Universität Basel

Research Project

MUSCLE_NET: Coactivator-controlled transcriptional networks regulating skeletal muscle cell plasticity

Third-party funded project

Project title MUSCLE_NET: Coactivator-controlled transcriptional networks regulating skeletal muscle cell plasticity
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Regular physical activity is linked to improved health and increased life expectancy. Inversely, a sedentary
life-style is a strong and independent risk factor for many chronic diseases, including obesity, type 2 diabetes
or cardiovascular disorders, but also pathologies that are not primarily associated with muscle, such as certain types of cancer or neurodegeneration. Interestingly however, the molecular mechanisms that mediate
the health beneficial effects of exercise, or those that trigger the pathological changes in diseases, are largely
unknown. Nevertheless, “exercise mimetics”, pharmacological agents that elicit a phenotype similar to that
of trained muscle, are part of an interesting new concept to prevent and treat many different pathologies. However, in order to be able to design and deploy specific and selective exercise mimetics without major side effects, a better knowledge of the molecular aspects of muscle plasticity in health and disease are indispensable. The transcriptional coactivator peroxisome proliferator-activated receptor γ coactivator 1α
(PGC-1α) is one of the major regulatory hubs of muscle adaptation to endurance training. Accordingly, enhanced expression of PGC-1α in muscle is sufficient to induce a trained phenotype in mice. Inversely, mice lacking a functional PGC-1α gene in skeletal muscle exhibit many signs of pathological inactivity. Finally, PGC-1α expression is dysregulated in pathological contexts in human muscle, including type 2 diabetes and aging. In contrast, physical activity is the major driver of PGC-1α gene expression in this tissue.
Therefore, the study of the regulation and function of PGC-1α in muscle has the potential to yield important
insights into the molecular mechanisms that control muscle health.

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