DESCRIPTION FOR THE GENERAL PUBLIC

Mitochondrial dysfunction is a prominent feature of chronic heart and brain disorders, including ischemic stroke and Alzheimer's and Parkinson's disease. The mitochondrial dysfunction has been also reported in lung diseases, chronic obstructive pulmonary diseases, lung cancer, asthma and cystic fibrosis. Recent studies have incontestably shown that mitochondria play a key role not only in the synthesis of ATP and production of reactive oxygen species but also in the regulation of mechanisms responsible for the initiation of cell death. Description and understanding of the endogenous, cytoprotective mechanisms preserving mitochondrial function during ischemia/reperfusion is goal of many studies. Data derived from electrophysiology, biochemistry, molecular genetics and morphological studies indicating the participation of mitochondria in apoptotic signal transduction, have therefore become the starting point for the exploration of cytoprotective strategies. Recently, a group of potassium channels from inner mitochondrial membrane has been identified. These proteins control potassium fluxes between mitochondrial intermembrane space and mitochondrial matrix what directly regulates mitochondrial functions. It has been found that activation of mitochondrial potassium channels with pharmacological substances preserves mitochondria against damage induced by various factors including ischemia/reperfusion. The regulation of mitochondrial reactive oxygen species as a consequence of the activation of mitochondrial potassium channels have been shown to be involved in the preconditioning phenomenon. Despite intensive research, the exact mechanism of cytoprotection involving the influx of potassium into the mitochondria still remains under investigation.

Recently it has been proposed that one of key factors inducing mitochondrial dysfunction of the airway epithelium might come from air pollution. Epidemiologic evidence links exposure to urban pollution particulate matter (PM) to morbidity and mortality (U.S. Environmental Protection Agency, 1996). Exposure to PM may account for as many as 60,000 cardiopulmonary deaths each year in the United States. The airway epithelium, as the principal site of particulate matter deposition, is critical to the effects of PM. A key mechanism by which PM exerts its effects is the generation of ROS, inducing antioxidant and inflammatory responses in exposed epithelial cells. Therefore, one of the key questions seem to be the role of the mitochondrial potassium channels in damage caused by urban particulate matters. Does activation of the mitochondrial potassium channels stimulate cytoprotective mechanisms of epithelial monolayer upon damage caused by urban particulate matters?

Therefore we propose this interdisciplinary project whose main goal will be verification of the contribution of the mitochondrial potassium channels to cytoprotection upon stress by urban PMs. Our preliminary data suggest that in the inner mitochondrial membrane human epithelial cells, mitoBK_{Ca} and mitoK_{ATP} channels are present. We plan to use wide spectrum of the modern molecular biology, biochemical, biophysical and electrophysiological techniques including generation new cell lines models in our project.

A better understanding of the relationships between mitochondrial metabolism and cell physiology can help in the development of the effective strategies for cytoprotection induction. Possibly, by being on the trail of one of the oldest cell protection mechanisms, we will learn how to improve the treatment of damage induced by particulate matter.