PRELUDIUM 11

TITLE: EFFECT OF MODULATION OF THE GPR39 RECEPTOR ON GLUTAMATERGIC AND GABAERGIC TRANSMISSION IN THE CONTEXT OF ANTIDEPRESSANT AND ANXIOLYTIC ACTIVITY

Depression is one of the most common mental disorders which affects millions of people worldwide. Main problems of the pharmacotherapy of depression include long waiting time for expected therapeutic effects, numerous side effects and treatment-resistant depressions that occur in some patients. Researchers are constantly working in order to understand, still unclear, pathomechanism of mood disorders and to explain the mechanism of action of currently used drugs.

Within this project I plan to focus on the role of the GPR39 zinc receptor in depression and anxiety - disorders that often co-occur in patients. In the past two decades there have been numerous reports supporting the role of zinc in depression, both in preclinical and clinical tests. There were also performed many studies on the relationship of the GPR39 with depression as well as its participation in the mechanism of action of some antidepressants. The aim of my project is to evaluate effects induced by modulation of the GPR39 receptor on two major neurotransmitter systems of the brain -gabaergic (inhibitory) and glutamatergic (stimulatory). For this purpose there will be performed behavioural tests in mice, used to measure potential antidepressant and anxiolytic effects. Animals will be treated with the compound stimulating the GPR39 function (TC G-1008), together with substances that affect functioning of the receptors of the two above mentioned systems. Mice will be given the acute and chronic treatment. Further studies will be performed to evaluate the adaptive changes that occur as a result of the modulation of the GPR39 and other selected receptors. It will be observed as decreased or increased levels of receptor proteins.

Collected data will significantly contribute to the explanation of the role of GPR39 in the pathogenesis of depressive and anxiety disorders . They will also significantly broaden the knowledge about interactions between the GPR39 and the transmission systems of the brain. Results obtained within the project will also provide information about the effects of TC G -1008 and may indicate the direction of development of innovative drugs for the treatment of psychiatric disorders.