ABSTRACT

The uterus is a key component of the female reproductive system in mammals, providing optimal conditions for embryo implantation and development. A growing concern affecting the proper functioning of the reproductive system in both women and animals is the recurrence of bacterial infections. These infections can lead to disruptions in the menstrual or estrous cycle and may interfere with the normal course of pregnancy. An important factor regulating the functioning of the female reproductive tract are peroxisome proliferator-activated receptors (PPARs), which also exhibit immunomodulatory properties. Studies have demonstrated the anti-inflammatory role of agonists of the gamma and alpha isoforms of these receptors in various experimental systems, however, the role of ligands targeting the beta/delta isoform remains unclear. The aim of the present study was to evaluate the effect of PPARβ/δ ligands (agonist – L-165,041; antagonist – GSK 3787) on immune response mediators in the porcine endometrium during lipopolysaccharide (LPS)-induced inflammation i*n vitro*, at selected phases of the estrous cycle: mid-luteal and follicular. The first part of the study involved global transcriptome analysis of the endometrium using RNA-Seq. In the second part, mRNA expression levels of selected inflammatory cytokines were assessed by Real Time PCR in endometrial tissue explants, while their concentrations in the culture medium were determined using the ELISA immunoenzymatic assay in two experimental models – ongoing and developing inflammatory states.

The obtained results revealed a differential impact of PPAR ligands on the transcriptomic profile of LPS-stimulated porcine endometrial tissue under *in vitro* conditions, depending on the phase of the estrous cycle and the type of ligand (agonist or antagonist). The conducted analyses suggest that PPARβ/δ ligands may modulate various processes associated with maintaining the physiological functions of the endometrium, such as angiogenesis, activation of the complement pathway, and NF-κB signaling pathway. Moreover, the data indicate that PPARβ/δ ligands exert pro-inflammatory effects by stimulating the expression of cytokines involved in the inflammatory response (*IL-1β, IL-6, IL-8, TNFα*) in the porcine endometrium during LPS-induced inflammation.

In conclusion, the results underscore the significant role of PPARβ/δ ligands in modulating the immune response during inflammatory processes within the endometrium and may serve as a basis for further research.