R toolkits such as Seurat (https://satijalab.org/seurat/) for reduction of dimensionality and clustering, Harmony (https://portals.broadinstitute.org/harmony/) for data integration and Slingshot (https://bioconductor.org/packages/devel/bioc/vignettes/slingshot/inst/doc/vignette.html) for trajectory inference.

The student will delineate the different cell populations which pre-exist in uninjured tissue and which arise during muscle tissue repair with the goal of identifying novel cellular subsets involved in these processes. The bioinformatic workflow will also on cell-to-cell communication using the Ligand-Receptor interaction tool CellChat (http://www.cellchat.org/).

The data obtained during the master internship will bring insight in muscle stem cell lineage hierarchy and help identify cellular sub-populations responsible for tissue repair. The long-term goal of this research project, extending beyond the master internship into a PhD project is to identify disease-specific cell subsets in animal models of neuro-muscular diseases and understand the basis of cellular cross-talks causing pathological fibrosis.

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: Garcia P, Jarassier W, Brun C, Giordani L, Peccate C, Agostini F, Kung W, Cheung TH, Le Grand F. Setdb1 safeguards genome integrity in muscle stem cells to allow for regenerative myogenesis and inflammation. bioRxiv 2023.06.08.544190; doi: https://doi.org/10.1101/2023.06.08.544