Ovarian cancer is a heterogeneous disease encompassing different histological types with distinct clinicopathological and molecular features. The most common type, characterized by the worst prognosis, is high grade serous ovarian cancer. Lack of efficient screening methods and high non-specificity of early symptoms lead to detection of the disease at advanced stage in the majority of patients. This directly translates into low 5-year survival rate (below 50%). Therefore, novel diagnostic, predictive and prognostic biomarkers in ovarian cancer are actively searched. It is worth mentioning that molecular intra-tumor heterogeneity is one of the factors responsible for a limited effectiveness of the therapy. The aim of the project is to characterize the heterogeneity of ovarian cancer and to construct a model of aberrant molecular pathways using the modern methods of systems biology: transcriptomics and metabolomics. The former 'omics' technique deals with the gene expression studies, while the latter one – with the analysis of the low-molecular weight products of metabolism (such as: carbohydrates, amino acids, fatty acids, nucleotides, vitamins, antioxidants, etc.)

The studied group will consist of the patients operated due to ovarian cancer, benign tumors and borderline tumors. The control group will be constituted by the patients qualified for surgical ovary removal due to non-malignant indications. The blood serum collected before and after the surgery, the tumor tissue samples (excised from 4-5 locations within the tumor) and the normal ovary samples (in the control group) will be studied in the project using *Nuclear Magnetic Resonance* (NMR) spectroscopy. The tissue specimens (after the NMR analysis) will be evaluated histopathologically to correlate the molecular heterogeneity with the histopathological one. Because abdominal dropsy is often one of the first symptoms of ovarian cancer, the ascites samples will also be collected. The differences in gene expression between different histological types of ovarian cancer and between cancer and stromal compartments within the tumor will be analyzed with use of spatial transcriptomics [*Visium Spatial Gene Expression (10x Genomics)*].

The multivariate analysis of the data is expected to evaluate:

- a correlation between the metabolic profiles of cancer tissue, serum and ascites and the clinic-pathological parameters;
- the differences in the metabolic profiles of the serum and tissue samples between the patients with ovarian cancer, benign tumors and borderline tumors, and the control group;
- a correlation between the metabolic profiles of tissue, ascites and serum in the patients with ovarian cancer;
- the differences in the metabolic profiles of serum collected before and after surgical removal of ovarian cancer;
- an intra-tumor metabolic heterogeneity in ovarian cancer, including an analysis of the relation between the tissue content (cancer cells, stroma, necrosis, etc.) and the metabolic profile;
- an inter-tumor metabolic heterogeneity, including an analysis of the differences between the distinct histological types of ovarian cancer;
- the intra-tumor and inter-tumor heterogeneities in the transcriptomic profiles of ovarian cancer.

The interpretation of the results obtained from the mentioned analyses of the serum, tissue and ascites samples will be facilitated by the metabolomic and transcriptomic studies of seven ovarian cancer cell lines (serous and non-serous) and 3 fibroblast (stromal) cell lines cultured *in vitro*.

The identified metabolomic and transcriptomic changes may serve as potential diagnostic and prognostic biomarkers useful in characterization of the patients status and in therapy personalization.