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Metagenomics- and metabolomics-based microbiome profiles to identify distal gut dysbiosis correlating with cancer therapeutic outcomes

Cancer is one of the leading causes of morbidity and mortality in Poland and western counties. One of the factors associated with the development of gastrointestinal cancers, including colorectal cancer (CRC), is the disbalance in composition of non-pathogenic bacteria colonizing the intestine, called dysbiosis. Intestinal bacteria may also be responsible for the effectiveness of anti-cancer therapies, namely the chemotherapy and the more and more commonly used immunotherapy, which can reactivate the immune system of a patient to fight cancer. In the case of chemotherapeutics the intestinal bacteria may change the metabolism of the drug through the generation of its toxic or non-toxic derivatives in the intestines, and in the case of immunotherapeutics the bacteria may modulate the antitumor efficacy of the drug by affecting the activity of the patient's immune system. In both cases, the composition of intestinal bacteria may determine the success of therapy.

The aim of this project is to link the bacterial composition and metabolites in stool samples with the effectiveness of anticancer treatment and the severity of side effects of chemo- or immunotherapy in studies conducted on cancer patients and in the experimental model of human CRC transplantation to mouse. The bacteria will be identified and quantified through the comparative analysis of 16S RNA gene that is present in all bacteria while the metabolites will be surveyed with the technique called the mass spectrometry.

We expect that determining the bacterial and metabolites composition in stool associated with the response to treatment in humans and in animal models of cancer, will confirm the assumptions about the modulating role of intestinal bacteria in chemo- and immunotherapy. In addition, we should identify new markers, bacteria or metabolites, whose presence could predict the effectiveness of anti-cancer therapy. The results of our research will form the basis for further work on the possibility of changes in the composition of the intestinal bacteria that ultimately could improve the effectiveness of anticancer treatment, and perhaps also prevent the development of cancer. Cancer is a major burden of disease worldwide, and the studies we propose fit into the prophylaxis and effective treatment of cancer.