

Autism spectrum disorders (ASD) is a group of neurodevelopmental disorders characterized by deficits in social interactions, social communication skills, repetitive and restrictive behaviors and unusual responses to sensory experiences that can vary in individuals along a continuum of severity. The average prevalence of ASD is estimated at 1%, affecting males 4 times more often than females. Despite extensive research the cause of ASD remains unknown, however studies show that both environmental factors and genetic factors may play a role in the development of autism. Thanks to the development of large-scale genomic sequencing, many genes associated with ASD have been identified.

The brain represents about 2% of the body weight, remarkably it uses about 20% of the energy consumed by our body. Thus, it is not surprising that regulation of energy metabolism is especially critical to the central nervous system and changes in energy production may lead to neurological diseases. Interestingly, recent data suggests that as many as 30% of children with ASD may experience metabolic abnormalities. Still, the role that metabolism may play in ASD remains unknown and has yet to be established.

Recently we identified a novel mutation in TRAP1 gene in two unrelated ASD patients and have created a mouse model with identical mutation to be able to study its effect on the brain physiology. Trap1 is a mitochondrial protein with function connected to regulation of metabolism. Based on our preliminary results, we can say that male, but not female mice with Trap1 mutation are less social and display deficits in transmitting information between neurons. We also detected differences in the energy use and amino acid levels in the brain of male Trap1 mutant mice.

In the proposed project, we are planning studies that will allow us to understand the role of Trap1 protein in the regulation of brain metabolism considering possible gender differences. We also aim at identifying affected metabolic pathways and potential targets for nutritional intervention. We expect that the knowledge gained during the implementation of the project will allow us to propose new therapeutic targets that may hold promise for the development of effective dietary therapy for ASD.