ABSTRACT

The uterus is a specialized organ that creates optimal conditions for embryo implantation and subsequent development. To prepare for this function, the endometrium undergoes cyclical structural changes during each sexual cycle. The proper progression of the menstrual or estrous cycle depends largely on the ability of the uterus to recognize and eliminate bacterial infections that lead to inflammation. Frequent bacterial infections that cause acute or chronic inflammation in the reproductive system contribute to the formation of endometrial polyps, miscarriages, and abnormalities in placental formation or even infertility in various species. Endometritis in livestock is one of the most common diseases challenging veterinary medicine. Recent research suggests that there is an urgent need for new treatments for chronic inflammation to improve herd reproductive performance and overall animal welfare. In recent years, the role of PPAR in regulating inflammatory processes has become a particularly interesting research topic. It is believed that PPARγ has an anti-inflammatory effect. However, to date, such studies have not been performed on the endometrium.

Therefore, the aim of this dissertation was to determine the effect of PPARγ ligands – a synthetic agonist (pioglitazone), a natural agonist (prostaglandin J_2, PGJ_2), and a selective antagonist (T0070907) – on the transcriptomic profile of porcine endometrium during *in vitro* induced inflammation by lipopolysaccharide (LPS) using the high-throughput RNA-Seq method. In addition, Real-time PCR and ELISA methods were used to determine the expression of pro- and anti-inflammatory mediators in two experimental systems – developing and ongoing inflammation.

The obtained results showed that LPS increased the expression of pro-inflammatory markers during the studied phases of the estrous cycle. In addition, bioinformatic analyzes determined signaling pathways involving genes whose expression was altered under the influence of LPS. The effect of LPS on the process of alternative splicing of genes critical for the proper functioning of the reproductive system was also demonstrated. In addition, blocking the PPARγ receptor during the mid-luteal phase it was shown to affect the largest number of genes with altered expression. These genes were mainly involved in the immune response with a pro-inflammatory profile and the process of granulocyte chemotaxis. In turn, in the follicular phase of the estrous cycle, an association between PPARγ ligands and the expression of genes involved in the DNA damage response was demonstrated. In addition, the modulatory role of PPARγ agonists in porcine endometrium during the inflammatory process was reported to be

more dependent on the estrous cycle phase than on the experimental system (developing and ongoing inflammation).

The results of this study comprehensively describe for the first time the effect of PPARγ-ligands on the immune response in porcine endometrium during *in vitro* induced inflammation. The important role of the PPARγ receptor in regulating inflammation in the endometrium during the mid-luteal and follicular phases of the estrus cycle was demonstrated. In addition to its anti-inflammatory properties, studies have shown that pioglitazone regulates the expression of genes involved in DNA repair mechanisms, including checkpoint activation, which halts cell cycle progression when abnormalities occur in the genome.