Practically all animal's organs and tissues, including cancers, are composed of heterogeneous population of cells. Nevertheless, almost all information about biological and biochemical properties of cells were obtained from studies in which monotypic (containing only one type of cells) cell cultures were used. These in vitro studies could be very valuable for investigating a cell biology and for designing and testing new drugs. However, during the last twenty years several lines of evidence has accumulated that the biology (morphology, biochemistry and function) of such cell cultures differs essentially from that of cells which are co-cultured with their in vivo partner cells. Recently published study has unveiled that the co-culturing of astrocytes and neurons significantly alters the expression of several metabolic enzymes, both in neurons and astrocytes. Intriguingly, the co-culturing decreases the concentration of glycolytic enzymes in neurons and elevates it in astrocytes. This strongly suggests that any metabolic and, presumably, functional characterization of a monotypic cell culture (e.g. the susceptibility of cancer cells to drugs) may provide data which is not representative for the properties, and hence the role, of studied cells in the organism.

The main goal of our study is to demonstrate how the co-culturing of major kinds of cells which constitute brain (astrocytes and neurons), heart (cardiomyocytes and fibroblasts) and lung cancer (non-small cell lung cancer cells and cancer-associated fibroblasts) changes the proteomes of these cells and hence, their metabolism and functional properties. We are also going to discover molecules released during the cells' crosstalk which regulate the expression of energy metabolism enzymes in co-cultured cells.

The second aim of our project is elucidation how interaction of various types of cells affect the organization of their energetic metabolism. Although the mechanisms of action of individual glycolytic enzymes have been described precisely, the predictions of their dynamic behavior are still far from accurate. Hence, understanding the properties of multi-enzymatic complexes may hold the key to precise description of metabolic pathways and to understanding of a cell behavior in norm and pathology.

This knowledge is crucial to understand the actual functional interdependence among various types of cells within an organ or a tissue, and to determine new targets for pharmacological intervention in cancer, and in heart and brain dysfunctions.