

Colorectal cancer is one of the most common type of cancer in Poland, in Europe and in US. There is huge problem with diagnosis of this disease, since colorectal cancer can be asymptomatic, and often it is diagnosed accidentally during screening tests – colonoscopy or sigmoidoscopy.

The carcinogenesis is associated with rapid proliferation of cancer cells, that result in significant changes in their metabolism, mainly amino acid, nucleic acid, carbohydrates and lipid metabolism. In the 20's of XX century Otto Warburg discovered elevated rate of anaerobic glycolysis in cancer cells. In these conditions glucose is transformed into pyruvate and further into acetyl-CoA that is a substrate for fatty acid and cholesterol synthesis. Fatty acids are a component of phospholipids. Phospholipids and cholesterol are a main component of cell membranes, and when cancer cells rapidly proliferate they need a great amounts of this lipids. The increased expression of genes of enzymes of fatty acid and cholesterol synthesis has been reported in various cancers. However other researchers suggested that increased synthesis of fatty acids in cancer cells may supply endogenous lipids used as an energy source.

Lipids are very heterogeneous group, but fatty acids are the main component of majority of them. Fatty acid could be present in blood and tissues in their free form or be a part of complex lipids. Lipids are a structural elements of every cell, they play a key role in cellular energy homeostasis, are store of energy in organism, they regulate many biochemical processes, are electric isolators, are antigens recognized by specific antibodies and could be used as medication. The beneficial properties of omega-3 and -6 fatty acids as well as unfavorable effects of diet rich in saturated fatty acids is well known. Fatty acids have a biological activity and they influence the metabolism of various cells, tissues and organs. Since the development of colorectal cancer is associated with deregulation of lipid metabolism, lipids may turn out to be the potential prognostic and diagnostic markers of this disease.

The aim of this project is to examine if colorectal cancer is associated with changes in lipid (fatty acid, phospholipid, triacylglycerols and cholesterol) composition in cancer tissue and to evaluate if the stage of colorectal cancer development is associated with lipid composition. Fatty acid composition will be also studied in patients serum and compared to serum of healthy subjects. Another objective of the project is to evaluate the anti-proliferative properties of inhibitors of lipid synthesis, selected based on the knowledge of changes of lipid composition in colorectal cancer tissue.

The published data concerns mainly on the overexpression of lipogenic enzymes in cancer tissue, but there is lack of lipidomic studies (detailed analysis of various groups of lipids) in colorectal cancer tissue – this will be evaluated during realization of this project. To discover the molecular mechanism of formation of lipid composition in cancer tissue the expression of genes of synthesis of fatty acids, cholesterol, phospholipids and triacylglycerols will be studied. Our Pilot study revealed significant changes of fatty acid composition in cancer tissue of colorectal cancer patients. Inter alia cancer tissue contains much higher levels of very long chain (containing 22-26 carbons) fatty acids than normal colon tissue of the same patients. Moreover we found elevated level of cerotic acid (26:0) in serum of patients with colorectal cancer. Confirmation of this result in greater group of patients would suggest that cerotic acid would be novel, non-invasive, lipid marker of colorectal cancer. In sum, the realization of the project will reveal if changes of lipid composition are associated with colorectal cancer progression, will allow to discover the biochemical basis of these changes, and to verify if it is possible to inhibit colorectal cancer proliferation by influencing lipid metabolism.