

In every organism cell division process is controlled by genes and by other cells of the body. When an organism loses control over this process, the cells begin to divide uncontrollably, which lead to the cancer development. Ovarian cancer is the leading cause of death among gynecological malignancies. According to the epidemiological data from 2016, 3717 women were diagnosed with ovarian cancer in Poland, and 2639 women died. There are two main reasons for high mortality among ovarian cancer patients. First, the initial phase of ovarian cancer development may be asymptomatic, making its detection difficult. In most cases, ovarian cancer is diagnosed when the disease is very advanced, with many metastases, which significantly reduces the effectiveness of treatment. Another reason for the high mortality rate is the low effectiveness of the treatment. The standard treatment for ovarian cancer involves surgical removal of the tumor, followed by chemotherapy to kill cancer cells that could not be removed during surgery.

Chemotherapy involves the administration of drugs, which should lead to cancer cells death by blocking a wide variety of processes. Unfortunately, cancer cells can defend themselves in various ways successfully and limit the effectiveness of chemotherapy. Additionally, metastases are usually more resistant to treatment than the primary tumor.

Many proteins involved in the process of metastasis and resistance have been described over the years, but new ones are still being described. Such proteins include SEMA3A, PCDH9, and S100A3. The change in expression of these proteins is associated with the progression of ovarian cancer and, as our research shows, also with the development of resistance to chemotherapy.

The aim of the project is to determine the exact role of SEMA3A, PCDH9, and S100A3 protein in the biology of ovarian cancer.

The first stage of the study will be performed on primary tumors and metastasis of ovarian cancer to determine the role of investigated proteins in ovarian cancer progression.

Next, the expression will be investigated in the drug-sensitive and resistant cell line to determine the role in chemotherapy resistance.

Functional studies will be performed to understand better the role of the studied proteins in both the progression and resistance of ovarian cancer. For this purpose, changes in the expression of the studied genes will be artificially carried out in ovarian cancer cells, which will demonstrate their role in the development of resistance to cytotoxic drugs and tumor progression. These studies will also allow us determine the mechanism of action of this protein in the studied process. As the test conditions of the cultured cells differ from those prevailing in the body, the final verification of the role of SEMA3A, PCDH9, and S100A3 proteins will be carried out in an *in vivo* model that much more resembles the conditions prevailing in the patient's body. Two research models will be applied: the xenograft chick embryo chorioallantoic membrane model (CAM) and in mice xenograft model.

This project covers the area of knowledge designated as medical biology. It involves the application of biology as basic science to explain the phenomena occurring in the human body during illness - which are of interest for practical science - medicine. The project will apply knowledge from various fields of biology, such as molecular biology - the study of life processes at the molecular level, cell biology - to demonstrate the presence of tested molecules in the cellular structures and histology - the study of the structure and function at the tissue level.

The application of basic scientific knowledge to explain the medical phenomenon - limited effectiveness of treatment in ovarian cancer - will deepen our knowledge about the causes of this phenomenon, which may lead to the introduction of new therapeutics and increase the effectiveness of treatment in the future.