One of the deficits characteristic for patients with autism spectrum disorder is changes in the processing of tactile input - the somatosensory information. People with autism often manifest hypersensitivity or hypersensitivity to touch. For some, any light tactile impression may be perceived much too intensely. For others, any touch, even strong touch, may escape attention. Particularly in children this can lead to significant problems in everyday life - defensive attitudes when interacting with peers, active avoidance of physical contact, negative emotional associations to new experiences, or even aggression in response to attempts of touch and interaction. These problems may be one of the aspects behind the deficits in social communication so common for autism. Unfortunately, the underlying mechanisms responsible for the altered processing of somatosensory information in autism are essentially unknown. This, in turn, prevents the development of targeted therapies that can help affected patients.

Autism spectrum disorder manifests very early in life. Its symptoms likely stem from slight changes in brain function, fine anatomy and/or circuit formation that originate from abnormal brain development in late gestation. As modern research suggests, one such change may take a form of an imbalance between the ratio of excitatory and inhibitory neurotransmission in the central nervous system. Inadequate amount of inhibition or an impossible to inhibit excess of excitatory signaling may be the cause of the tactile hyper- or hypersensitivity in autism. Most studies that attempted to explore this problem have focused on the cerebral cortex. However, cortex is not the only structure responsible for the processing of sensory information. For the brain to work properly all of its structures have to work in unison. Researchers are starting to pay increasing attention to study not only to the cortex itself, but also to its connections to structures lying deeper within the brain. One such structure is the thalamus. Together with the cortex, they form a fine-tuned network of thalamocortical neural loops responsible for initial filtering, processing, distribution and integration of sensory input, including the tactile information, throughout central nervous system. It is known that anatomical and functional alterations in thalamocortical circuits are often identified in patients with autism, but the exact nature, causes and effects of such deficits are not well characterized. Therefore, **the goal of this project is to analyze the relation between impaired excitatory and inhibitory neurotransmission on proper somatosensory signal processing in thalamocortical circuits and autism-like behaviors.**

This research will be conducted on genetically modified mice, in which either the excitatory or inhibitory neurons lack the *Tsc2* gene. Mutations in this gene in humans lead to tuberous sclerosis. About 50% of patients with this disease are also diagnosed with autism spectrum disorder. This indicates a common etiology for the changes in brain function in tuberous sclerosis and autism at the level of genetic, molecular and/or developmental abnormalities. Hence, the genetic link between these two disorders makes the *Tsc2* knockout animals a good model for elucidating the molecular basis of autism's etiology.

In the project we will perform a comprehensive analysis of neuronal activity within the somatosensory thalamocortical loops in mice affected with the *Tsc2* mutation, as well as examine their propensity for social contact and willingness to enter into physical interactions with their conspecifics. Behavioral studies will be carried out using modern methods that allow an automated analysis of the social behavior of individual mice living in a group. **Through these studies, it will be possible to link specific deficits in the functioning of selected brain structures with specific sensory and social deficits - aspects that are characteristic and important in the diagnosis of autism. Characterizing the dynamics and physiological range of activity of the aforementioned neuronal circuits may open the way to develop therapeutic strategies for various symptoms of autism spectrum disorder.**