
SUMMARY

Obesity is considered to be a worldwide epidemic disease characterized by an accumulation of AT. Increased adiposity can perturb normal metabolic functions and lead to the development of diseases like insulin resistance and other metabolic disorders. A large amount of clinical studies have been shown that changes in inflammatory signaling in adipose tissue cells, increased infiltration of immune cells into AT as well as stress of endoplasmic reticulum belong to the key molecular steps leading to the development of metabolic disturbances associated with this disease.

Adverse metabolic effects of AT accumulation can be diminished by calorie restriction resulting in weight loss. In addition, stress of endoplasmic reticulum could be alleviated by chemical chaperones including bile acids. These two approaches for the treatment of obesity or the obesity-associated disturbances were basis for this PhD thesis.

In the first part of this work, we studied inflammation status of gluteal in comparison with abdominal AT and differentiation and secretory capacity of adipocytes after weight loss in obese patients. We revealed that inflammatory profile of gluteal AT, estimated by mRNA level of macrophages and cytokines as markers of inflammatory status of the body, did not explain the different clinical impact of subcutaneous abdominal and gluteal AT. We proved that weight loss is associated with an improvement of adipogenic capacity of preadipocytes in obese women as well as with change of the inflammatory status of adipocytes from more to less pro-inflammatory profile.

The second part of this PhD study consists from two cross-sectional clinical studies focused on the determination of the role of stress of endoplasmic reticulum and bile acids in AT and blood cells exposed to different experimental conditions.

We investigated effects of ursodeoxycholic acid (UDCA) and tauroursodeoxycholic acid (TUDCA) on preadipocytes and adipocytes derived from human AT of obese patients. Our results demonstrate that from two studied bile acids, only UDCA, is able to influence physiology of AT cells and neither from two tested bile acids were able to suppress the stress of endoplasmic reticulum.

Except for the excess of AT, also food intake is accompanied by transiently elevated concentrations of inflammatory markers in the bloodstream, so-called postprandial inflammation. We hypothesised that stress of endoplasmic reticulum could be one of the possible triggers of postprandial inflammation. However, our results showed that postprandial inflammation was not accompanied by the stress of endoplasmic reticulum and was not preventable by UDCA.

To sum up, results of this thesis contributed to the understanding of the impact of weight loss and chemical chaperones on the molecular characteristics of AT. At the same time, the outcomes of the thesis stressed the need of further investigation of the individual AT depots, role of bile acids in human AT physiology and triggers of postprandial inflammation.