Endometriosis is a gynecological disease. It describes the condition, where endometrial tissue (from uterus wall) is growing where it shouldn’t, often peritoneum as well as on the surface of the ovaries, uterus, bladder or intestines. It can also occur in distant places from the uterus, eg in the umbilicus, pleura, nasal sinuses or brain. Understanding the causes of endometriosis and the processes responsible for the various stages of its development has been the subject of many studies. Hypotheses related to the genesis of this disease are based on different sources of its occurrence. The most popular theory presupposes the formation of an ectopic endometrium by the autografting of properly localized endometrial mucosa (eutopic endometrium), which also contains stem-like endometrial cells. They have many features in common with mesenchymal stem cells (MSCs) residing in different tissues. Other hypotheses are based on the possibility of mesothelial cell transformation under the influence of hormones such as estrogens, the existence of residues from Müller's ducts or the participation of stem cells in the formation of the ectopic localized endometrium.

An important role in the formation of endometriosis is attributed to existing immune conditions, which are responsible for the removal of the resulting ectopic endometrium. It is also indicated changes in the hormonal microenvironment, which can modify the ectopic cells in the endometrium. As a result, these disorders create the possibility of developing endometriosis under conditions of hypoxia, which hinders its physiological as well as pharmacological elimination.

Both processes, immune response and hypoxia are closely related and can participate in the selection of pathological stem cells that are responsible for the initiation, progression and development of endometriosis. Therefore, activities targeting stem-like endometrial cells are a promising strategy for the treatment of endometriosis, which until now is considered the most common cause of female infertility. During the development of endometriosis, angiogenesis is the main reaction to hypoxia. This is a typical example of common features of endometriosis and carcinogenesis.

The aim of the project is to explain the mechanisms leading to endometriosis, in particular related to the microenvironment of the endometriosis foci responsible for the individual stages of its formation and progress.

Research will be conducted using animal model of endometriosis in mice. Research tasks leading to the project's objective will include active intervention in pathogenic processes through appropriate modulation of the immune response and through normalization of hypoxia in surgically induced endometriosis combined with immunomodulation using specially constructed genetic vaccines. As immunomodulators, we plan to construct cell-based established immortal lines of innovative genetic vaccines directed against epitopes of endometriotic cells, especially pathological stem cells. Cells of endometriosis, ovarian cancer or endometrial cancer will be modified with genes encoding immune system stimulants (so-called molecular adjuvants) and induced pluripotent stem cell (iPSC), formed from allogeneic fibroblasts. In addition, we are planning to further characterize the microenvironment of endometriosis by inducing normalization of hypoxia with myo-inositol tris pyrophosphate (ITPP), which acts as a allosteric effector of hemoglobin. It allows the release of oxygen from hemoglobin to the inside of tumors or endometrial changes. Cancers can inhibit this process, which leads to hypoxia and the automatic inclusion of tumor defense mechanisms or endometriosis before elimination. Increasing the pO_2 level will activate factors that inhibit angiogenesis and, as a result, significantly improve the treatment outcomes of the so often diagnosed young women's disorder.