

Depression is the most common mental disorder. Based on the global statistics, approximately 15-18% of the people manifested symptoms of depression. World Health Organization (WHO) is predicted that by the year 2020, depression will be the second leading cause of world disability. The relationship between suicide and depressive disorders is an important issue (the suicide attempts and/or suicidal ideations are reported in up to 20% of depressed patients). Depression is a heterogeneous disease with multifactorial etiology. Genetic, neurochemical and environmental factors probably interact at many different levels to play a role in the onset and progression of this disorder.

Depression often occurs in association with other medical conditions such as cancers, diabetes or neurodegenerative disorders. Nowadays, this is not only a clinical, but also social and economic problem. Patients who experience depression have a limited ability to work, which results in their absences and generates billions in losses for businesses around the world. The mental condition of patients (related with persistent sadness, fear, anxiety) is a state which significantly impairs proper functioning of individuals in normal life.

Despite decades of research on depression, the mechanisms of antidepressant action, are not sufficiently known. Modern antidepressants require long-term use, which is necessary to achieve satisfactory therapeutic effect. Many patients take their antidepressant for 14 weeks or less. No effects for typically used antidepressant treatment is common occurrence and have a crucial role on the further clinical course of this disease. Moreover, there is no certainty that received drug will be effective, since about 30% of patients are resistant to antidepressant treatments. Taking this into consideration, seems to be necessary to undertake the studies aimed at deepening the knowledge about the molecular as well as cellular mechanisms involved in development of depressive disorders and gives opportunity to create novel therapeutic and diagnostic methods.

A growing number of evidences confirm the role of inflammation in the pathogenesis of major depressive disorder (MDD). Increased levels of pro-inflammatory cytokines have repeatedly been reported in depressed patients. Molecular signs of inflammation linked to depression, have been identified in clinical, *post-mortem* and animal studies. For a long time, the inflammatory theory of depression was considered as one of the several, presented only individually dysfunctional. New evidence shows that depression is not only caused by inflammatory alterations but also is related with activation of oxidative stress pathway, that contributes to the induction of apoptosis in astrocytes and oligodendrocytes. In addition, synergism between activated inflammatory system and increased oxidative stress, may be a crucial mechanism underlying depression.

Inflammatory and oxidative stress processes are regulated by factors/proteins, in which the Nrf2 nuclear transcription factor has important relevance to development of depression. The Nrf2 has also been proposed as a novel pharmacological target for neuropathology related with disturbance of inflammatory and oxidative stress in depression.

The aim of the presented project is to examine the role of Nrf2 nuclear transcription factor in the regulation of OB-induced depressive-like behavior in mice. In preclinical studies some animal models of depression are used, which allow mimicking depressive symptoms similar to the symptoms occurring in human. In the first part of this project the potential antidepressant effect of (*R,S*) – Sulforaphane (isothiocyanate; selective activator of Nrf2 nuclear transcription factor) in mice subjected to the olfactory bulbectomy procedure will be investigated. Next, the levels and/or activity of selected proteins and genes encoding them, will be determined using advanced molecular techniques. Results of these analyses allow to confirm (or exclude) the role of Nrf2 activation in the regulation of depression-like behavior.

The obtained results of proposed project, will contribute to a better understanding of the pathomechanisms of depression and potential therapeutic usefulness of Nrf2-activating compounds.

The results of this work will be presented at national and international conferences. In addition, the obtained results will be included in the PhD Thesis of the Principal Investigator.