The major function of the female gonads is biosynthesis of steroid hormones as well as the release of the mature egg cell (oocyte) for fertilization which is essential for successful propagation of the species. The functional unit within mammalian ovaries is the ovarian follicle which contains a single oocyte that is surrounded by granulosa and theca cells. When ovarian follicles firstly occurs, which takes place during prenatal or neonatal period, they are formed as primordial follicles. The pool of primordial follicles in the ovary or "ovarian reserve" is a major factor in the fertility potential, because it represents the total population of oocytes during female reproductive lifetime. Folliculogenesis is the process in which a recruited primordial follicle grows and develops into a preovulatory stage with the potential to either ovulate its egg to be fertilized or to die by atresia. The mechanisms regulating follicle recruitment, growth and development are under the control of hormones and locally produced growth factors, which are themselves products of the follicle. After ovulation, the remaining follicle cells transform into a temporary endocrine organ, corpus luteum, that synthesizes and secretes steroids, mainly progesterone, needed to prepare the endometrium of the uterus for implantation. Considerable attention has recently been focused on endocrine active chemicals (EACs) that disrupt the reproductive system by altering steroid receptors function. EACs which arise from many different sources (pesticides, industrial chemicals, pharmaceuticals and phytochemicals) may interfere with the natural regulation of endocrine systems by either mimicking or blocking the function of natural hormones. It is well known that hormones in the body work in exquisitely fine balance. So the balance between androgens and estrogens within the ovary may be important during neonatal period. Moreover, many female reproductive disorders observed during adulthood originate from the neonatal period which is a critical stage towards the reproductive potency. Therefore it seems that exposure to androgen and estrogen excess or deficiency during neonatal period can affect gonad formation and disrupt reproductive functions during adulthood. Consequently, it is important to study the effects of neonatal exposure to chemicals that antagonize or mimic the function of androgens and estrogens to establish their role in ovarian follicle development and corpus luteum function. Indeed, our previous research showing that diminished androgen action during neonatal period in pigs affects the ovarian function in adult life. Thus, the aim of our project is to provide new information of androgen and estrogen excess or deficiency during neonatal period, experimentally induced by exposure to chosen EACs, on intraovarian factors involved in regulation of follicular development as well as corpus luteum function. The latter will entail the attention of steroid production within the corpus luteum and changes in epigenetic control of luteal gene expression. Epigenetics has been a hot topic for research over the past decade. Epigenetic control of gene expression results in switching on and switching off of genes. It is known that epigenetic modifications are dynamic and susceptible to environmental influences, including EACs. This phenomena is achieved by DNA methylation, histone modification and microRNAs (miRNAs). DNA methylation correlates with suppression of gene expression and is established and modified in response to environmental factors by three DNA methyltransferases (DNMTs), DNMT1, DNMT3a and DNMT3b, which all will be examined in our project. The second epigenetic modifiers are miRNAs molecules. The identification of miRNA as major posttranscriptional gene regulators has led to an explosion in our knowledge of the role of miRNAs in organ function. MiRNAs comprise a large family of ~22 nucleotides long non-coding RNAs. They are expressed in a tissue-specific or developmental stage-specific manner, thereby greatly contributing to cell-type-specific profiles of protein expression. MiRNAs form a base pairs with target messenger RNAs in their special region, known as 3' untranslated region (3'UTR) and cause translational suppression and reduction of target protein expression. To fulfill the objectives of the planned project, specific tasks and methods of molecular biology will be introduced, including next-generation sequencing (NGS). Sets of experiments are planned to study in adult pigs the effect of neonatal exposure to examined EACs on (1) ovarian morphology, (2) plasma concentration of hormones, including AMH, (3) expression of FSHR, intraovarian factors and their receptors that are important in follicular development regulation, (4) corpus luteum function and (5) changes in DNMTs expression and miRNA profile in luteal cells. Understanding the long-term or irreversible effect of steroids excess or deficiency during neonatal period on the function of adult ovaries will provide a basic data for further research of the female reproductive potency and may put more light on ovarian physiology following developmental exposure to endocrine disruptors. Certainly the pig has been a valuable biomedical model organism for molecular biomedical research due to the fact that its anatomy, genetics and physiology reflect human biology more closely than the classic animal models.