Abstract

Perturbation in signaling cascades regulating basic metabolic processes in adipocytes and hepatocytes often result in metabolic imbalance and metabolic diseases. In adipocytes increased lipogenesis and lipolysis in combination with reduced energy dissipation are the hallmarks of obesity and type 2 diabetes (T2D). Increased lipogenesis also contributes to the development of non-alcoholic fatty liver disease (NAFLD). Conversely, induction of negative energy balance during cancer-associated cachexia (CAC) is partially caused by increased metabolic activity of adipocytes. In my research group we aim at understanding of the complex signaling network regulating the above-mentioned basic metabolic processes. For this purpose we combine cell biology, biochemical and omics approaches with mouse genetics. Using high throughput siRNA based screening we identified a number of novel kinases regulating lipolysis. Using targeted mouse genetics approach we identified several members of Protein kinase D family as central regulators of adipocytes and hepatocyte metabolism. In future, we plan to investigate the identified pathways in the context of metabolic diseases. In parallel, we will utilize screening approaches to identify novel, non-canonical signaling modules (phosphatases and components of the ubiquitin system) regulating abundance, localization and phosphorylation of targets of Pkds and, in the long term, also other kinases implicated in regulation of metabolism.
By identifying and characterizing the essential signaling networks in liver and adipose tissue the project will contribute to more targeted pharmacological strategies for treatment of metabolic diseases such as obesity, T2D and CAC.