Regeneration of the injured spinal cord is one of the most challenging, unsolved tasks in medicine. In case of severe spinal cord injury (SCI) resulting in deep impairment of function, spontaneous recovery is extremely limited and, despite many trials, patients still don't have effective therapies. The majority of spinal cord injuries are due to road traffic crashes, falls or violence. Taking into account increasing intensity of traffic and that people with a SCI are two to five times more likely to die prematurely than people without a spinal cord injury; SCI should not only be considered as a personal tragedy, but also it carried substantial costs for the individual and society.

Undoubted progress in research led to promising trials of combined therapies using electrical stimulation and pharmacotherapy, which, however, also revealed their limitations. There is still need for further search for effective approaches that stimulate both the nervous and muscle function. One of the most promising approaches to cure injured spinal cord is the use of potential of neurotrophins – cellular, releasable proteins, that promote neuronal survival. Although there were many experiments that focused on administration of those substances after SCI, none of them resulted in clinical applications yet. General reason of failures is that our knowledge about the mechanisms of their action and mechanisms of neuronal regeneration and reorganization is still very incomplete. Every project that contributes to advanced understanding of these processes is of the essence here.

The aim of this study is to provide an insight in the structure and molecular changes related to function of peripheral synapses in hindlimb muscles, after spinal cord injury (SCI) and treatment with brain–derived neurotrophic factor (BDNF).

Conducted experiments revealed that in a model of complete SCI, early robust locomotor improvement may be achieved in rodents, if the level of BDNF is up-regulated. Unfortunately, after several weeks symptoms of functional over-reactivity develop. The aim of this proposal is therefore to explore and explain the early, positive effect of BDNF on hindlimb sensory-motor system of the rat after complete SCI, with a focus on neuromuscular junctions, and changes which may prone the system to hyperexcitability.

In project animals will be subjected to complete spinal cord transection at low thoracic segment. BDNF upregulation will be evoked by intraspinal administration of safe viral vector AAV carrying BDNF transgene. The tasks of the current proposal will be achieved by the means of novel, highly sensitive method of imaging of local gene expression combined with protein localization, accompanied by electron microscope imaging of synapse ultrastructure. Neurotransmitter receptors and their accessory molecules, BDNF receptors, Symptoms of secretory activity of perijunctional Schwann cells and myocyte components will be studied. Obtained data are expected to provide wider knowledge and more complete picture of how BDNF administered to the spinal cord influences peripheral synaptic machinery after injury. Such knowledge will be valuable for developing therapies that improve the quality of life of people with SCI and muscular atrophies.