Synapses are specialized domains of the plasma membrane, which are points of contact and communication between neurons. Most excitatory synapses are located on the dendritic spines which are small protrusions of dendrite membrane. A subset of dendritic spines is a subject to constant change - some appear, other disappear and those existing follow their size change. The dynamic turnover of spines and their shape changes are associated with synaptic plasticity and memory. Improper turnover and changes in the morphology of synapses are associated with different neuropsychiatric and neurodegenerative disorders such as mental retardation, epilepsy, addiction, schizophrenia, fragile X syndrome, Alzheimer's and many others.

Glycogen synthase kinase-3 beta (GSK-3β) is one of the key proteins regulating synaptic plasticity because of its role in excitatory synaptic transmission, but its contribution to abnormal dendritic spine structure and its relationship to the pathogenesis of the fore mentioned diseases is poorly understood. To this end we will use two mouse models with increased activity and devoid of GSK-3β protein and by combining imaging, behavior and optogenetics we will characterize role of dendritic spine structure in cognition and emotional response.

First, we will examine shape of dendritic spines in different brain structures of mice with defective GSK-3β activity using fluorescent dye. Next we will analyze mice with defective GSK-3β activity with respect to different behavioral paradigms including social behavior, cognition, addiction predisposition, willingness to explore new environments, short and long term memory and anxiety. In the last part of the project we will analyze the role of dendritic spines in controlling behavior using optogentics. First we will express light sensitive opsin channel in neurons that participate in the acquisition of memory trace. Then using optogentic low frequency stimulation or high frequency stimulation we will force dendritic spines to change their shape during memory retrieval to define role of dendritic spine shape in learning and memory.

This project will allow for better understanding how dendritic spines contribute to learning and memory as well as to brain diseases.