SUMMARY

Obesity and overfeeding are associated not only with increased circulating levels of nutrients and metabolites, but also with increased risk of the development of additional disorders, such as cardiovascular diseases, cancer or insulin resistance. Plausible link between obesity and its comorbidities is inflammatory state, observed on the whole body level as well as in AT. As possible initiators of this inflammation, hypertrophied adipocytes were suggested. Adipocytes *per se* secrete a spectrum of heterogeneous molecules including cytokines. Under the stress conditions, adipocytes and subsequently AT resident immune cells switch to pro-inflammatory state and via secretory signaling attract additional immune cells. Furthermore, hypertrophic adipocytes release higher levels of metabolites that may also contribute to pro-inflammatory polarization of immune cells, mainly macrophages.

General aim of this thesis was to investigate connection between impaired levels of nutrients and pro-inflammatory statue and activation of immune cells in healthy (obese and lean) subjects.

In the Part one of this thesis, we analyzed acute reaction of immune cells in circulation and AT on artificially elevated levels of nutrients, imitating its increased values typical for metabolic syndrome. HFM ingestion led to inflammatory reaction detectable in circulating monocytes but not associated with ER stress. Similarly, short-term HG and hyperlipidemia induced a pro-inflammatory response associated with altered relative content of immune cells in blood and SAAT. Moreover, changes induced by acute hyperlipidemia were associated with enhanced release of pro-atherogenic mediators.

In the studies included in the Part two, we extended our knowledge about beneficial effects of weight reduction on pro-inflammatory and metabolic statue of obese patients. Moderate weight loss was accompanied by amelioration of levels of pro-inflammatory markers in circulation and in AT. The effect on mRNA levels of immunity-related markers was similar in abdominal and gluteal subcutaneous AT. Expression changes of one of these markers, CD163, which were induced by weight loss, were not associated with changes of insulin sensitivity. Furthermore, weight loss reprogrammed precursors of adipocytes and reduced their intrinsic inflammatory potential.

In conclusion, in short-term interventions we confirmed that impaired levels of glucose and lipid metabolites (FA, TAG) are associated with activation of immune

cells in humans. On the other hand, weight reduction led to improvement of secretory function of adipocytes *per se* and inflammatory status of AT on mRNA level. Results of this thesis thus contribute to understanding of obesity and overfeeding associated inflammation, even so further investigation of the functional changes in AT by nutrients and obesity is warranted.