

Autoimmune chronic inflammatory diseases, affecting as much as 5-7% of the general population, represent a considerable portion of human morbidity and many are known to be heritable. The clinical observations strongly suggest that even in genetically predisposed person, some trigger (an environmental exposure or change in the internal environment) is required for initiation of autoreactivity. However, for most autoimmune diseases, the trigger is unknown. Over the last decade, it has become apparent that obesity is an enhancer of chronic inflammation, and white adipose tissue products – adipokines and gastric hormone ghrelin have attracted attention for their immunomodulatory roles representing promising avenues for pharmacotherapy of autoimmune chronic inflammatory diseases.

The purpose of this dissertation was to extend our understanding of the roles of adipokines and ghrelin in chronic inflammation using an experimental model of rheumatoid arthritis, adjuvant arthritis (AA) in rats. The chronic inflammation was studied under the condition of (a) normofeeding, (b) overfeeding (using a model of early-life diet-induced obesity, comprising small litter size and high-fat diet consumption) and (c) 40% foodrestriction to reveal to what extent nutritional factors affect adipokine and ghrelin levels and subsequently the outcome of chronic arthritis.

Results from the AA studies under the condition of normofeeding showed that chronic inflammation of AA is associated with decreased circulating leptin and adiponectin levels, and increased circulating visfatin and ghrelin levels. Results on adipokines and ghrelin obtained under the condition of overfeeding in AA were not significantly differing from those of normofeeding. However, overfed AA rats displayed more severe arthrograph score and systemic inflammation than normally-fed AA rats. On the other hand, food-restriction during AA considerably attenuated arthritis severity and systemic inflammation and was associated with a more profound fall of leptin and more increased surge of ghrelin than in the other feeding conditions.