DESCRIPTION FOR THE GENERAL PUBLIC

Mitochondrial dysfunction is a key characteristic of chronic heart and brain disorders, such as ischemic stroke, Alzheimer's disease, and Parkinson's disease. It has also been identified in various intestinal diseases, leading to barrier disruption, lung cancer, and cystic fibrosis. Recent studies have conclusively demonstrated that mitochondria are crucial not only for ATP synthesis and reactive oxygen species (ROS) production but also for regulating the mechanisms that initiate cell death.

Understanding and describing the endogenous, cytoprotective mechanisms that preserve mitochondrial function during ischemia/reperfusion is the focus of many studies. Evidence from electrophysiology, biochemistry, molecular biology, and morphological studies suggests that mitochondria play a role in apoptotic signal transduction, providing a foundation for exploring cytoprotective strategies.

Recently, a group of potassium channels located in the inner mitochondrial membrane has been identified. These proteins regulate potassium fluxes between the mitochondrial intermembrane space and the mitochondrial matrix, directly influencing mitochondrial functions. Pharmacological activation of these mitochondrial potassium channels has been shown to protect mitochondria from damage caused by various factors, including ischemia/reperfusion. The regulation of mitochondrial ROS as a result of mitochondrial potassium channel activation has been implicated in the phenomenon of preconditioning. Despite extensive research, the precise mechanisms of cytoprotection involving potassium influx into the mitochondria remain under investigation.

Last time, it was proposed that one of the key factors inducing mitochondrial dysfunction of the intestinal epithelium might come from nanoplastics (NPs). NPs have become a growing concern for human health due to their pervasive presence in the environment and their potential for bioaccumulation. It is well established that, the intestinal epithelium, the single-cell layer lining the gut, plays a crucial role in nutrient absorption and as a barrier against harmful substances. A key mechanism by which NPs exert its effects is the generation of ROS, inducing antioxidant and inflammatory responses in exposed epithelial cells. While current research indicates that nanoplastics can negatively impact the intestinal epithelium, leading to barrier disruption, inflammation, oxidative stress, and microbiome alterations, further studies are crucial to fully understand these interactions and their implications for human health. Therefore, one of the key questions seems to be the role of the mitochondrial potassium channels in damage caused by nanoplastics. Does activation of the mitochondrial potassium channels stimulate cytoprotective mechanisms of epithelial monolayer upon damage caused by nanoplastics?

Therefore, we propose this interdisciplinary project with the primary goal of verifying the contribution of mitochondrial potassium channels to cytoprotection under stress induced by NPs. Our preliminary data suggest the presence of the mitoBK$_{Ca}$ channel in the inner mitochondrial membrane of human intestinal epithelial cells. To achieve our objectives, we plan to employ a wide range of modern molecular biology, biochemical, biophysical, and electrophysiological techniques, including the generation of new cell line models.

A better understanding of the relationships between mitochondrial metabolism and cell physiology can aid in developing effective strategies for inducing cytoprotection. By investigating one of the oldest cell protection mechanisms, we may discover ways to improve treatments for damage caused by nanoplastics.