Description for the general public

The human body consists of a huge number of cells, and cells are built out of organelles. The efficient functioning of cells can occur thanks to efficient communication between cellular structures. Intracellular processes require energy, which is produced in organelles called mitochondria, which are often compared to powerhouses. However, the simple production of energy by the mitochondria is not sufficient for the proper functioning of the cell. Like powerhouses, mitochondria, in addition to energy production, must communicate with the surrounding environment. Dysfunctional communication may lead to abnormalities in cell functioning and, in extreme cases, cellular death.

In mitochondrial disorders, as in the case of a powerhouse failure, the best way to restore their proper functioning is to reduce the energy demand, which is associated with the inhibition of production in other parts of the cell. The most energy-consuming process in a cell is the synthesis of proteins that are building blocks of cell structures, but also perform many other important functions. Additionally, a decrease in cellular proteins production causes a reduction of a protein load on the mitochondria. This situation, although beneficial for mitochondrial repair mechanisms, cannot last too long. Cells, like urban agglomerations, have to restore production after some time, because otherwise, it could lead to a catastrophe. Mitochondria send a signal that despite their dysfunction, production of proteins must be restored. This induces adaptations in the functioning of the cell, which on the one hand allow cells to survive, but on the other hand, may have surprising consequences. These adaptive responses may lead to the protein aggregation, which is often observed in neurodegenerative diseases such as Alzheimer's disease, in which β-amyloid and Tau protein aggregates are observed in the patients’ brains. In our previous studies, we discovered cellular adaptive responses associated with protein synthesis under prolonged mitochondrial stress. Therefore, the goal of our project is to determine the contribution of these adaptive responses to Tau protein aggregation during mitochondrial dysfunctions.

Using mammalian cell cultures, we will examine how signals from dysfunctional mitochondria affect the aggregation of proteins. For this purpose, using advanced techniques of microscopy and analysis of cell properties, we will check how biochemical and genetic manipulations in adaptive cellular responses to mitochondrial stress, will affect the aggregation of Tau protein. We are also planning to investigate which proteins can co-aggregate with the Tau protein and find proteins that interact with Tau and potentially modifying it under mitochondrial stress. We hope that the results of our project, in which we propose a new concept of protein aggregation induction in neurodegenerative diseases, will allow us not only to acquire new knowledge about the processes taking place in Alzheimer's disease but also to propose new prevention strategies for this disease.