

The ovaries fulfill to main functions in the organism of a female. They are the source of steroid hormones (progestagens, androgens and estrogens) and gametes (oocytes). As indicated by epidemiological studies ovarian tumors after the breast cancer are the most frequent neoplasms occurring in women. They are usually malignant with symptoms appearing late what in many cases impedes effective treatment. Taken into account various cellular origin of ovarian tumors studies on the subject which ovarian cells play a role in oncogenesis of this organ are of utmost importance.

Given the increasing pollution of the environment it is increasingly recognized that Endocrine Disrupting Compounds (EDCs) can be one of the factors having deleterious effects on processes occurring in the ovary. EDCs can derive from various sources e.g. agriculture, chemical and pharmaceutical industry. They have the ability to interfere with steroid hormone receptors and thus mimic or inhibit the action of endogenous hormones. Therefore continuous exposition to even small concentration of such compounds can lead to the development of tumors. In light of these observations it seems important to establish if and in what way compounds that block or mimic action of endogenous steroids influence initiation of oncogenesis and its course within the ovary.

In the last years it would be hard to find more hot topic in biological sciences than stem cells (SCs) being both the greatest hope of contemporary medicine and the source of ethical dilemmas. They stand out from other cells by their unrestricted ability to divide and differentiate. In other words SCs are immortal – self-renovable, having just amazing ability to differentiate in an appropriate microenvironment into other cells of the organism. For better understanding of SCs nature, according to their ability to differentiate they have been divided into: *pluripotent* – giving rise to cells that can derive from all three germ layers; *multipotent* - giving rise to cells that can derive from one germ layer; *unipotent* - regenerating cells of only one kind; while according to their origin on: *embryonic* – from early embryos expressing pluripotent character (**ESCs**) and *fetal* – from cord blood and fetal tissues expressing multipotent character (**FSCs**). The real breakthrough in regenerative medicine was the discovery of the presence of mature adult stem cells (ASCs) in tissues of mature organisms. ASCs have been found inter alia in the bone marrow, peripheral blood, cornea, liver, skin and gut. The knowledge of ASCs isolation, selection and culture methods can be of great importance in therapy of degenerative diseases, artificial organs production or organ reconstruction after accidents. In the last years using among other methods studies on the expression of c-Kit receptor in the ovary a population of putative stem cells (PSCs) has been identified. This is a heterogeneous population consisting of many types of small, round cells with 5 – 7 µm in diameter. It is supposed that among PSCs there are ASCs, that are responsible for regeneration of tissues of mature organisms. There is also a hypothesis assuming that ASCs, as a result of accumulation of mutations in them, can be involved in the formation of cancer stem cells (**CSCs**). Consequently elucidation of the transformation mechanism of ASCs into CSCs seems to be especially important for the understanding of such processes as initiation and further development of a tumor.

Our previous studies with specific markers confirmed that in the ovaries of mature pigs cells that can be multi- and pluripotential stem cells are present. Based on these results, the aim of this grant proposal is to determine ovarian adult stem cells potential to differentiate, also towards CSCs. The specific aim would be to determine if and in what way selected compounds belonging to EDCs mimicking or blocking androgen action (anabolic steroids: nandrolone, boldione), are involved in directional (CSCs) differentiation of ovarian cells. Selective identification of CSCs, analysis of their proliferation rate, and also programmed cell death pathways (apoptosis and autophagy) will allow to follow the process of adult and cancer stem cells transformation into endothelial cells and study the mechanism of this phenomenon. This is important because differentiation into the endothelium is of importance in the formation of new blood vessel supplying the tumor (tumor angiogenesis). Studies carried out in recent years indicate that the pig due to its special similarity to the human in terms of both anatomy of internal organs and the course of physiological processes is the most suitable animal model used in biomedical studies. Therefore in the proposed grant the source of stem cells will be ovaries of pigs obtained from the abattoir. Results obtained thanks to the carried out experiments and standardization of ovarian stem cells isolation, selection and in vitro culture methods will allow to follow signaling pathways stimulating such cells to migration, mobilization and differentiation. Elucidation and understanding of mechanisms of action of selected compounds showing endocrine activity in the porcine ovary will complement and enrich the present state of knowledge concerning reproductive potential of a female which seems important in view of reports indicating increasing exposition to such substances present in the environment.