Alarming statistic reports, classify brain stroke as one of the most common cause of premature death in the European Union and the most common cause of long-term disability among adults. However, **the true burden related with ischemic stroke** is not the number of deaths, **but rather the neurological impairment resulting from it**. It is estimated that only one in four stroke survivors is able to return to carrier life, which means that huge amount of public funds are spent on the medical care of stroke survivors. Despite remarkable progress in drug discovery and a decade of clinical trials in brain stroke, no pharmacological agent able to promote the recovery from stroke, has been successfully introduced to the clinical practice. These evidences clearly highlight that the development of novel therapeutic strategies remains an unmet clinical need.

Ischemic stroke is caused by the blockage of blood flow in the cerebral vessel. Under hypoxic conditions, in the place where the blood supply was interrupted, local necrosis is created, and the tissue surrounding this area is called **the "penumba region".** In this area, the blood reaches a limited amount, resulting in the gradual onset of subsequent cascade of pathological processes involving biochemical changes, chronic neuroinflammation, as well as the **activation of pathological tonic GABA-ergic neurotransmission**. Neurons within the penumbra region are functionally impaired but anatomically undamaged, **which makes this zone potentially salvageable and appropriate for therapeutic interventions**. It has been shown that administration of neuroprotective agent improves the recovery after stroke and reduces further neuronal lost. However, if the proper neuroprotective treatment is not initiated, cells within the penumbra region slowly die.

The results of our research team, as well as other teams, showed that switching the pathological tonic GABA-ergic neurotransmission into phasic GABA-ergic current in the penumbra region, very quickly helps to restore the proper neuron function and reduce neurological deficits resulting from brain stroke. In order to enhance the phasic GABA-current it is crucial to modulate the activity of synaptic subpopulations of receptors, particularly interacting with the α1-GABA-A receptor. **In this project we will develop a library of selective α1-GABA-A, that will be able to intensify the phasic GABA-ergic signalling in the penumbra region, and thus restore the proper neurotransmission and reduce neurological impairment resulting from stroke.**

As currently there is no pharmacotherapy approved for the treatment of neurological impairments for brain stroke survivors, the results of this project will pave the way for search for new therapeutic possibilities and may become a starting point for the development of novel pharmacological agents.