One of the most common causes of death worldwide is ischemia of brain and heart. Recent studies reported that mitochondria not only take part in the energy metabolism of the cell but also are involved in cell death and survival. Mitochondrial have been proposed to play a role in cardio- and neuroprotection. Data indicate that pharmacological activation of mitochondrial potassium channels plays a role in cytoprotection of heart and neuronal tissues. There is strong experimental evidence that activation of mitochondrial large-conductance calcium-activated potassium channels (mitoBK$_{Ca}$) is crucial for the protection of heart during ischemia/reperfusion underscoring the vital role of these channels during myocardial infarction. Moreover, it is known that in human diseases and aging dysfunctions of mitochondrial respiratory chain play also an important role. Hypothetically, interactions between mitoBK$_{Ca}$ and respiratory chain complexes located in the inner mitochondrial membrane might have an influence on some of these dysfunctions.

To this time analysis and characterization of supercomplexes of mitochondrial proteins was difficult, because there were unstable after solubilization even in mild detergents - primarily digitonin was used to that. Data indicate that by using polymer nanodiscs it is possible to isolate stable protein complexes. Data obtained previously in our laboratory showed that mitoBK$_{Ca}$ could be uniquely regulated by respiratory chain substrates and it was suggested that mitoBK$_{Ca}$ might be physically associated with respiratory complexes. My preliminary results revealed that by using a styrene-maleic acid copolymer (SMA) it is possible to solubilize mitoBK$_{Ca}$ as large supercomplexe(s), which may contain respiratory chain proteins.

Therefore, the goal of this project is the application of polymer nanodiscs to isolate and characterize supercomplexes between mitochondrial potassium channel mitoBK$_{Ca}$ and other proteins from the mitochondrial inner membrane, including complexes of the mitochondrial respiratory chain. To do this state-of-the-art biochemical and biophysical methods will employ. In the end, my research might help to understand the mechanism and role of interaction between mitoBK$_{Ca}$ and respiratory chain complexes and answer the question of how potassium channels protect mitochondria. In the future, this knowledge might help in designing better drugs for ischemia-related diseases: brain and heart failure.