C1. The abstract

The process of early pregnancy is the critical because at this time the highest mortality of embryos is observed. Interactions between conceptuses (embryos with associated membranes) and the inner mucous membrane (endometrium) covering the lumen of mammalian uterus are the complicated molecular dialogue involving various players such as: hormones, cytokines, transcription factors and growth factors. As the embryos are in 50% immunologically distinct for maternal system, the modulation of maternal response protecting from rejection of embryos is highly important. Progesterone called as "pregnancy hormone" is the main hormone responsible for making the uterine environment ready for embryos implantation. Progesterone is secreted by the corpora lutea (CL) – transient endocrine organs formed in ovulatory place in ovaries. However, the maintenance of corpus luteum action is dependent on "recognition" of conceptuses presence in the uterine lumen by maternal organism. Hence, the conceptuses must signalize their presence through embryonic signals secretion. In the pig, the main embryonic signals are estrogens, mainly estradiol-17β (E2). Porcine conceptuses secrete elevated amounts of estradiol-17β on days 11-12 and after day 15 of pregnancy. Enhanced synthesis and secretion of estradiol-17β on days 11-12 of pregnancy is defined as the maternal recognition of pregnancy. During this time, estradiol-17β of conceptus origin prevents corpora lutea against detrimental factors (such as prostaglandin F2α) leading to CL degradation that is unique among mammalian species as the capacity of embryos to estrogen synthesis and secretion was observed in bovine, ovine and equine however, pig is the only species in which secretion of progesterone and CL functioning is protected by estrogens of conceptus origin. The second period of elevated estradiol-17β synthesis and secretion after day 15 of pregnancy is concurrent with the onset of implantation process.

Estradiol-17β exerts its action through estrogen receptors localized inside the cells. Interestingly, the changes of estrogen receptors abundance in endometrium and conceptuses coincides with estrogen secretion by embryos. It should be emphasized that is the major and highly important embryonic signal as its impaired secretion leads to pregnancy loss. Too small number of embryos followed by insufficient amount of estrogens in uterine lumen leads to corpora lutea regression resulting in pregnancy termination. On the other hand, the timing of estrogen secretion is also critical for successful pregnancy establishment as excessive amount of estrogens before the time of maternal recognition of pregnancy may also result in pregnancy failure.

It has been reported that the presence of embryos may regulated the expression of factors involved in maternal recognition and implantation mechanisms. Particular factors important for pregnancy establishment and development that are regulated by estradiol-17β were also identified. However, the mechanisms of direct effect of estradiol-17β on global gene expression profile in the porcine endometrium has not been studied yet. Moreover, in this project we are going to determine whether the differential expression of selected genes in porcine endometrium is due to DNA methylation processes triggered by embryonic signal E2 that has not been studied in any species till now. Despite of described profile of estrogen receptors expression in the porcine conceptuses, a role of E2 in conceptus cells still remains unclear.

Regarding above facts, the aim of current project is to determine the changes in the global gene expression profile in the porcine endometrium evoked by estradiol-17β action and finding the answer whether this changes may be related to DNA methylation processes. To reach our goal we are going to use innovative *in vivo* model in which the estradiol-17β was administered locally into uterine lumen to mimic conceptus signaling. The next aim of proposed project is to determine the effect of estradiol-17β on the expression of embryonic genes involved in conceptus development and implantation as well as to determine the effect of E2 on proliferation and adhesion of conceptus cells. Our research will be conducted in the well-equipped and modern laboratories (laboratory of *in vitro* techniques, molecular biology laboratory) of the Institute of Animal Reproduction and Food Research of PAS in Olsztyn and in the top international research units collaborating with our Institute. As the embryonic signals are species-specific, the molecular processes triggered by their action are universal for most mammals. Therefore, the realization of our research will increase the knowledge in the field of biology of reproduction and will be helpful in reducing the embryonic mortality rate during such a critical steps as early pregnancy, implantation and fetus development.