

The role of PAQR receptors in the regulation of the corpus luteum function in cow

The corpus luteum (CL) is a transient secretory organ that develops from granulosa cells and theca interna after the rupture of ovarian follicle in female mammals. The main hormone produced by the CL is progesterone (P4), which determines the proper course of the estrous cycle, blastocyst implantation, and maintenance and development of pregnancy in many mammalian species. The physiological effect of P4 on cells is mediated through its nuclear receptors (nPR) and via nongenomic way through membrane receptors (mPR), including PGRMC (progesterone membrane component) and PAQR (progestin and adipoQ receptors). While, the impact of P4 on the genomic pathway is fairly well understood, the role and the pathways of nongenomic action of this hormone in the functioning of the female reproductive tract remains poorly understood. Our previous studies confirmed the presence of PAQR receptor isoforms (7, 8, and 5) in luteal cells and endothelial cells of blood vessels in bovine CL. Our results indicate that the expression of these receptors in CL is varied and depends on the phase of the estrous cycle and pregnancy. The proper functioning of the CL depends on such processes as steroid hormone synthesis, tissue remodelling, formation of a network of blood vessels and apoptosis. It has been suggested that PAQR receptors may be involved in these processes, but there is no data on their role in ovarian function.

Based on the above a research hypothesis was formulated, which assumes that PAQRs participate in the regulation of bovine CL function through their (i) participation in the modulation of intracellular signals, (ii) influence on the expression of selected genes and proteins, and (iii) regulation of the processes of steroidogenesis, prostaglandin secretion, angiogenesis and apoptosis in luteal cells and the endothelium of blood vessels.

In this project proposal, we will plan to characterize the coexistence profile of different membrane progesterone receptors in the cow ovary. Next, we will determine the factors that can regulate the expression of these receptors in CL cells. We will perform functional analyses to determine the participation of PAQRs in steroidogenesis, prostaglandin secretion, angiogenesis and apoptosis processes in luteal and endothelial cells of the CL. Finally, we will verify the molecular mechanisms underlying the action of P4/PAQR in bovine CL cells by identifying genes, proteins and protein kinase pathways involved in this process.

The proposed studies are basic, however important for the understanding of female fertility disorders. We hope to collect new data on the participation of PAQR in the regulation of CL function, which may help to better understand of the mechanism of P4 effect on the regulation of the estrous cycle and protection of early pregnancy. Proper functioning of the CL is crucial for mammalian reproduction and disorders in CL activity might be a cause of improper endometrium development as well as problems with the embryo implantation and early miscarriages. Therefore, understanding the mechanisms regulating the function of this organ, at the level of cellular and subcellular regulation, may also have some practical significance in medical and veterinary practice. Moreover, understanding the relationship between the genomic and non-genomic effects of P4 in cells may facilitate the identification of molecular causes of some cases of female infertility.