**Ovarian cancer is the one of the most lethal gynecological malignacies. Its high mortality rate is a result of the lack of screening methods and specific symptoms of the disease, which is related to the extremely heterogeneity of ovarian cancer, including genomic, transcriptomic, proteomic, and, the very least known, immunologic aspects.**

Currently, we acknowledge that the immune system plays a dual role in cancer. It can not only suppress tumor growth by eliminating cancer cells or inhibiting their outgrowth but also promote tumor progression either by selecting tumor cells that are more fit to survive in an immunocompetent host or by establishing conditions within the tumor microenvironment that facilitate tumor outgrowth. Cancer development and progression is highly dependent on the specific tumor microenvironment, which is crucial in prognosis and influences treatment efficiency. However, the development of effective anti-cancer therapies has been challenged by the overall complexity of tumors, particularly in ovarian cancer. **Understanding how the composition of the tumor microenvironment changes during cancer development and progression is a prerequisite for projecting therapeutic strategies able to tackle the tumor at a specific evolutionary stage which is important for selection of the most suitable therapy.**

The mechanisms of ovarian cancer cells escape from immune surveillance, tissue invasion, and metastasis remain unexplained. The latest advances in the field of tumor immunology and immunotherapy emphasize that ovarian cancer cells can evade hosts immune response and stimulate tumor development by deactivation or death of crucial immune system effector cells, i.e. T-cells and NK cells. One of the negative regulators of activated T cells is programmed cell death receptor 1 (PD-1) and its ligands (PD-L1, PD-L2). However, T-cells and NK cells frequently express multiple co-inhibitors. The analogous role to PD-1/PD-L1/PD-L2 pathway in evade antitumor immune response plays T cell immunoglobulin and ITIM domain (TIGIT) and T cell immunoglobulin-3 (TIM-3) and its ligand galectin 9 (Gal-9) axis. The reversal of immunosuppressive tumor microenvironments of ovarian cancer and sensitization of these tumors to immunotherapeutics can be a strategy in the ovarian cancer treatment. However, many factors affecting this effectiveness are unknown and the data concerning the co-expression of these immune checkpoints in ovarian cancer is scant. Similarly, the data concerning the regulation of expression of above mentioned immune checkpoints by microRNAs and cytokines is limited.

Moreover, the clinical outcomes of OC patients depend on many factors including the International Federation of Gynecology and Obstetrics (FIGO) stage, differentiation grade and histological type of the tumor. Thus, the search for immunological triggers in patients with different clinical manifestations of the disease concerning the treatment results obtained seems to be relevant. The co-expression status of immune checkpoint molecules on T cells in the OC TMEs is pivotal to understand the complex immune inhibitory mechanism in OC patients.

**Thus, I hypothesize that the strong immunosupression found in ovarian cancer is the result of immune factors, such as TIGIT, TIM-3/Gal-9, and PD-1/PD-L1/PD-L2, secreted by immune/cancer cells, and regulated by microRNAs and cytokines. The synergistic model of action of these immune factors may be a promising target in ovarian cancer treatment.**

Therefore, the main objective of the proposed project is to conduct multiparametric analyses of immune system cells co-expressing immune checkpoints, i.e. immune factors of PD-1/PD-L1/PD-L2, TIGIT/DNAM-1/CD155, and TIM-3/Gal-9 axis, their soluble forms, and regulate them proper cytokines (IL-2, IL-4, IL-6, IL-10, IL-17A, TNF-α, IFN-γ) and microRNAs (miR-21, miR-34a, miR-424, miR-513, miR-570) in ovarian cancer patients' peripheral blood and tumor microenvironments, i.e. peripheral blood and tumor, and then correlate the results to patients' data in comparison to benign tumors (peripheral blood and tumor) and healthy blood donors (peripheral blood).

**The results of this project might help (immuno)oncologists for patient stratification based on PD-1/PD-L1 pathway inhibitors. They may also help to select a prognostic and/or diagnostic biomarker for use in the liquid biopsy to differentiate between malignancy and benign tumors.**