

Stroke is one of the major causes of death and disability in adults worldwide. In Poland every year approximately 70 000 people suffer from stroke. About 80% of strokes are ischemic. Unfortunately, there are no neuroprotective strategies that will be effective in stroke.

During the early phase of cerebral ischemia there is a huge increase of extracellular glutamate which causes the overstimulation of glutamatergic receptors and leads to irreversible damage of neural and glial cells. Glutamate is released into the synaptic cleft from vesicles located in presynaptic terminals. The neurotransmitter is loaded into these vesicles through vesicular glutamate transporters (VGLUTs).

The main goal of the project is to investigate the role of vesicular glutamate transporters (VGLUTs) in cerebral ischemia. In order to provide a more detailed insight, two models will be used in the study: i) *in vivo* model of focal brain ischemia caused by middle cerebral artery occlusion in rats and ii) *in vitro* model of oxygen-glucose deprivation in primary neuronal cells. Efficacy of VGLUTs inhibition by CSK6B *in vivo* will be compared with two established preconditioning methods. For *in vitro* studies one preconditioning strategy will serve as a comparator.

So far, results of studies on neuroprotection failed in clinical trials in stroke patients. Thus, modulation of VGLUTs influencing glutamate release seems to be an interesting option to study in depth in the context of cerebral ischemia. Moreover, since glutamate-mediated toxicity plays a significant role in many neurodegenerative disorders (e.g., amyotrophic lateral sclerosis, Parkinson's disease) and VGLUTs were found to be important for pathophysiology of epilepsy, schizophrenia, or neuropathic pain, results of this project can be hopefully useful for studies on other neurological pathologies, which still wait for effective therapeutic strategies.