Project 1.2 Strategies to increase the performance of skeletal muscles and brown adipose tissue to combat obesity and related diseases.

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Background:

According to the World Health Organization in 2016, over 1.9 billion people were overweight, including 650 million obese ones. Obesity arises from elevated calorie intake in combination with insufficient energy utilization by the organism. It predisposes to multiple diseases including type 2 diabetes (T2D). Strategies aiming to elevate energy utilization by the organism might ameliorate obesity and related diseases. In this context different types of adipose tissue gained recently a lot of attention, since metabolically inactive adipocytes (white adipocytes) can be converted by genetic or pharmacological means to the active beige adipocytes which dissipate energy in the form of heat and might protect against obesity. Energy is also dissipated in large amounts by muscles.
Skeletal muscles are rich in mitochondria and possess a high capacity for energy consumption. High capacity for energy production and utilization is necessary to generate muscle strength and to ensure their performance over a prolonged period. However, obesity, especially in older patients, is often associated with loss of mitochondrial function and consequently with dynapenia (loss of muscular strength) as well as with sarcopenia (loss of musculature). These diseases significantly decrease quality of life and are often life-threatening.
Recently, we uncovered Extracellular regulated kinase 3 (ERK3) as the major kinase regulating adipocytes function. We showed that ERK3 is stabilized in response to β-adrenergic signaling by forming the complex with its co-factor MAP kinase-activated protein kinase 5 (MK5) in the protein kinase A (PKA)-dependent manner. This leads to the induction of lipolysis but also suppresses energy dissipation, which promotes obesity and diabetes. Consequently, deletion or inhibition of ERK3/MK5 is an attractive strategy to treat obesity. However, the mechanisms underlying increased energy dissipation in the absence of ERK3/MK5 signaling remain unclear.
We have also shown that the ERK3/MK5 pathway in adipose tissue suppresses mitochondrial function. Our preliminary data indicate that in obese mice specific deletion of ERK3 in skeletal muscles results in increased mitochondrial number and elevated energy dissipation partially ameliorating obesity. However, the impact of the ERK3/MK5 pathway on the development of dynapenia and sarcopenia as well as mechanisms of action of these kinases were not investigated so far.

Aim:

This project aims to determine the mechanism of ERK3/MK5 action in white and beige adipose tissue as well as in muscles using cell biology, biochemical and genetic methods in combination with the omics approaches. The long-term goal is to determine an effective strategy to increase energy dissipation by manipulating ERK/MK5 pathway in adipocytes and to combat the development of dynapenia and sarcopenia, two most frequent muscular dysfunctions by manipulating this pathway in muscles.

Requirements:

- master's degree (awarded or to be defended soon) in biology, biotechnology, biomedicine, veterinary or related subject;
- good knowledge of English;
- strong motivation and commitment to science;

- preferably experience in laboratory work, in particular working with animals (proven internships and placements would be an advantage).