

Project 1.2 The role of impaired metabolism in PACS2 Syndrome development

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Background:

PACS2 Syndrome is an ultra-rare genetic disease caused by autosomal dominant mutation in PACS2 gene that leads to developmental and epileptic encephalopathy (DEEs). In the cell, the PACS2 protein is located at the contact sites between mitochondria and the endoplasmic reticulum. The planned research will include a comprehensive analysis of metabolic parameters, lipidomic profile, proteomic profile and calcium homeostasis in control fibroblasts and those from patients with the PACS2 Syndrome. The status of oxidative stress and antioxidant protection will also be determined. The research will also include the characterization of MAM fraction (containing the contact sites between mitochondria and the endoplasmic reticulum) and mitochondria isolated from tissues obtained from the PACS2 mouse model. We plan to determine which of the tested parameters may be essential for the development of the disease - PACS2 Syndrome.

Aim:

The aim of the project is to determine, based on functional and proteomic data, the correlation between the level of proteins involved in key metabolic pathways and the observed changes in bioenergetic parameters, the level of reactive oxygen species, the level of oxidative damage, calcium homeostasis and lipid metabolism in cells derived from patients with PACS2 Syndrome. The primary goal is to answer the question to what extent the "multi-parameter metabolic profile" of patient fibroblasts differs from healthy cells. Additional proteomic studies of MAM fraction and mitochondrial bioenergetics will be of great cognitive value. Research conducted in the range of the project will contribute to a better understanding of the pathomechanism of this disease by increasing our knowledge of the impact of mutations in the PACS2 gene on cellular metabolism.

Requirements:

- A master's degree (or an equivalent) in biology, biochemistry, molecular biology, molecular biomedicine, medicine, genetics or biotechnology,
- good command of spoken and written English,
- knowledge of the standard biochemistry and molecular biology techniques,
- a strong motivation and ability to drive the project independently,
- well-developed collaborative skills,
- curiosity for discovery of biological processes,
- knowledge of statistics, experience of working with cell cultures, laboratory animals,

documented scientific activity (e.g. publications, presentations at conferences, research internships, awards, scholarships) will be an additional advantage.