SUMMARY

It is apparent that the imbalance in energy intake and expenditure coming hand-to-hand with the „westernisation“ of our lifestyle leads to an elevated number of overweight and obese individuals that are commonly in a greater risk of developing chronic complications (e.g. insulin resistance, type 2 diabetes and cardiovascular diseases) with increased mortality.

The development of obesity-related complications closely relate with dysfunction of adipose tissue leading to the peripheral insulin resistance and metabolic disruption of insulin sensitive organs (e.g. muscle, liver) subsequently inducing whole body insulin resistance. Since adipose tissue is the biggest endocrine organ in the human body producing many hormones influencing functions of adipose tissue itself or other organs, alteration of their spectrum has been revealed as one of the possible inductors or contributors disturbing body energy homeostasis. Adipose tissue serves as a major site for storage of surplus nutritions, however, long-term positive energy imbalance and high dose calorie intake lead not only to expansion of fat mass but mainly to the pathological changes of the tissue. In states of obesity, adipose tissue is under constant metabolic stress, resulting in the activation of the stress and inflammatory response. It leads to the remodeling of adipose tissue with increased macrophage accumulation, the important source of proinflammatory cytokines in adipose tissue. Abnormal release of cytokines, adipokines and FFAs, that act in a paracrine or autocrine fashion amplify the proinflammatory state within adipose tissue and cause local insulin resistance. Increased fat load increases adipocyte cell size that leads to a shift in the pattern of secreted adipokines as a result of dysregulated adipocyte metabolism. This might have different pathological consequences regarding location of the fat tissue. A number of products secreted by adipose tissue (e.g. adipokines, fatty acids) are affected in a depot-related manner. In fact, differences in protein production or gene expression of many adipocytokines were demonstrated in VAT when compared to SAT. Adiponectin stands out among multiple adipokines due to its most abundant expression in adipose tissue, high plasma levels, its pleiotripoc beneficial effects not only in metabolism and its unusual negative correlation with fat mass and obesity-related complications. Adiponectin has been suggested to play an important role in pathogenesis of obesity-related complications, e.g. insulin resistance and T2DM. Therefore, adiponectin and its regulation has attracted an enormous attention and has become a promising target in treating of obesity-related disorders. Two main thearapeutic approaches might be applied to manipulate a protein levels, namely, administration of the recombinant protein, or augmentation of its endogenous production. The production of recombinant adiponectin has met number of difficulties due to its complicated multimeric but biologically important structure.

Because of this and adiponectin relatively high plasma levels [113] the effort to improve adiponectin endogenous production and to increase its plasma levels by pharmacological or non-pharmacological approaches has became more attractive field of preclinical research. Many pharmacological drugs (e.g. TZDs, statins) have been proved to manipulate adiponectin production at different levels (mRNA expression, post-translational processing or secretion process). Next approach is to treat obesity itself and in consequence to normalize adiponectin levels. The typical strategies for obesity treatment are divided into 3 categories: non-pharmacological (diet and increased physical activity), pharmacological (anti-obesity drug treatment) and surgical (e.g. gastric banding). Caloric restriction-induced weight loss is a powerful and effective tool to improve metabolic parameters and insulin sensitivity and the possibility of increasing adiponectin levels promoted by dietary interventions has attracted increased attention and has been also one of the goals of our studies in frame of this work.

In our studies we focused particularly on the adiponectin isoforms regulation in relation to molecular adaptations of human adipose tissue by dietary interventions. With respect to the secretory activity of adipose tissue we investigated possible mechanisms influencing the profile of adiponectin isoforms expressed in obesity. Based on our results and results of many other studies it seems that production of adiponectin and the increase of its levels in circulation might be effectively achieved by lifestyle modifications, however, relatively large weight reduction is needed. Our study comparing the secretion of adiponectin by the two main adipose tissue depots (SAT and VAT) revealed that adiponectin isoform profile differs between depots with regard to obesity state. Therefore, differential metabolism and functions of the fat depots might play a role in adiponectin regulation and suggest one of the possible mechanisms affecting adiponectin isoform expression in obesity. Further investigations of adiponectin regulation, particularly the isoforms processing, are needed to understand mechanism of its deterioration in obesity and to be able to reveal novel approaches of increasing adiponectin levels in obesity-related disorders.