SUMMARY

The role of chemerin in the ovary of the domestic pig (*Sus scrofa domestica* L.)

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The ovaries are among the most active and morphologically diversified organs. The crucial factors regulating the functioning of the ovaries are gonadotrophins, steroid hormones and insulin. Nevertheless, their proper functioning may also be influenced by factors that modulate the processes taking place in the ovaries depending on the energy resources of the body or the occurrence of a local inflammatory reaction. Literature data indicate that **chemerin** is one of these factors. This hormone was primarily known for its role in the modulation of immune response and regulation of energy homeostasis in the body. The latest research also demonstrated that chemerin is locally produced in the ovaries and may be involved in the proper functioning of these structures. However, there was a lack of information on the expression and function of chemerin in the ovaries of the domestic pig — one of the most important livestock species that is also used as a model organism in biomedical research. Moreover, comprehensive studies of the effect of chemerin on the regulation of ovarian functioning have not been conducted in any species. On the basis of the available literature data, it has been hypothesized that chemerin is involved in the regulation of the functioning of pig ovaries. **Hence, the aim of this doctoral thesis was to determine the expression and localization of chemerin and its receptors (CMKLR1, GPR1 and CCRL2) in the ovaries of the domestic pig, as well as to investigate the influence of chemerin on key processes in the gonads, i.e. steroidogenesis, angiogenesis and apoptosis**.

The studies were performed on the ovaries of prepubertal animals and mature pigs during the oestrous cycle and/or early pregnancy. The research material consisted of porcine ovarian follicles and corpora lutea. During the realization of this doctoral thesis, the following research methods were used: quantitative polymerase chain reaction (qRT-PCR), Western Blot, fluorescent immunohistochemistry, *in vitro* cell

cultures, radioimmunoassay (RIA), enzyme-linked immunosorbent assay (ELISA) and statistical analysis.

The obtained results demonstrated that chemerin is produced locally in the ovaries of pigs, and this hormone directly affects ovarian cells functioning, as it was also confirmed by the presence of chemerin receptors in all the examined structures. Changes in the abundance of the relevant transcripts and proteins indicated that the expression of chemerin and its receptors is dependent on the sexual maturity of pigs and the stage of the oestrous cycle or the period of early pregnancy. The immunolocalization of chemerin and its receptors was found in the porcine follicles at various stages of growth/maturation, and in the porcine corpora lutea during the periods of formation, highest activity, and regression. It was also shown that the physiological concentrations of chemerin in the porcine follicular fluid ranged from 104.64 ± 5.28 ng/ml to 186.46 ± 5.66 ng/ml (mean ± standard error of the mean), and it was found that the concentrations of this hormone varied depending on the physiological state of the animals. Moreover, chemerin was shown to modulate (increase or decrease, depending on the phase of the oestrous cycle or stage of early pregnancy) the basal (unstimulated) and luteinizing hormone/follicle-stimulating hormone- and/or insulin-stimulated secretion of steroid hormones (progesterone, androstenedione, testosterone, oestrone and oestradiol) by the porcine ovarian cells. It was also found that chemerin stimulated the secretion of key angiogenic factors (vascular endothelial growth factor A — VEGF-A and basic fibroblast growth factor — bFGF) by the porcine luteal cells and increased the protein abundance of angiogenic factors' receptors (VEGFR1, VEGFR2, VEGFR3, FGFR1, FGFR2) in these cells. Furthermore, it was reported that chemerin modulated (increased or decreased, depending on the phase of the oestrous cycle) the protein abundance of factors of the extrinsic death receptor pathway (apoptosis-related factor — Fas and Fas receptor ligand — FasL) and the intrinsic mitochondrial pathway (apoptosis regulator Bcl-2) of apoptosis, and it also decreased the protein abundance of crucial factor of the execution pathway of apoptosis (caspase-3) in the porcine luteal cells. **The results obtained in this doctoral dissertation indicated that chemerin is the important factor regulating the functioning of the porcine ovaries.**

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