

The losses due to mastitis reach billion dollars or Euros in America and Europe every year, respectively. The presence of pathogen bacteria in milk, producing thermostable toxins causes a risk to the health of consumers. Moreover, the expression of pro-inflammatory cytokines, even at low levels but for a long time promotes diseases such as allergies, asthma, atherosclerosis, Alzheimer's disease, fibrosis, rheumatoid arthritis, depression, obesity, or cachexia in humans. Thus, consuming milk with an elevated content of pro-inflammatory agents could negatively influence consumers' health (milk from quarters with sub-clinical mastitis or from quarters adjacent to infected one is used for human consumption if the cow is not treated with antibiotics). Cattle udder consists of four mammary glands and they are considered anatomically and physiologically independent with its own vascular and nervous system, and suspensory apparatus. However, some researchers indicated that the external lining of connective tissue showed leakiness. Thus, substances stimulating the immune system can penetrate this barrier and induce the immune answer also in the uninfected adjacent quarters. It might be possible that blood leukocytes aimed at the infected gland may enter also the healthy glands disturbing their homeostasis. Some researchers suggest that the mastitis in one gland influences immune response in the uninfected adjacent glands. Thus, the udder cannot be considered as four isolated glands. In the preliminary analysis, we obtained differences between expressions of some cytokines and acute-phase proteins in healthy quarters adjacent to the staphylococci infected quarter vs. their expression in the quarters derived from the whole healthy udders. However, there is limited information on the influence of the infection of one quarter on the homeostasis of the adjacent quarters. Several papers and our own preliminary analysis show that the somatic cell count in the milk of "healthy" quarters adjacent to the infected one is also elevated. It also indicates that the inflammation of one udder quarter disturbs the homeostasis in the adjacent quarters. Therefore it was decided to check, whether natural and chronic staphylococcal infection of the udder quarter (or quarters) of the dairy cow has an impact on the genomic, proteomic, and epigenomic phenomena occurring in tissues of the uninfected adjacent quarter(s). It is assumed that the pathophysiological processes occurring in the infected quarters affect the physiology of the adjacent uninfected quarters, by regulating transcription or translation processes through, among others, epigenetic phenomena. The analysis of methylation status of selected genes and miRNA transcriptome will allow identifying the impact of the infections on epigenetic regulations and on the changes in expression of genes that are involved in response to its infection. In this study will be also performed transcriptomic analyzes of miRNA genes as well as the expression of selected immune genes at mRNA and protein levels. The experimental material will consist of samples of mammary gland parenchyma with predominance of tissues derived separately from individual udder quarters from each cow infected with coagulase-positive or coagulase-negative staphylococci and samples taken from the adjacent quarters of the same cow but free from pathogen bacteria. The control group will be secretory tissue and milk somatic cells collected from the udders of healthy cows -all four quarters free from bacterial infections. The comparison with genomic, proteomic, and epigenomic phenomena occurring in secretory tissue and MSC of the same quarter will be conducted. It is expected to receive different expressions of selected genes in healthy tissues adjacent to the infected than in completely healthy udders, which will mean indirect bacterial regulation of expression of these genes. Moreover, since the expression of casein genes will be studied, the economic losses in casein production (yield of casein curd) in healthy but adjacent to infected quarters will be also estimated.