

Project 9.5 The role of mTOR-Brg1 interaction in normal and aberrant neuronal activity (NCN/MAESTRO)

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www: <https://shorturl.at/yMUY8>

Background:

Gene expression is key for brain development and function and 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. mTOR kinase is one of the basic regulators of metabolism. 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 Brg1. Using advanced molecular, cellular biology and microscopy methods we plan to study how mTOR-Brg1 interaction affects Brg1 cellular functions as well as neuronal activity, epileptogenesis and social interactions. The research will use in vitro cultured neurons (rat and human) and *Danio rerio*. The results will contribute to a better understanding of the role of mTOR in physiology and brain diseases.

Aim:

Based on our previous research, we hypothesize that neuronal activity causes mTOR to move to the nucleus, where it regulates the chromatin-modelling complexes and gene expression. At the same time, we hypothesize that this sequence of events is disturbed in tuberous sclerosis complex leading to epilepsy as well as disturbances in social interactions characteristic of autism spectrum diseases. The aim of the project is to verify these hypotheses.

Requirements:

- Master's degree in biology, biochemistry or related field,
- good knowledge of basics of molecular and cell biology and/or neurobiology,
- basic hands-on experience in one of the fields: molecular & cell biology, genetic engineering, fluorescent microscopy, or gene expression analysis using next generation sequencing
- written and spoken fluency in English,
- willingness to learn and take new challenges, ability to work independently, analytical thinking,
- good interpersonal skills and a collaborative attitude

Number of positions available: 1

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