Project 1.6. Protein depalmitoylation in the regulation of synaptic plasticity in neuropsychiatric diseases

Supervisor: Prof. Jakub Włodarczyk/ Auxiliary Supervisor: Dr. Monika Zereba-Koziol
Laboratory: Cell Biophysics
WWW: http://en.nencki.edu.pl/laboratory-of-cell-biophysics

Background: Stress impairs the structure and function of synapses in the brain. This results in long-term impairments of synaptic plasticity underlying memory processes. Under physiological conditions, signal transduction and activity-dependent changes in nerve cells are regulated at many different levels. According to the latest research, post-translational modifications such as S-palmitoylation of synaptic proteins are one of the key processes regulating proper signal transmission in the brain. S-palmitoylation is a lipid modification of proteins, involving the attachment of a palmitic acid to a cystein residue in protein molecule. On the other hand, protein depalmitoylation is a process in which palmitic acid is removed from modified proteins. Palmitoylation and depalmitoylation serve as regulators of the function of synaptic proteins and are strictly regulated by two groups of proteins i.e. palmitoyltransferases and thioesterases.

Aim: The goal of this project is to determine the role of the PPT1 depalmitoylating enzyme in the pathogenesis of stress-related neuropsychic diseases. In the project, we propose an approach in which we will use both modern proteomics based methods such as mass spectrometry as well as fluorescence microscopy based methods to assess changes in palmitylation regulated by the PPT1 enzyme. The study will be performed both in vivo in animal model of depression and in vitro on cell cultures.