OPUS Project:

Deciphering progression of triple negative breast cancer – analysis of tumor-associated cells in the bloodstream using single cell sequencing and methods of artificial intelligence

Modern oncology is shaped by two main challenges: early detection of cancers and offering patients personalized, tailored dynamic care. To find solutions, hundreds of academic labs and biotech firms are turning to artificial intelligence, working to develop machine-learning algorithms that could help decipher weak signals in the blood, identifying cancers when they are small or indicating patients' response to treatment in real time.

So far, machine-learning algorithms designed to detect minute quantities of tumor DNA and RNA in a blood sample – the goal of so-called liquid biopsies – have performed well in clinical validation studies, but no self-learning algorithm has yet been approved for clinical use. Nevertheless, liquid biopsies have the potential to outperform imaging and tissue biopsies in detecting and monitoring cancers by looking for changes in DNA, RNA, and proteins directly in the blood.

It is planned to explore the subject of liquid biopsies in the aspect of Circulating Tumor Cells and tumor-associated cells such as neutrophils and Tumor Educated Platelets, present in the bloodstream of breast cancer patients. Most sensitive and innovative molecular techniques will be applied to analyze cells' RNA at a single cell resolution, with the use of machine learning. Such approach will unravel the underlying biology of blood cells interactions in triple-negative breast cancer (TNBC) which accounts for 15-20% of cases and is characterized by aggressive course, high recurrence rates and poorest long-term survival out of all breast cancer subtypes.

The main aim of the project is to elucidate single-cell level heterogeneity and changes within peripheral blood of TNBC patients undergoing systemic treatment. Obtained knowledge will possibly identify molecular profiles critical for TNBC progression and response to treatment. This is important as TNBC has very limited options of targeted therapy, and chemotherapy remains a mainstay of systemic treatment. There are still no reliable biomarkers allowing to predict and monitor efficiently the patient's response to treatment and TNBC's high heterogeneity only obstructs therapeutic success. A better evaluation system for TNBC is urgently required. Hence, the hypothesis of this project is that single-cell RNA sequencing and profiling of liquid biopsies collected from TNBC patients could predict response to neoadjuvant treatment, indicating which patients demonstrate complete response and benefit from therapy. The main aim of the project is to elucidate single-cell level heterogeneity and changes within peripheral blood of TNBC patients undergoing systemic treatment. The following objectives will be met to achieve this aim: 1) single-cell analysis of CTC and neutrophil-enriched blood fraction; 2) Tumor Educated Platelets profiling; 3) transcriptome analysis of cancer cell-platelet in vitro co-cultures treated with chemotherapeutic agents.

The project will be realized at the Laboratory of Translational Oncology (Medical University of Gdańsk), in close collaboration with Department of Clinical Science (University of Bergen, Norway) and Centre for BioSystems Science and Engineering (Indian Institute of Science, Bangalore, India). Knowledge transfer as well as sharing experiences and best practices will be strengthened by the support of Breast Cancer Unit (Medical University of Gdańsk) and VU University Medical Center (Cancer Center Amsterdam, Netherlands).