The objective of the Project

Coenzym Q (quinone), lipid-soluble, vitamin-like substance is present in most eukaryotic cells, primarily in mitochondria. It is a component of the mitochondrial electron transport chain and participates in aerobic cellular respiration, generating energy in the form of ATP. Mitochondrial coenzyme Q (mQ) is an important antioxidant that decrease the harmful oxidation of other molecules. Beside this good side, mQ is also critically involved in mitochondrial reactive oxygen species (mROS) production, causing the oxidative damage (known as oxidative stress). Namely, production of mROS depends on the reduction level of mQ. Surprisingly, there is no much kinetic data describing the relationship between mROS formation and the mQ reduction level in mitochondria.

Our aim is to understand the role of mQ reduction level in mROS generation as it is important in normal cell operation and development of pathology. We will elucidate the dependence of mROS formation on the redox state of mQ pool in mitochondria of different eukaryotic organisms, i.e., representatives of fungi, protists and animals (mammals). Our aim is to describe general and organism/tissue-specific features of the relationship between mROS formation and the mQ reduction level under a variety of metabolic conditions, including oxidative stress conditions. We will elucidate the link between the dependence of mROS production on the mQ reduction level (and mQ amount) with physiological cell operation, including oxidative stress that could lead to mitochondria/cell dysfunction.

The basic research to be carried out

We will compare the dependence of mROS formation on the redox state of mQ pool in mitochondria of different eukaryotic organisms, including unicellular organisms and cultured human endothelial cells (an example of slightly mitochondrial energy-dependent cells), and from rat tissues/organs with high energy requirements (brain, skeletal muscle, liver and kidney). We will study various mitochondria respiring conditions and mitochondria isolated from control and oxidative stress-treated cells (unicellular organisms and endothelial cells).

We will measure mROS formation, the mQ reduction level (and content) in parallel with changes in mitochondrial membrane potential and oxygen uptake in various isolated mitochondria. A quantitative importance of mitochondrial and cellular Q content relative to ROS production and consumed oxygen amount will be also studied in unicellular organisms and cultured mammalian cells. Additionally, the expression level of proteins important in prooxidant and antioxidant function of mitochondria as well as the level of lipid and protein peroxidation will be studied.

Present reasons for choosing the research topic

Data regarding mQ reduction level under different mitochondria respiring conditions are very limited. Moreover, there is no kinetic data describing the dependence of mROS formation on mQ reduction level in isolated mitochondria. Therefore, we will undertake a systematic study for detecting the Q content in mitochondria, cells, and whole-tissue homogenates and the mQ reduction level under given mitochondrial oxygen consumption and membrane potential conditions in relation to mROS formation, by a previously standardized methods identical for all samples.

The phenomena described in this project will be important for understanding mechanisms governing mROS production and will have a significant impact on physiological and bioenergetic research of mitochondria function and disease. Modulation of mROS formation, which in large measure depends on mQ reduction level, could be a promising target for therapy in various dysfunctions, such as cardiovascular or degenerative diseases. Studies in different eukaryotic organisms (yeast, protists and mammals) will provide an insight into mitochondrial ROS formation as a general biological phenomenon and also into its specific features in particular organisms.