

## ABSTRACT

Obesity is the world's most widespread metabolic disease and its continuous rise in prevalence is alarming. The severity of obesity is that it is associated with a significant increase in the risk of metabolic diseases such as type 2 diabetes mellitus, hyperlipidemia, cardiovascular disease and some types of cancer. Obesity thus contributes significantly to increasing the cost of healthcare system. Preventing the aforementioned diseases is essential to reduce this burden. This is based both on the prevention of obesity itself, on the other hand, on the knowledge and consequent influence on the mechanisms of metabolic disorders associated with obesity. These disorders are based on changes in key metabolic organs: adipose tissue, liver, skeletal muscle and pancreas. The present thesis is focused on obesity-induced disorders of adipose tissue at the metabolic, endocrine and immune levels, presented as dysfunctional adipose tissue. Special attention was paid to the detrimental effect of elevated levels of basic macronutrients (carbohydrates and lipids) and, on the other hand, to the beneficial effects of low calorie diets on molecular characteristics of adipose tissue. The acquired knowledge illuminates the mechanisms of action of nutritional stimuli on adipose tissue dysfunction at the molecular and cellular level and thus provides an important basis for the prevention of obesity and related metabolic disorders. Thus, the link between nutritional risk factors and the etiology of dysfunctional adipose tissue provides scientifically-based facts necessary to adjust nutritional recommendations. This approach could be called "Molecular Preventive Medicine".

This thesis is elaborated in the form of a set of publications dealing with the effect of interventions leading to the elevation of circulating levels of nutrients - hyperlipidemia, hyperglycemia on the one side, and calorie restriction on the other - on subcutaneous adipose tissue characteristics. A total of 6 publications that were created at the Department for the Study of Obesity and Diabetes, newly renamed as Department of Pathophysiology on the Third Faculty of Medicine of Charles University are included. This Department has been engaged in the research of adipose tissue, obesity, metabolic complications of obesity and their prevention for a long time. The thesis is thematically divided into two parts. In the first part, the common theme is the influence of short-term interventions on the pro-inflammatory profile both at the level of adipose tissue and in the circulation. In publication No. 1 and 2 is evaluated the effect of short-term hyperlipidemia and hyperglycemia on the adipose tissue immune profile of obese women. Publication No. 3 describes the effect of a single-dose high-

fat meal on inflammatory changes in circulation in young healthy men. Publication No. 4 is focused on the regulation of fatty acid mobilization from adipose tissue during exercise influenced by antidiabetic medication - metformin. The second part of the thesis, which includes publications No. 5 and 6, focuses on the effect of hypocalorie diet and its various phases on the modulation of metabolic, endocrine and immune functions of adipose tissue in obese women.

The studies in this thesis provide contributions to the knowledge of the regulation of pro-inflammatory state of the organism and the role of energy intake and the level of basic macronutrients in this process. These fragments of knowledge can help to understand the functional changes at the level of the adipose tissue and thus lead to the effective development of preventive and treatment strategies.