Universität Basel

Research Project

Molecular mechanisms controlling the crosstalk between skeletal muscle and neurons

Third-party funded project

Project title Molecular mechanisms controlling the crosstalk between skeletal muscle and neurons
Principal Investigator(s) Handschin, Christoph ;
Organisation / Research unit
Departement Biozentrum / Growth & Development (Handschin)
Department
Project start 01.04.2019
Probable end 31.03.2023
Status Completed

Skeletal muscle exhibits an enormous cellular plasticity to adapt to external and internal stimuli. For example, exercise triggers a pleiotropic adaptation in metabolic and contractile properties in muscle fibers, angiogenesis and increased vascularization within muscle tissue, as well as systemic metabolic remodeling in various other organs. Even though exercise exerts numerous health benefits, the molecular mechanisms that control muscle cell plasticity are still poorly understood. In particular, it is largely unclear how long-term adaptations of training are controlled, e.g. those related to the remodeling of the neuromuscular junction. Our grant aims at elucidating the transcriptional networks that control muscle cell identity in acute exercise and chronic exercise training. Preliminary data indicate that epigenetic adaptations in trained muscle might facilitate the gene expression changes elicited by individual exercise bouts. Besides a general analysis of these networks using a combination of next generation sequencing approaches and computational predictions, we will also specifically focus on potential mediators of a crosstalk between muscle fibers and neurons. We have previously published a hitherto unexpected retrograde effect of muscle on morphological and functional aspects of the motor neuron, mediated by so-far unknown effectors. Moreover, preliminary findings describing a potent effect of exercise and muscle peroxisome proliferator-activated receptor γ coactivator 1α (PGC-1α), a regulatory nexus of endurance exercise adaptation, on motor coordination and balance, and hence presumably proprioceptive and/or vestibular input indicate an even more extensive retrograde signaling between muscle and neuronal circuits. We thus plan to study the interaction of the neuromuscular, proprioceptive and vestibular systems, and to identify the respective mediators in this crosstalk. Retro- and anterograde mapping of proprioceptive and vestibular input on specific motor neuron pools will allow a fine-grained quantification of changes in these systems. These studies will not only contribute to a better understanding of neuromuscular physiology, but also help to identify factors that modulate neuromuscular junction stability, motor coordination and balance, all of which are affected in different pathological settings, e.g. in sarcopenia and aging.

Financed by
Swiss National Science Foundation (SNSF)

Add publication

Add documents

Specify cooperation partners