Ovarian cancer is the leading cause of death among gynecological cancers. In 2020, 4 669 Polish women were diagnosed with ovarian cancer, and 3 131 patients died from this disease. 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 at an advanced stage, with many metastases, which significantly reduces the effectiveness of treatment. Another reason for the high mortality rate is the low response to standard treatment. Surgery is still the main treatment option for primary ovarian tumors. After surgery, chemotherapy treatment is recommended to eradicate cancer cells that could still be present in the tumor niche to minimize the possibility of relapse.

Chemotherapy involves administering drugs, which should lead to cancer cells death by blocking a wide variety of processes. Unfortunately, cancer is a complex structure intricately controlled by several signaling pathways. Thus, cancer cells can become resistant to drugs by the different possible mechanisms. Furthermore, tumor heterogeneity, particularly the presence of cancer stem cells (CSC), plays a crucial role in the development of drug resistance. Recently studies showed that the Sonic Hedgehog (Shh) pathway, one of the well-known CSC-specific pathways, is involved in low response to chemotherapy. This pathway can be stimulated in a canonical and non-canonical way by a protein called Osteopontin.

The project aims to inhibit canonical and alternative activation of the Shh pathway to reduce the expression of resistance genes/proteins and increase the effectiveness of chemotherapy.

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. Further studies will determine whether the most important player in the Shh pathway is responsible for cancer cells resistance to therapy.

Functional studies will be performed to shed new light on the role of the Shh pathway 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, demonstrating their role in developing resistance to cytotoxic drugs and tumor progression. These studies will also allow us to determine the mechanism of action of this protein in the studied process. Finally, the role of the Shh pathway will be investigated using *in vivo* models that much more resemble the conditions prevailing in the patient's body. Two research models will be applied: the xenograft chick embryo chorioallantoic membrane model (CAM) and the mice xenograft model. In both models, human ovarian cancer cells will be used.

The presented project will help better understand the molecular mechanisms that regulate the Shh pathway, and scientists can use this knowledge to develop a more effective therapeutic approach. Thus, proposed research can expand our understanding of the Shh signaling pathway in ovarian cancer cells. This information can lead to identifying new targets for cancer treatment and improving response to currently used therapy.