Project title: Effect of different dietary fatty acids on autophagy induction and metabolic activity in hypertrophic adipocytes

Obesity is currently recognized as one of the diseases of affluence. The number of obese people has been constantly increasing over the last decades. Statistical data show that worldwide obesity has more than doubled since 1980 and in 2014 exceeded 600 million people. Fat tissue (also termed adipose tissue), was once considered to play only a role of passive energy storage and heat loss protection; however, nowadays it is defined as the largest secretory organ of the body with high metabolic activity. Adipose tissue cells, including fat cells (adipocytes), are able to produce and secrete many biologically active substances called adipokines. Excessive accumulation of fat in the body leads to disorders in glucose and lipid metabolism. Moreover, obesity is connected with a state of chronic inflammation in adipose tissue, causing adverse changes in the secretory profile of this tissue. Described changes constitute an important factor for development of obesity-related diseases, such as type 2 diabetes, non-alcoholic fatty liver disease, hypertension and coronary heart disease.

Recently, researchers have discovered that autophagy may play a substantial role in differentiation and functioning of adipose tissue. Autophagy, a cellular process of "self eating", enables cells to digest dead or damaged elements of their cytoplasm. Maintenance of inner balance in cells is highly dependent on the proper functioning of autophagy, because products of autophagic digestion can be reused again by the cell, providing cell with efficient recycling process. Discovery of the important role of autophagy in cells was recognized as a significant achievement in biology, and in 2016 professor Yoshinori Ohsumi was awarded with the Nobel Prize in Physiology or Medicine for his discoveries of mechanisms for autophagy. Studies conducted in the XX century have shown that genes related to autophagy are also involved in regulation of adipocytes maturation (termed adipogenesis). Furthermore, results of some research demonstrate that obesity is accompanied by increased autophagic activity in fat tissue; however its role in this context has not been fully explained so far. Many questions arise regarding the mechanisms of autophagy induction and exogenous factors which can regulate autophagic activity in adipocytes. It is possible that fatty acids are among the factors which can impact autophagy activity in fat cells. It has been proven that various types of fatty acids may exert different effects on metabolism and secretory functions of adipose tissue; however, the exact mechanism of these actions is not fully understood. In addition, it is unclear whether increased autophagy in the adipose tissue of obese individuals is beneficial or deleterious. Therefore, research on physiology and pathophysiology of adipose tissue seems to be a promising direction of scientific studies, which may lead to the development of new strategies for the prevention and treatment of obesity and related diseases. Consequently, **this project aims to determine the role of different types of fatty acids in regulation of autophagy in adipocytes with excessive fat accumulation (termed hypertrophy).**

Using *in vitro* cell culture model of hypertrophic adipocytes (3T3-L1 mouse cell line) and *in vivo* animal model of mice fed a diet with high fat content, we want to explore the possible causes of autophagy induction in „obese" adipocytes (e.g. endoplasmic reticulum stress, oxidative stress, mitochondrial dysfunctions). In addition, we want to determine whether different types of fatty acids: palmitic acid, lauric acid, oleic acid, eicosapentaenoic acid and docosahexaenoic acid, may differently influence the autophagic activity in hypertrophic adipocytes; and whether the activity of autophagy is connected with the secretory profile of adipocytes (secretion of pro- and anti-inflammatory adipokines). Furthermore, the *in vivo* part of the study, in which obesity will be induced in mice by feeding them diet with high fat content, aims to verify whether diets with the same fat content but differing in lipids composition due to different sources of lipids: lard, coconut oil, olive oil and fish oil, (thus, containing the fatty acids investigated in the in vitro part of the study), will have a different effect on adipose tissue physiology and secretory profile. We are also planning to investigate the influence of these different high fat diets on autophagy induction in adipocytes of obese mice. To our knowledge this is the first research project using such comprehensive approach to study the role of multiple fatty acids: saturated, monounsaturated and polyunsaturated, in regulation of physiology and functions of hypertrophic adipocytes, thus mimicking the state observed in obese people. This research will be carried out using modern molecular biology methods (RT-PCR, Western-Blot, ELISA), chromatographic methods (GC-MS, LC-MS) and confocal microscopy.