Depression is one the most severe illness affecting modern society. Depression is not only a medical problem, but also an economic challenge, because treatment of depression requires constant financial effort. Unfortunately, the currently method of treatment of depression are unsatisfactory. It is estimated that a few to several percent of patients are suffering from resistant depression

The lack of efficacy of currently used drugs forces researchers for development of the new treatment strategies and for better understanding of biological mechanisms of depression. Currently used drugs modulate monoaminergic systems (mainly noradrenergic and serotonergic), but as has been mentioned this strategy is not satisfactory.

In the last years, researchers focused attention on the zinc abnormalities as a potential factor involved in the pathogenesis of depression. Results obtained both in clinical and preclinical studies showed that deficiency of this trace element is associated with depression in human or depressive-like symptoms in animals. Zinc is ubiquitous ion which is engaged in many cellular processes. But blockade of glutamate NMDA receptor by zinc is the most important biological effect for potential role of this element in pathogenesis of depression.. In particular, it is very possible that enhanced and long lasting activation of cortical and hippocampal extrasynaptic NMDA receptors is involved in pathological processes. The enhanced neural transmission by NMDA receptor may lead to the loss of the synaptic connections and neural death. The role of NMDA receptors in the pathophysiology of depression, or at least in the recovery processes, is emphasized by administration of ketamine - NMDA receptor antagonist that single dose lead to relieving of depression symptoms. From molecular point of view, administration of ketamine is correlated with activation of intracellular transduction pathways like mTOR and ERK/CREB involving in processes of synaptogenesis, neural plasticity and neuron survival.

What important, zinc deficiency lead to enhance activity of glutamate system in central nervous system. Based on above assumptions, the main goal of this project is to determine the relationship between zinc deficiency and transduction signalling pathway involved in the synaptogenesis. These studies will be performed mainly on rats. However the experiments with transgenic mice are also planned in order to understanding the role of signalling pathway involved in the expression of depressive-like symptoms induced by zinc deficiency. Furthermore, the molecular mechanisms underlying zinc deficiency will be determine using a different methods such as western blotting, ELISA, electrophysiology and immunochemistry.