

Project Title: Dissecting the mechanism of mitochondrial fatty acid oxidation dysregulation in breast cancer

Principal Investigator: Olga Razorenova

Triple-negative breast cancer is the only breast cancer subtype that lacks FDA-approved targeted therapies. Recently, a metabolic process-fatty acid oxidation-has been identified as a cause of triple-negative breast cancer metastasis. My research group established that there is a protein-CUB-domain containing protein 1 (CDCP1)-in triple negative breast cancer cells, which is a driver of this metabolic process and accordingly metastasis. There is a considerable interest in targeting this protein to prevent metastasis and inhibitors are being developed. Importantly, the inhibitors are targeting CDCP1 on the cell membrane and we have recently shown that it also localizes in another cellular compartment: mitochondria. Here we are going to investigate its role in mitochondrial metabolism and assess the potential of targeting CDCP1 as well as the proteins it regulates in mitochondria. Thus, the results of this study will have a number of implications, which will affect breast cancer therapeutic development: a novel class of CDCP1 targeting therapeutics (targeting CDCP1 in mitochondrial compartment of the cell) will be justified for development, novel molecules in CDCP1 pathway driving mitochondrial metabolism will be positioned to be therapeutic targets for drug development. A potent oncogene-Src-will be assessed as a mediator of CDCP1 signaling in mitochondria and Src targeting specifically in mitochondria will be assessed as a potential therapeutic strategy. This study contributes to my long-term goal: to design effective therapeutic strategies for triple-negative breast cancer based on targeting key molecules involved in fatty acid metabolism and metastasis.