Project 1.12 Mitochondrial potassium channels as sensors and regulators of redox signaling

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www: https://infraredmito.nencki.edu.pl/

Background:

Mitochondria are essential for ATP synthesis, metabolic regulation, and apoptosis. Dysregulated mitochondrial function and redox homeostasis contribute to many diseases, highlighting the importance of maintaining mitochondrial health. As the primary source of reactive oxygen species (ROS), mitochondria play a dual role: uncontrolled ROS increase leads to cell death, while controlled ROS synthesis supports processes like inflammation or cancer metabolic reprogramming.

Mitochondrial potassium (mitoK) channels are key to these pathways. Their activation induces cytoprotection, partly by regulating mitochondrial ROS synthesis. MitoK channels also are part of a redox signaling loop, as their activity is influenced by redox signals. However, the detailed mechanisms of mitoK channel redox regulation remain unknown. We suspect that through regulation by redox signals, mitoK directly regulate mitochondrial and cellular function and are part of a feedback loop that regulates the mitochondrial transcriptome/proteome, and metabolome. Additionally, in stress conditions redox regulation of mitoK channels is crucial for their cytoprotective function.

Aim:

The project aims to investigate the redox regulation of mitochondrial potassium (mitoK) channels and their impact on mitochondrial function and cellular physiology. We will explore how the redox state influences the activity of mitoBKCa and mitoKATP channels using various cellular models, including mouse cardiomyocytes, U-87 MG glioblastoma cells, and HEK293. We will identify key redox-regulating domains and amino acids within the proteins forming mitoK channels.

The project will also evaluate the effects of mitoK channel redox regulation on mitochondrial function under normoxia and hypoxia. Furthermore, it aims to understand mitoK channels as transducers of redox signals, focusing on their role in mitochondrial metabolism, cytoprotection, and oxidative stress-induced cytotoxicity. Advanced techniques will analyze mitochondrial transcriptome, metabolome, and lipidome for a comprehensive understanding of mitoK function.

Requirements:

- we are seeking a motivated, creative, and collaborative individual with a background in chemistry, biophysics, biology, biotechnology, or a related field,
- candidates should possess basic knowledge of biochemical techniques and/or molecular biology and biophysical methods,
- additionally, a strong command of both spoken and written English is required.