Project 1.1. Determination of the impact of the ERK3/MK5 pathway on the development of cancer-associated cachexia

Project description

Storage and degradation of triglycerides (in the process of lipolysis) from lipid droplet is the key evolutionary adaptation to cope with the prolonged periods of fasting. However, the induction of uncontrolled lipolysis in adipocytes independently of the nutritional demand of the organism is an event contributing to the development of multiple metabolic diseases including cancer-associated cachexia (CAC). In our previous studies, we identified that atypical member of Mitogen-Activated Protein Kinase (MAPK), extracellular regulated kinase 3 (ERK3), and its interaction partner, MAPK-activated protein kinase 5 (MK5) promote lipolysis in adipocytes of mice and humans. The same complex of kinases regulates energy dissipation by adipocyte, another key event evoked during cachexia. In multiple types of cancers, CAC is the direct cause of death of the patients. Therefore, there is an urgent need to develop anti-cachexic therapies.

Aim of the project

In the framework of this project, we will test the impact of the ERK3/MK5 complex of kinases on the development of CAC. For this purpose, we will utilize mouse models of CAC in which we will ablate or increase the signaling via ERK3/MK5 complex using genetic and pharmacological means.