Project 7.1 The role of MTARC2 protein-related metabolism changes in the intestinal tumorigenesis

Supervisor: Michał Mikula, PhD
Institute: Maria Skłodowska-Curie National Research Institute of Oncology
Unit: Department of Genetics
www: https://www.pib-nio.pl/

Background:

Cancer cells metabolize essential nutrients much faster than non-cancerous cells, including through mitochondrial fatty acid oxidation which leads to a dramatic increase in glucose uptake and lactate production, even in the presence of oxygen. MTARC 1 and MTARC2 proteins, are molybdenum-containing enzymes and are located in the outer membrane of mitochondria. Both proteins are components of a catalytic enzyme complex that performs reduction reactions of N-hydroxylated structures. The most extensively described physiological function of the MTARC complex is its participation in cellular energy processes related to lipid metabolism. Prof. Mikula's team was the first to describe reduced MTARC2 expression in colorectal adenomas and adenocarcinomas. To date, however, endogenous MTARC substrates directly linked to lipid metabolism in healthy tissues or cancer tissue have not been identified, and how the complex affects the process of colorectal cancer (CRC) carcinogenesis has not been studied. The project in cooperation with Prof. Mlynarz of the Wroclaw University of Technology.

Aim:

Herein we will test the hypothesis that inhibition of MTARC2 expression in CRC induces reprogramming of metabolic pathways toward greater utilization of fatty acids in the energy processes of the cancer cell. The project includes the following research tasks: 1). Analyze of MTARC2 protein deletion on the rewiring of molecular and metabolic pathways specific to the cancer cell; 2). To evaluate the effect of Mtarc2 deletion on intestinal adenocarcinoma/tumor formation and lifespan in an Apc min/+ mouse model; 3). To determine whether DNA methylation of the MTARC2 locus correlates with protein expression in CRC tissues.

Requirements:

- MSc in biology, chemistry, or related life science fields,
- previous experience with NGS technology and NGS data analyses will be an advantage,
- performing cell culture, Seahorse assay and xenografts implantation,
- total RNA and chromatin isolation from cell culture,
- performing ChIP assays and ChIP-Seq libraries; QC of samples prior to and during NGS libraries preparations,
- NGS libraries preparations,
- involvement in data analyses and results dissemination.