One of the remarkable features of the brain is its ability to acquire, interpret and store the upcoming information. These processes are assured by the properties of the nervous tissue, where the individual neurons create a complex network by forming synaptic connections among each other, thus allowing signal transfer. Modifications in the number or strength of the aforementioned contacts are thought to underlie brain's learning capability and they are called synaptic plasticity. According to the newest concept, synapse consists of the four different components: the pre- and postsynaptic membrane, astroglia and the adjacent extracellular matrix. The postsynaptic part of the synapse is frequently localized at the membranous protrusion extending from a neurons' dendrite called dendritic spine. Enhanced network activity (ex. during memory acquisition) often results in morphological alterations of these structure (involving spine volume changes), which are believed to accompany modifications in synapse strength. Since dendritic spines are tightly surrounded by the extracellular matrix (ECM), changes in their shape may depend on the interactions with the ECM components. The ECM forms a meshwork-like scaffold which tightly enwraps neuronal cells. ECM molecules have a potential to influence dendritic spines through the contact with their specific receptors localized at the spine membrane. The numerous components of the extracellular matrix play divergent roles in the plasticity of dendritic spines. In our research project, we decided to focus on a protein called matrix metalloproteinase-9, MMP-9. Recently, this ECM modifier has been shown to be a key player in synaptic plasticity, able to induce dendritic spine maturation. The enzymatic activity of MMP-9 allows it to cleave different ECM components and ECM receptors at dendritic spine. Such proteolytic activity at the synapse proximity controls synaptic changes, thus affects memory formation and storage. Interestingly, the time window in which MMP-9 is active, seems to be strictly regulated in order to assure proper changes in dendritic spine structure. The immediate enzyme inactivation is controlled by its endogenous inhibitor, TIMP-1 protein. As it was mentioned above, the presence of a variety of specific molecules at the spine membrane allows it to contact with the cell extracellular matrix. Our preliminary data points out that the two of them are not only the novel MMP-9 substrates, but they may also serve a crucial function in the regulation of structural plasticity of dendritic spines. These are the CD44 adhesion molecule and β-dystroglycan (β-DG). However, the exact role of these two proteins in spine morphological changes is not described in the literature, our pilot experiments give us more than one premise in support of the notion that CD44 and β-DG can regulate spine structure. Having these information, we decided to study the role of these synaptic molecules in the context of proteolytic-dependent dendritic spine maturation. The "molecular interplay" between CD44/β-DG and MMP-9 has a potential to fundamentally influence such complex process as structural synaptic plasticity. Our goal is to disentangle, what are the changes in the postsynaptic protein (CD44/β-DG) composition during activity-dependent processes. At the same time, we will assess whether, and how such modifications in synapse molecular architecture affect dendritic spine morphology and plasticity. Subsequently, we will perform a set of quantitative experiments in order to get and compare the precise copy number of CD44/β-DG at the immature and mature synapses. Additionally, we designed a study in which we plan to modify CD44/β-DG gene expression in living animals to unravel the specific roles for each investigated molecule for mature synapse stabilization in vivo.

The plasticity of the nervous system is one of the most intriguing aspects in the contemporary neuroscience. However, the knowledge on how the brain is processing and storing the information is still far from being complete. In the research project we will explore the complex relationship between proteolytic modifications is synaptic molecular architecture and dendritic spines structural plasticity. By the use of different experimental approaches such as: cellular models of complex neuronal network, confocal microscopy, in vitro modifications of gene expression, transgenic animals and in vivo brain imaging we aim to provide the answers on fundamental neuroscience questions, which will help to understand, how "synapses are learning" at the molecular level.

Since, dendritic spines are considered to be the "locus of plastic changes" in the nervous system, we decided to perform the research allowing to understand the molecular mechanisms of spine formation and its long-lasting stabilization, which not only underlay physiological plasticity of the synapse, but they are also engaged in different pathological conditions. We think that studying, how the postsynaptic proteins dynamics affects dendritic spine molecular architecture will substantially expand the knowledge of such complex process as neuronal synaptic plasticity.