The role of embryonic signal in epigenetic regulation of genes involved in corpus luteum function during early pregnancy in the pig

Reduced fertility in animals and humans are mainly related to problems with impaired communication between embryos and maternal organism. During early pregnancy in most mammals including pigs developing embryos signalize their presence in the maternal reproductive tract by secretion of specific factors (mainly hormones). In response, maternal organism triggers the cascade of physiological processes preventing the rejection of embryos and ensuring their implantation. This period is usually called as the maternal recognition of pregnancy. Corpus luteum is a transient endocrine gland which produces and secrets progesterone (P4) which is commonly called as "pregnancy hormone". Progesterone is responsible for preparing the uterine environment for establishment of pregnancy (implantation) and its proper development. The luteal phase is a period during which corpus luteum realizes its function (mainly P4 secretion). Porcine corpus luteum is unique among animals since it is the only source of P4 throughout entire pregnancy. In the case of the lack of fertilization, corpus luteum declines (undergoes luteal regression) in the process called luteolysis. During early pregnancy the activity of corpus luteum depends on the embryonic signals which determine its prolonged lifespan and maintain its secretory function. Embryonic signals prevents corpus luteum from factors inducing luteolysis. Estradiol-17β (E2) is the main embryonic signal in the pig. E2 prevents corpora lutea against luteolytic PGF2α by changing its endometrial secretion from the endocrine (into uterine venous drainage) to the exocrine (into uterine lumen) manner. Proper embryonic signaling is not the only requirement for successful pregnancy establishment and development. The corpus luteum function ensuring sustained secretion of progesterone is important for embryonic growth and developments as well as for its proper implantation. Thus the detailed knowledge about physiological mechanisms regulating secretory function of corpus luteum is essential in understanding the processes involved in early pregnancy establishment and development.

According to current knowledge, E2 directly stimulates progesterone secretion by corpus luteum in the pig. Interestingly, studies on mechanisms underlying tumorigenesis revealed that estrogens are involved in the epigenetic processes such us DNA methylation and histone modifications that lead to altered expression of genes. There are few studies concerning the role of DNA methylation in the control of expression of particular genes involved in processes such as oocyte maturation, steroids synthesis or corpus luteum formation. However, the role of E2 in epigenetic processes regulating the expression of genes involved in the corpus luteum function has not been widely studied yet. Therefore, in the present project **the role of porcine embryonic signal (estradiol-17β) in epigenetic processes such as DNA methylation regulating the expression of genes involved in corpus luteum function during early pregnancy will be determined**. Basing on literature data and on results from our preliminary data **we hypothesize** that **estradiol-17β after reaching corpora lutea induces DNA methylation that leads to altered expression of genes involved in corpus luteum function**.

The main outcome of present project is presentation of novel role for porcine embryonic signal in mechanisms ensuring pregnancy establishment and development. Verification of project hypothesis will give the answer to the question whether and how the embryos by secreting its signal (estradiol-17β) can regulate the dynamic of epigenetic processes occurring in corpus luteum? Confirmation of hypothesis surely would improve the knowledge about mechanisms ensuring pregnancy establishment that will significantly increase the development of science in the field of reproductive biology. Moreover, results obtained in the proposed project may be used in application studies on assisted reproductive techniques improvement.