

## **Amotl1 mutant mice as a novel model of human psychiatric disorders associated with social dysfunctions**

The central nervous system (CNS) is composed of the brain and spinal cord and it constitutes a part of the nervous system. The main function of the CNS is to register, analyze and react to the stimuli coming from outside and from inside of the body. The CNS is also responsible for complex cognitive processes like thinking, learning and memory. Neurons are the fundamental units of the nervous system. Single neuron consists of a cell body and two types of extensions: single long projection– axon and numerous short extensions – dendrites. Abnormalities in dendritic tree growth and dendritic spines formation are often reported to cause intellectual impairments and are known to be associated with numerous neurological disorders like schizophrenia, Rett syndrome or autism spectrum disorders.

In the proposed research we will characterize Amotl1 knockout (KO) mice as a novel mouse model of neurodevelopmental psychiatric disorders and explore the role of Amotl1 in the brain. Numerous studies documented the role of Amotl1 in the regulation of cellular polarity and cancerogenesis, however, its function in the brain has not been studied. Interestingly, Genome-wide Association Study revealed that Amotl1 could be the potential genetic factor related to mood disorders (GeneCards) and several studies implicated *Amotl1* locus with schizophrenia. Our preliminary results strongly suggest that Amotl1 KO mice have morphological and behavioral abnormalities apparent in mouse models of psychiatric disorders. Although similar structural or functional defects appear in many neurodegenerative disorders like autism or anxiety-related disorders, the results from MRI studies and behavioral tests are the most similar to those observed in mouse models of schizophrenia. In this project we will focus on characterization of behavioral deficits and alterations of brain morphology including structural MRI analysis of mouse brain as well as analysis of neuronal morphology in Amotl1 mutant mice. The experiments planned in this study will significantly contribute to the field and will include cutting-edge techniques.

Brain disorders constitute one of the greatest challenges to the health system. Conducting research dedicated to understanding the behavioral, structural and molecular abnormalities related to schizophrenia and other neurological diseases can help in developing new strategies for treatment and prevention of various psychiatric disorders. Experiments proposed in this grant application are innovative and in the long run have the potential to be a substantial contribution to the field of neurobiology and medicine.