Title:
The molecular mechanisms of skeletal muscle plasticity: from bulk muscle to individual single muscle cells and non-muscle cells multi-OMIC analyses

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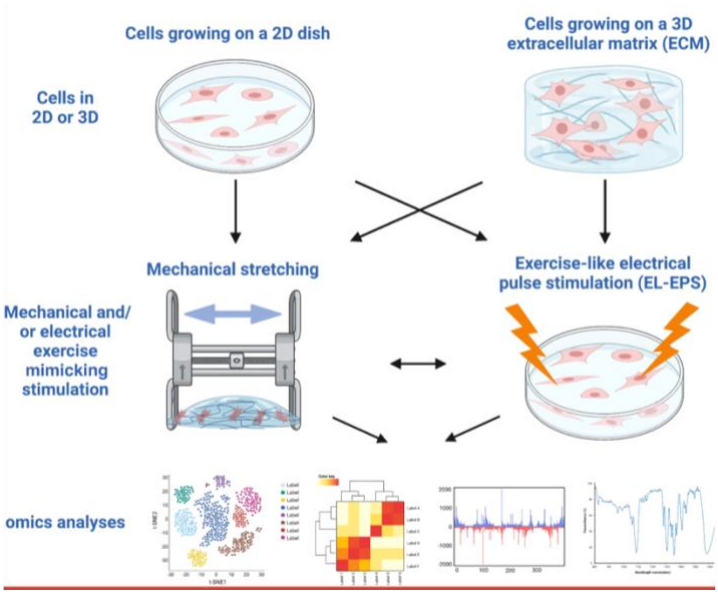
Research Theme/Topic:
Physiology, Cell biology, Regenerative medicine

It is widely recognized that skeletal muscle plasticity is paramount importance for human health. Our laboratory has been studying the cellular and molecular mechanisms of skeletal muscle plasticity using mechanical and energetic analysis of individual muscle fibres coupled to intracellular signaling analyses on bulk muscle samples from mice models and humans for decades.
Recently, transcriptomic analysis of single nuclei (snRNA-Seq) has highlighted that ~1/3 of nuclei in muscle samples is not from muscle fibres, but from mononuclear residents cells (e.g. fibroadipogenic precursors cells (FAPs), glial cells, immune cells)(*1*). Such cell populations can play a key role not only in muscle regeneration, but also in normal muscle homeostasis. Moreover, proteomic(*2*) and transcriptomic analysis of individual muscle fibres have shown large heterogeneity in the response of different fibre types to external stimuli.
This project will develop single cell approaches to resolve the myofiber and cell type-specific mechanisms governing muscle adaptations. This will be achieved by performing extensive targeted and un-targeted multi-OMIC analyses (metabolomic, epigenomic, transcriptomic and proteomic) on isolated single fibres(*3*) and/or on enriched cell populations from muscle tissue and muscle-derived cells using magnetic-activated cell sorting (MACs)/fluorescence-activated cell sorting (FACs) to distinguish fibre/cell type-specific responses to external stimuli. Since muscle cells may retain or ´remember´ characteristics from their in vivo niche during culture(*4*), the research will utilize 3-D bioengineered skeletal muscle tissue culture models to explore the mechanisms of anabolic and catabolic stimuli in isolated myoblasts(*5*) (see figure).
The project will be performed in collaboration with Italian and foreign laboratories.



References

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