For many years, astrocytes were underestimated in their role in the brain. However, recent research indicates that astrocytes are indeed key participants in regulating brain activity, development, and function. Astrocytes perform diverse functions within the central nervous system, such as providing trophic and metabolic support to neurons, promoting synapse formation, regulating neuronal excitability, and maintaining brain homeostasis. The focus has shifted from the question of whether astrocytes regulate neuronal function to understanding the mechanisms that control and coordinate this regulation. To better understand how astrocytes influence the development, maturation, and function of neurons, it is crucial to uncover the internal mechanisms that guide astrocytic function.

My research indicates that one of the internal pathways involved in the maturation of astrocytes is the Wnt/β-catenin signaling. Deletion of TCF7L2, a key transcriptional effector of the Wnt/β-catenin pathway, revealed its role in the development and maturation of postnatal cortical astrocytes, as well as its involvement in limiting synaptic numbers and regulating social behaviors. However, compared to cortical astrocytes, where the level of TCF7L2 decreases with age, in hippocampal astrocytes, the expression of this protein remains high until adulthood. These data suggest that the β-catenin signaling pathway is active in hippocampal astrocytes not only during the embryonic and postnatal periods but also in adulthood.

To better understand how the regulation of hippocampal neuron function by astrocytes is coordinated, within this project, I will investigate the involvement of the β-catenin pathway and one of its effectors, the TCF7L2 factor, in the functioning of astrocytes. This specific effector is a transcription factor, a special protein that binds to DNA in the cell nucleus, regulating the expression of relevant genes. I will conduct my studies using transgenic mice, ensuring optimal living conditions and eliminating potential stress. By analyzing hippocampal cells in mice lacking the TCF7L2 factor, I will examine which genes are regulated by the investigated transcription factor in different populations of astrocytes and neurons. Additionally, I will assess how this factor affects the morphology of neurons and the number of synapses and conduct electrophysiological studies of neurons. Finally, I will conduct behavioral studies on mice to evaluate whether the investigated transcription factor influences their cognitive functions.

The research conducted in the project aims to expand our knowledge of the fundamental mechanisms of regulating the functioning of neurons by astrocytes. Such an in-depth perspective may contribute to the development of new therapies and innovative methods for treating diseases that increasingly affect our society.