ABSTRACT

THE ROLE OF CHEMERIN IN THE UTERUS OF DOMESTIC PIG (*Sus scrofa domestica* L.) DURING THE OESTROUS CYCLE AND EARLY PREGNANCY

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Ubiquitously occurring overweight and obesity are growing problems, resulting in an increased incidence of infertility. In addition to energy storage, the adipose tissue is also the largest organ of internal secretion. It has been found that the adipose tissue is a source of many factors, including the adipokines – bioactive peptides that affect many organs to maintain physiological homeostasis. More and more reports indicate the role of adipokines as a link between the metabolic status of animals and their reproductive capacity. Adipokines include several factors, among them chemerin – product of *RARRES2* (also known as *TIG2*) gene. Chemerin exhibits its biological activity through binding to specific G protein-coupled receptors, which include chemokine receptor 1 (CMKLR1), G protein-coupled receptors form the chemerin system. Chemerin has a pleiotropic effect, and numerous reports indicate its participation in the functioning of the female reproductive system. Nevertheless, little is known about the function of this adipokine in the uterus, particularly of the domestic pig.

The aim of this study was to confirm the research hypothesis, which assumes the participation of chemerin in the regulation of the functioning of the uterus of the domestic pig (*Sus scrofa domestica* L.) during the oestrous cycle and early pregnancy. In order to verify the hypothesis, the following research tasks were performed:

1. determination of the expression of chemerin and its receptors' (CMKLR1, GPR1 and CCRL2) genes and proteins by real-time PCR and Western blot, respectively, in the endometrium and myometrium of the porcine uterus in the different phases of the oestrous cycle (days 2 to 3, 10 to 12, 14 to 16 and 17 to 19) and during early pregnancy (days 10 to 11, 12 to 13, 15 to 16, 27 to 28 and 30 to 32) as well as in the trophoblasts and conceptuses;

- 2. determination of the concentrations of chemerin in the uterine luminal flushings (ULF) of pigs by enzyme-linked immunosorbent assay (ELISA) in the different phases of the oestrous cycle (days 2 to 3, 10 to 12, 14 to 16 and 17 to 19) and during early pregnancy (days 10 to 11, 12 to 13, 15 to 16 and 27 to 28);
- 3. determination of the effect of oestradiol (E₂) and progesterone (P₄) on *RARRES2* gene expression and chemerin secretion (real-time PCR and ELISA) as well as expression of CMKLR1, GPR1 and CCRL2 genes and proteins (real-time PCR and Western blot) in the porcine endometrium during the above-mentioned periods of early pregnancy and in the mid-luteal phase of the oestrous cycle (days 10 to 11);
- 4. determination of the chemerin effect on the secretion of E_2 and P_4 (RIA) and the expression of steroidogenic factors/enzymes (StAR, P450_{SCC}, 3 β HSD, P450_{C17}, P450_{AROM}; Western blot) in the endometrium of pigs during the abovementioned periods of early pregnancy and in the mid-luteal phase of the oestrous cycle (days 10 to 11);
- determination of the chemerin effect on the phosphorylation of ERK1/2 and Akt signalling pathways (Western blot) in the porcine endometrium on days 10 to 11 of the oestrous cycle.

The results obtained during the implementation of this work allow to conclude that:

- the presence of the chemerin system in the porcine uterus, trophoblasts and conceptuses suggests that chemerin, also locally produced, may influence the regulation of uterine reproductive functions through its receptors;
- changes of the abundance of chemerin system transcripts and proteins in the porcine uterus and concentration of the hormone in ULF during the oestrous cycle and early pregnancy suggest that the expression of chemerin and its receptors is dependent on the hormonal status of animals;
- E₂ and P₄ have the effect on the chemerin system expression in the uterine endometrium during early pregnancy, which indicates that steroid hormones may be an important regulator of the chemerin and its receptors' expression in the uterus of domestic pig;
- 4. chemerin affects the secretion of E₂ and P₄ in the endometrium and regulates the expression of proteins involved in the formation of these two steroids, which is most likely mediated by ERK1/2 and Akt signalling pathways. It suggests that

chemerin may regulate reproductive processes by affecting the process of steroid ogenesis in the uterus of pig.

Chemerin by influencing the process of steroidogenesis in the endometrium may play an important role in the functioning of the female reproductive system during the oestrous cycle and the peri-implantation period. In addition, chemerin may be a factor maintaining a proper environment for developing embryos.

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