

Over 1.9 billion people world-wide are obese or overweight. Obesity itself is rather an esthetic and gravitational problem. However, it promotes deposition of toxic lipids in such organs like adipose tissue or skeletal muscles, which changes the metabolism of the organism by affecting so called signaling cascades. Under normal circumstances function of each cell of our organism is under tight control of hormonal and nutritional cues, which arise in response to the changes in physiological settings. Muscles and/or adipocytes need to rearrange their metabolism in response to feeding or fasting, physical activity or resting as well as ambient temperature or cold challenge and many other physiological setting. All of these are coordinated through activation by hormones and nutrients of so called signaling cascades which coordinate an appropriate change in the cellular metabolism. This ensures proper glucose, lipid and other nutrients levels in our blood and adequate supply of these nutrients to all of the organs. However, aberrant deposition of lipids in the many organs mis-regulates these signaling cascades and leads to the aberrant glucose and other nutrient handling and consequently promotes dysfunction of adipose tissue, skeletal muscle and other tissues. Ultimately, mis-regulation of signaling cascades during obesity promotes diabetes as well as fatty liver disease or muscle weakness. In our project we want to identify dysfunctional signaling cascades evoked during obesity and other metabolic diseases. To study these cascades we will utilize genetic, biochemical, molecular biology and pharmacological approaches to interfere with specific signaling cascades in adipose tissue and skeletal muscles in order to prevent obesity and muscle weakness. Our recent data indicate that signaling complex composed of Extracellular-regulated kinase 3 (ERK3) and MAP Kinase-Activated Protein Kinase 5 (MK5), represents a crucial signaling node which regulates adipocytes and muscle function and therefore might be central for development of obesity and associated diseases. In current proposal we will investigate the impact of these molecules in adipocytes and muscle on development of obesity, diabetes and muscle diseases such as sarcopenia and dynapenia. Our long term goal is to develop strategies to treat obesity and obesity-associated diabetes as well as muscular dysfunction.