

Functions of Amotl1 protein in the dopaminergic and serotonergic systems

Our behavior, consciousness, memory, and daily functioning are possible thanks to communication between different brain parts. This communication is mainly supported by the neurons, which release neurotransmitters to ensure the proper transmission of information between cells. Different neuronal populations secrete specific neurotransmitters that target selected populations of neurons expressing specialized receptors. Among the neurotransmitters is dopamine, produced by the dopaminergic neurons, which is associated with pleasure and reward. On the other hand, serotonin, secreted by serotonergic neurons, regulates mood, sleep, or withdrawal. One fascinating particularity of these neurons is that despite their relatively small amount, they send projections and can modulate the activity of most of the brain's parts. The two systems are fundamental for the proper functioning of our brain, and defects in one or both of these neurotransmitter systems are associated with many psychiatric disorders, such as drug abuse, depression, schizophrenia, bipolar disorder, ADHD, and Parkinson's disease.

The proposed project aims to characterize the functions of a protein called AMOTL1 in regulating dopaminergic and serotonergic neurons. So far, the role of AMOTL1 has been studied mainly in cell polarization, adhesion, and cancer progression but not in the CNS. AMOTL1 belongs to a family of proteins called angiomotins, including AMOT and AMOTL2. These proteins are closely related and have a similar organization of protein domains. However, despite their high degrees of structural similarities, each angiomin presents unique functions.

Interestingly, the roles of the Angiomotins in the brain are poorly understood. However, there are reports that AMOT controls neuronal development and maturation. These studies are just the beginning of understanding the functions of Angiomotins in the brain. Our preliminary results indicate that AMOTL1 also has an essential role in regulating the activity of dopaminergic and serotonergic neurons. Therefore, the current project aims to examine in detail the functions of AMOTL1 in both neurotransmitter systems. The experiments will be conducted on mice lacking the AMOTL1 gene expression in each type of neuronal population. We will check how AMOTL1 deletion affects neuronal activity. Our experiments will include behavioral analysis, brain tissue examination, and molecular studies to comprehensively understand AMOTL1 functions in each cell type.

Defects in brain functioning and neurological processes are among the health care system's biggest challenges. Thanks to support from the Polish National Science Center (NCN), the obtained results could help develop new treatments for nervous system diseases.