**Project 1.8. Investigation of the structure of the mitochondrial permeability transition pore**

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**WWW:** https://wieckowski-mitolab.nencki.edu.pl/
https://www.nencki.edu.pl/laboratories/laboratory-of-mitochondrial-biology-and-metabolism/

**Background:**

The mitochondrial permeability transition (mPT) is a highly conserved phenomenon in evolutionary history, with key features conserved in yeast, mammals and plants. Under favorable conditions including calcium ($Ca^{2+}$) overload, oxidative stress, increased phosphates concentration, and decreased adenine nucleotide availability, the inner mitochondrial membrane becomes highly permeable to solutes with a molecular weight of up to 1,500 Da. Mitochondrial permeability transition pore (mPTP) opening is often associated to disease conditions and considered as critical mechanism in the development of several acute pathological conditions, including neurodegenerative disorders, heart failure, and age-dependent diseases, as well as in organ damage caused by the toxicity induced by several compounds. Mitochondrial permeability transition pore and its structure is one of the most intriguing phenomena in cell biology. This phenomenon has been studied for almost 50 years and still no definitive answer has been provided regarding its mechanisms and structure. From originally being considered an in vitro artifact to the current notion that the mPTP is a clear phenomenon a long road has been travelled. The evolving mPTP models and mechanisms, which have involved many proposed mitochondrial protein components, also result from methodological advances and the use of more complex biological models.

**Aim:**

The main goal of the project is complex characterization of mitochondrial permeability transition pore. We believe that such comprehensive analysis will suggest potential therapeutic strategies in which mitochondrial permeability transition pore is modulated to alleviate the consequences of mitochondrial dysfunction. We aim to clarify the potential structure of mPTP and its involvement in nonalcoholic fatty liver disease development and progression. Moreover, we plan to elucidate the potential melatonin binding site in the mPTP complex. Taking into consideration all controversies about mPTP structure we want to prove the most probable mPTP structure at the different level of complexity.

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