Endometrial cancer is one of the most common cancers of the female reproductive organs and the fourth most common cancer in women. It occurs most often in the perimenopausal age. The two most commonly used classifications of endometrial cancer advancement differentiate endometrial cancer tumors basing on the depth of invasion into healthy tissues and the presence of tumor metastases. Treatment of endometrial cancer patients depends on the stage of cancer at diagnosis. Endometrial cancer risk factors include diabetes, obesity, physical inactivity, and low fertility. Early menstruation and late-onset menopause, menstrual disorders, childlessness, and the use of estrogen hormone replacement therapy also increase the risk of the disease. In recent years, the incidence of endometrial cancer has increased and the disease appears earlier, therefore endometrial cancer treatment is a significant clinical problem. Endometrial cancer is divided into two main types which differ in histological structure, pathogenesis, frequency, and prognosis. Type I is responsible for most cases of endometrial cancer. It is glandular cancer and is induced by estrogen, the female sex hormone. In contrast to that, type II is rarer and more malignant.

MicroRNAs are short, single-stranded, non-coding RNA molecules that regulate the expression of many genes, thus influencing the level of various proteins in the cell. In this way, they regulate many hallmarks of neoplastic cells, including cell division, invasion to surrounding tissues, and their metastasis. MicroRNAs can stimulate the tumor or inhibit its growth. Numerous scientific papers describe the role of microRNAs in the development of neoplasms, including endometrial cancer. MicroRNA molecules are frequently studied as potential tumor biomarkers because they are stable and can be detected in various body fluids, e.g. blood. Estrogen induces the proliferation of healthy endometrium, but its action is opposed by progesterone. In endometrial cancer, this balance is destabilized and estrogen signaling is a key pathway regulating endometrial cancer development and progression Nevertheless, the molecular basis for the effects of estrogen in endometrial cancer remains poorly understood. The reports on the influence of estrogen on the biogenesis of microRNA molecules mainly concern the breast cancer model.

Our study aims to investigate the effects of estrogen on microRNAs in endometrial cancer. For this purpose, we plan to identify microRNAs whose expression is increased by estrogen and assess their level in both types of endometrial cancer tissues and healthy endometrium, and then investigate the impact of selected microRNAs in endometrial cancer cells and describe their mechanism of action.

In the first step of the study, microRNAs that are induced by estradiol will be identified. Subsequently, the expression of the selected microRNAs will be assessed in endometrial cancer tissues and healthy endometrium by real-time quantitative PCR. For this purpose, the technique of laser microdissection will be used, which allows the excision of the selected tissue fragments and then the analysis of this material without disturbances resulting from the presence of the surrounding tissue.

Selected three microRNAs, which are induced by estradiol in endometrial cancer cell lines and whose expression differs between endometrial cancer type I and type II and between endometrial cancer type I and healthy tissue will be tested in functional tests in model endometrial cancer cell lines to determine the influence of microRNAs on various tumor hallmarks, including cell division, migration, and invasion to surrounding tissues. In the last stage of the research, we will try to answer the question about the mechanism of microRNAs' action. For this purpose, activation of key signaling pathways will be assessed in endometrial cancer cells after microRNA transfection using methods of quantitative real-time PCR and western blot that allows assessing the amount of proteins.

We believe that our research will help us better understand the pathogenesis of endometrial cancer. Project outcomes could serve as a basis for further research into the role of microRNAs as endometrial cancer biomarkers, both as markers of disease and its prognostic factors.