MASTER 2 BMC
PARCOURS GENOPATH
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Titre du sujet de stage : Epigenetic regulation of Muscle stem cell plasticity.

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Sujet de stage:
Skeletal muscle contains two types of muscle cells: multinucleated innervated muscle fibers that confer muscle contractility and resident quiescent muscle stem cells that can repair or replace injured muscle fibers. Skeletal muscle atrophy results from defects in these two cell types: (a) alteration of the protein degradation/protein synthesis ratio in muscle fibers (b) impaired muscle fiber regeneration by resident muscle stem cells (MuSCs).

In response to injury, a subset of MuSCs is activated, proliferate and either fuse to form multinucleated myotubes or return to quiescence to avoid emptying the pool of stem cells. Although the ability of MuSCs to form new myofibers has long been known, their capacity to self-renewal or remain in quiescent phase has only began to be understood. The maintenance of their quiescence and their activation are controlled by a complex array of signals including mechanical properties of the matrix, inflammatory molecules secreted by macrophages in response to muscle injury, as well as signaling molecules such as Wnt and TGF beta family members.

All these signals are translated into specific cascades of gene expression that indeed monitor MuSC fate and development. Even slight changes in such finely controlled processes can affect the determination of cell lineage and differentiation. Object of this internship is to dissect the epigenetic control of MuSC fate and cellular plasticity, with particular interest to histone variants and histone demethylation. Indeed understanding the epigenomic remodeling events occurring during MuSC fate choice would be of high interest for medical applications such as regenerative medicine.

Technologies utilisées : Primary cell culture, molecular biology, histology, immunofluorescence, imaging, chromatin immunoprecipitation (ChIP), CUT&RUN, ATAC-seq and single muscle stem cell RNA-seq.

Mots clés : Epigenetics – histone modification – transcription – chromatin – muscle regeneration – single cell.

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