Depressive disorders is the most common mental illness worldwide. Statistics show that about 15-18% of the global population manifested symptoms of depression. What is worse, according to the American Academy of Child and Adolescent Psychiatry, an estimated 2% of young children, and 4% to 8% of adolescents, suffer from the disease. While, WHO (World Health Organization) states, that by the year 2020, depression is projected to reach second place in the ranking of Disability Adjusted Life Years (DALY) calculated for all ages. Moreover, depression is associated with high suicidality (about 50% of individuals who have committed suicide carried a primary diagnosis of depression). Depression also often accompanies other diseases, including cancer or diabetes. Depressive disorders are not only a clinical problem but also the key social and economic problems, which due to the inability of patients to work generates billions in losses for businesses around the world.

The efficacy of available antidepressants are relatively low and the therapeutic response appears after a prolonged period of their application (min. 14 days). Furthermore many patients do not respond to pharmacological treatment (drug resistance), or have them relapse. A promising alternative to conventional antidepressants may be the use of combination therapy. Several data indicate that some drugs (for example neuroleptics), or other compounds (eg. lithium) may enhance the effects of given together antidepressants. Both clinical and preclinical studies also showed the benefits of zinc supplementation in antidepressant therapy. Interestingly, co-administration with inactive (in monotherapy) doses of various antidepressants and zinc resulted in a reduction of depressive symptoms. This therapy proved to be effective also in drug-resistant patients. It is even hypothesized that a zinc deficiency may have a dominant role in the development of drug resistance. Unfortunately, despite many years of research on the role of zinc in both the pathogenesis and treatment of depression, are still relatively poorly understood mechanisms, which would explain why zinc may enhance the effects of antidepressant drugs. Their carefully examine, primarily would provide some evidence for the efficacy of the combination therapy and would explain what changes occurring at the cellular level determine its effectiveness. Get the answers to these questions, may lead, in the future, to the development of new forms of therapy of depression (based on new scientific evidence) and, above all, to change approach to medical practitioners treating patients.

To characterize the cellular mechanisms associated with the synergistic effects of zinc and antidepressants for depression symptoms, this scientific project focuses on a series of studies using animal model of depression (Animal models of depression are research tools used to investigate depression and action of antidepressants as a simulation to investigate the symptomatology and pathophysiology of depressive illness or used to screen novel antidepressants). The administration of antidepressants or other alternative, effective therapy results in a reduction or elimination of symptoms of depression, which proves their potential effectiveness. The first aim of our study is to examine the effect of treatment with zinc and fluoxetine (one of the commonly used clinical antidepressants from SSRIs group) on the behavior of mice subjected to chronic restrained stress (CRS; one of the best-validated models of depression) procedure. In the second part of the project, a series of biochemical studies in the blood serum and brain tissues (hippocampus, frontal cortex) will be performed to examining the changes in the level (or activities) of various proteins (including proteins involved in the epigenetic regulation) and genes encoding them after co-treatment with zinc and fluoxetine. Obtained results will allow to confirm or exclude the importance of each proteins tested in the action of zinc potentiation.

This project will allow, for the first time, to describe in a comprehensive manner the alterations in the brain after combined administration of zinc and fluoxetine. At the same time, it will be possible to distinguish changes monotherapy of zinc or fluoxetine between poly-therapy of zinc and fluoxetine administration. The results of work will be the subject of presentations at international scientific conferences, scientific publications, and partially to the achievements of dissertation project manager. Moreover, they can be an introduction to further, more extensive research and can provide new search for effective antidepressant therapies.