Obesity is an increasing problem in well-developed regions of world. In obesity, an excessive adipose tissue accumulation dysregulate the physiological processes in the body. Accumulated fat cells – adipocytes, together with their progenitors - adipose stromal cells (ASCs) influence the surrounding cell populations by releasing of a plethora of molecules called adipokines. This, in turn, is an important risk factor not only for the development of cardiovascular diseases, but also influences the development of cancer, in particular colorectal cancers (CRC).

Tumor development is a long process, consisting of several stages: initiation, promotion and progression. Metastasis begins from invasion of tumor cells into closer and more distant tissues and organs. During metastasis, in particular colonization of distant organs, an important role play cells from tumor microenvironment and molecules secreted by them. Therefore, the targets of modern anti-cancer therapies are not only cancer cells but also cells from tumor niche, like fibroblasts, keratinocytes, immune cells or adipocytes, which may facilitate the cancer spreading.

Despite the fact, that the last years of research gives a new ideas and tools for better diagnosis and patient's treatment, in Poland CRC is still the second reason of mortality in patients suffering from malignant tumors. The molecular mechanisms that provide cancer cells with metastatic properties in patients affected by obesity remain unexplored. It means, that studies about colorectal cancer biology, which could help to find a new, more effective diagnostic and therapeutic targets are still valid and necessary.

Therefore, the objective of this project is to study the involvement of adipocyte and their progenitors' secretome on CRC progression. We would like to investigate if excess of molecules secreted by adipogenic niche should be taken into account as the therapeutic target in obese patients during treatment of CRC.

In the first stage of the study, we will use a unique direct co-culture system to simulate *in vitro* the cellular environment in the body, where different cell types are grown together in one culture dish. In this settings we will evaluate the effect of co-culture of ASCs or adipocytes on behavior (proliferation, migration, invasion) of primary and metastatic CRC cells. Next we will concentrate on the characterization of the modifications in the secretion level of different adipokines present in adipogenic niche cells induced by CRC cells. We will determine role of identified molecules in regulation of colorectal cancer progression. In the last part, we will conduct an analysis using samples collected from patients with CRC. These studies will verify our current observations obtained using cell lines and allow us to predict whether the level of expression of selected adipokines can serve as a diagnostic marker or therapeutic target as well as a prognostic factor in patients with colorectal cancer.

The proposed project aims to expand the knowledge about the biology of CRC and the contribution of adipogenic niche cells to its formation, what is especially important nowadays, when obesity is a rapidly growing problem. Understanding of these mechanisms could be a significant step in the development of diagnostic methods, creation of new therapeutic strategies and the prevention of this cancer.