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ABSTRACT

Chemerin effect on the endometrial transcriptomic and proteomic profile of the domestic pig (*Sus scrofa domestica* L.) during implantation period

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The doctoral thesis was written under the supervision of prof. dr hab. Nina Smolińska in the Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn.

The doctoral thesis comprises two papers published in 2022 (1 - *Biology of Reproduction*. 2022. doi: 10.1093/biolre/ioac063; 2 - *Cells*. 2022. doi: 10.3390/cells11071161), focused on the influence of chemerin on transcriptomic and proteomic changes in the porcine endometrium (*Sus scrofa domestica* L.) during implantation.

It is well known that the body's metabolism and reproductive functions are closely related. Chemerin is one of the many adipokines, biologically active molecules, secreted by adipocytes (adipose tissue cells), involved in the regulation of energy homeostasis. The adipokine was first identified in 2003 as a ligand of three receptors: chemokine like receptor 1 (CMKLR1, ChemR23), G protein-coupled receptor-1 (GPR1), C-C chemokine receptor-like 2 (CCRL2). Serum chemerin circulates as a prohormone, which is modified when necessary to a biologically active form *via* a proteolytic cleavage. Chemerin, a hormone classified as both, a chemokine and an adipokine, regulates numerous physiological processes. It is involved, among others, in the control of food intake, nutrient metabolism, inflammation, stress response and reproduction. Studies on pigs have shown that the expression of chemerin and its receptors (the chemerin system) occurs in the structures of the hypothalamic-pituitary-gonadal axis, as well as in the uterus, trophoblasts and embryos. Additionally, mRNA and protein levels of the chemerin system depend on the specific hormonal status of the pig. Moreover, it has been shown that the concentrations of chemerin protein in the endometrium increase during implantation. Additionally, it has been indicated that the hormone concentrations in the

uterine flushings increase during maternal recognition of pregnancy and implantation. The above results may suggest a potential role of chemerin in the processes related to embryo implantation.

We hypothesized that chemerin might affect the transcriptome and proteome of the porcine endometrium, and in consequence, influence the production of many factors essential for a proper course of gestation and embryo development. The aim of this study was to determine the chemerin effect on the endometrial transcriptomic and proteomic profiles of the domestic pig during implantation (15 to 16 days of pregnancy). The assumed aim of the research was achieved by the accomplishment of the following tasks:

1) the chemerin effect on the global gene expression in the porcine endometrium, including changes in the long non-coding RNAs (lncRNAs) expression profiles and alternative spliced (AS) events was determined using Next Generation Sequencing (NGS, RNA-seq);
2) the effect of chemerin on the global protein expression in the porcine endometrium was determined using Liquid Chromatography with Tandem Mass Spectrometry (LC-MS/MS).

In the present study, we identified 130 differentially expressed genes (DEGs) under the influence of chemerin. DEGs were assigned to 73 functional annotations. Twelve identified lncRNAs indicated a difference in the expression profile after chemerin administration. Additionally, we detected 386 differentially AS events. As a result of the proteomic analysis, we identified 352 differentially regulated proteins (DRPs) which were associated with 47 functional annotations. Ontology analyses have indicated the participation of the above genes and proteins in the processes of cell migration and adhesion, angiogenesis, immune response and steroidogenesis.

The obtained results provide a basis for a better understanding of the influence of chemerin on the global expression of genes and proteins in the porcine endometrium during the implantation period. It can be assumed that chemerin is an crucial factor regulating the proper course of gestation and embryo implantation.

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