DESCRIPTION FOR THE GENERAL PUBLIC

The comorbidity of type 2 diabetes and schizophrenia has been long recognized, but the mechanisms of this phenomenon remain unclear. One possibility is that these two disorders share genetic risk factors. We suppose, based on evidence resulting from published data and our research, that one of the genes associated with type 2 diabetes might be one of them. It was recently discovered that TCF7L2 is a central regulator of genes that are involved in glucose and lipid metabolism in liver cells. This explains, at least partly, its role in developing type 2 diabetes. The pioneering research of our group demonstrated that TCF7L2 is also present in a high level in the thalamus, which is a brain structure involved in transmission and modification of information from sense organs. The thalamus plays a very important role in the proper functioning of the brain and is involved in many pathological conditions including schizophrenia. The role of TCF7L2 in the brain is not known. In our project, we hypothesize that TCF7L2 regulates metabolism in the thalamus, just as it happens in the liver, and that its abnormal activity in the brain can lead to behavioral deficits. The aim of the project is to test these hypotheses. In this project, we will study genetically modified mice which have removed *Tcf7l2* gene specifically in the thalamus. This model has been already generated in our laboratory. In part of the experiments, we will induce diabetes in these and control mice by feeding them with a high-fat diet. To find out if TCF7L2 is involved in maintaining proper metabolism in the thalamus, we will measure the expression of metabolic genes and levels of metabolites, using advanced methods such nuclear magnetic resonance spectroscopy. The mice will be also subjected to behavioral testing. The test results should clarify what is the functional role of the TCF7L2 in the brain and provide evidence for understanding the biological basis of mental disorders and their comorbidity with metabolic disorders.