

Cytokines are mediators of the immune response. In addition, the cytokine involvement in the regulation of female reproductive process is strongly emphasized. They are implicated in the modulation ovarian steroidogenesis, folliculogenesis and the remodeling of the endometrium during the estrous/menstrual cycle. Cytokines are important during embryo implantation, the process crucial for establishing the proper course and maintenance of pregnancy in mammals. The unique dialogue between mother and fetus requires modulation of maternal immune response to antigenically different embryo. In turn, disturbances in the number of cells secreting cytokines and unbalanced amounts of cytokines secreted by these cells frequently accompany disorders of the reproductive system.

Our previous results indicate that there is an interaction between cytokines and peroxisome proliferator-activated receptors (PPARs) in the endometrial tissue of the pig. PPARs are ligand-dependent nuclear receptors and as transcription factors are involved in the regulation of female reproductive functions. We have shown that cytokines such as interleukin 6 (IL-6) and interferon (γ) affected the expression of the PPAR α – essential for pregnancy maintenance – in porcine endometrium during the estrous cycle and peri-implantation period. These above led us to hypothesize that: PPAR are involved in the regulation of cytokine synthesis in the endometrium of pigs during early pregnancy/the estrous cycle and during acute inflammation; and in addition, the PPAR may be an important factor in the development of inflammatory process in the reproductive system. This hypothesis will be verified in a series of experiments carried out *in vitro*. The research will be conducted on porcine endometrial slices. In the first task we will determine the involvement of PPAR (α , β , γ) in the synthesis of pro- and anti-inflammatory cytokines as well as nuclear factor κ B (signaling molecules involved in the process of immune response) in endometrial tissue during two key processes deciding about the establishment and maintenance of pregnancy – phase of maternal recognition of pregnancy and the initial phase of implantation. The role of PPARs in cytokines synthesis will be also examined during key stages of the luteal phase of the estrous cycle. The purpose of the second task is to determine the role of PPAR (α , β , γ) in synthesis of pro- and anti-inflammatory cytokines and nuclear factor κ B in endometrial tissue during acute inflammation induced by bacterial endotoxin LPS. In turn, the objective of the third task is to determine the involvement of PPAR (α , β , γ) in the development of inflammatory process (LPS-induced) in the endometrium of pigs. In this task, we expect that change the activity of individual isoforms of PPAR (through applied ligands) would change the sensitivity of the tissue to bacterial endotoxin that causes inflammation and perhaps will be the key factor in the development of inflammation in the reproductive tract.

The results of proposed studies will provide new information regarding the interaction between PPARs and cytokines during different stages of the estrous cycle and early pregnancy. They will also describe PPARs role in the porcine endometrium during inflammatory processes, evoked *in vitro* by lipopolysaccharide. The use of the pig as an experimental model is justified due to its similarity to humans with regards to many anatomical and physiological characteristics. Understanding the mechanisms that control early pregnancy course as well as inflammation in female reproductive system is important due to a basic nature of proposed studies. They are justified because peri-implantation period in gilts, but also in other species, is characterized by the highest mortality of embryos (about 40 %). In turn, the inflammation in the reproductive system contribute to the problems associated with the possibility of becoming pregnant and interfere with normal pregnancy course. There is evidence that 14-24 % of gilts with endometritis may be removed from breeding herds. Thus, the planned research will contribute to a better understanding of the mechanisms controlling the periimplantation and the development of inflammatory processes in the reproductive system in pigs.