In the 1980s, breakthrough discoveries were made about the molecular basis of brain function. The basic discovery of this new field called molecular neuroscience was to prove that long-lasting changes in brain activity, and more specifically in the nerve cells that build it, require changes in gene expression. These changes led to the production of proteins necessary for many cellular processes, including synaptic communication. Gene expression is regulated by a complex protein apparatus, which, among other things, is responsible for changes in the spatial packing of DNA in the cellular nucleus. These include proteins which, using the energy contained in ATP, induce mechanical changes in the packing of DNA in higher order structures (chromatin). Mutations in elements of these protein complexes lead to changes in brain anatomy and functioning and co-exist with mental retardation, autism spectrum disorders or epilepsy.

In recent years, more and more attention is being paid to the links between the metabolism of nerve cells and their ability to respond to stimuli reaching them. One of the basic regulators of metabolism is mTOR protein. On the one hand, it senses the state of the cell's resources and on the other hand it is a sensor of extracellular stimuli, including neuronal activity. The integration of these two information ultimately determines the ability of the cell to respond to a given stimulus and adapt its metabolism to new conditions. Mutations in the mTOR regulating genes, i.e. TSC1 or TSC2 lead to multi-organ diseases with serious neurological and neuropsychological symptoms. One of such diseases is tuberous sclerosis complex characterized by the occurrence of epilepsy, mental retardation and autism spectrum disorders.

mTOR acts on many proteins changing their function, but occurs mainly in cytoplasm. However, the results of our previous research and the preliminary data which form the basis of this research proposal indicate that neuronal activity causes mTOR to move to the nucleus of the cell, where it interacts with proteins that modify the spatial packing of DNA. On this basis, we hypothesize that under favorable conditions of sufficient cellular resources (e.g. energy), neuronal activity causes mTOR to move to the nucleus, where it regulates the cellular functions of chromatin-modelling complexes, including expression of genes important for neuronal activity. At the same time, we hypothesize that this sequence of events is disturbed in tuberous sclerosis complex leading to a characteristic disorder of nerve cell activity, which causes epilepsy as well as disturbances in social interactions characteristic of autism spectrum diseases. The aim of the project is to verify this hypothesis using advanced molecular, cellular biology and microscopy methods. The research will use in vitro cultured neurons and Danio rerio. The results will contribute to a better understanding of the role of mTOR in physiology and brain diseases. At the same time they can be an inspiration for scientists working on other mTOR-related diseases such as cancer and metabolic diseases.