

Vitamin B<sub>12</sub> (cobalamin) deficiency, leads to significant changes in cell metabolism, the clinical manifestations of which predominantly are hematological (anemia), neurological and psychiatric symptoms. Limb numbness, depression, memory deficits, personality disorders and ataxia may occur. The mechanism of nervous system dysfunction associated with vitamin B<sub>12</sub> deficiency has not yet been fully elucidated. Despite advances in medicine, these disorders may be irreversible. Recent scientific reports indicate the role of vitamin B<sub>12</sub> deficiency in the pathogenesis of neurodegenerative diseases, including Alzheimer's disease, multiple sclerosis, and Parkinson's disease.

It is worth emphasizing, that in addition to absorption disorders and diet deficiencies, the risk factors for hipocobalaminemia include old age and chronic pharmacotherapy of the common antidiabetic drug, metformin, as well as gastric acid secretion inhibitors, used to treat gastric ulcers and gastroesophageal reflux. Vitamin B<sub>12</sub> deficiency is therefore a current health problem in the aging and drug-abusing society.

The aim of the first step of this project is to develop an *in vitro* model of cobalamin deficiency by optimizing the conditions of nervous system cells culture in the presence of vitamin B<sub>12</sub> antagonist – hydroxocobalamin [c-lactam]. Intracellular metabolic disorders in the state of cobalamin deficiency result in the accumulation of homocysteine and methylmalonic acid. The extra- and intracellular concentrations of these metabolites, as markers of cobalamin deficiency in cell culture, will be determined by immunoenzymatic assays. The next step will be to investigate the effect of vitamin B<sub>12</sub> deficiency on the homeostasis of nervous system cells. It is planned to determine the intracellular concentration of reactive oxygen species and the level of reduced thiols, as well as analysis of antioxidant enzymes activity. Moreover, the project involves the investigation of apoptosis and cell cycle in the cells population, under conditions of vitamin B<sub>12</sub> deficiency.

This project provides an opportunity to broaden the knowledge regarding the pathomechanism of hipocobalaminemia-induced nervous system disorders, and to explain, at the cellular level, the role of vitamin B<sub>12</sub> deficiency in the development of neurodegenerative diseases.