Project 1.5 Modulation of the injured nerve microenvironment to support axon regeneration and spinal cord motoneuron survival

Supervisor: Małgorzata Zawadzka PhD, DSc
Laboratory: Laboratory of Neuromuscular Plasticity

Background:

The Ph.D. candidate will participate in the implementation of research tasks of the NCN OPUS project, entitled " Modulation of the injured nerve microenvironment to support axon regeneration and spinal cord motoneuron survival - molecular mechanisms and functional implications".

The ability of axonal regeneration after peripheral nerve injury is significantly higher in adults than in neonates. Developing motoneurons are very sensitive to breaking the connection with the muscles they innervate, which are the source of trophic factors necessary for their proper functioning. In rats, during the critical period of development, in the first five days of life, the majority of motorneurons die after injury to their axons. This specific sensitivity of neurons to axonal injury declines during the first week of life. When axons are injured on or after the day fifth of birth, the entire neuron pool survives and reinnervates the muscles. Mechanisms responsible for this impairment of peripheral nerve regeneration in the early period of postnatal development remain unknown.

In the proposed project, we will verify the hypothesis that transplantation of an experimentally modified sciatic nerve will improve the regeneration of damaged axons, reduce the mortality of motor neurons and enable the reconstruction of motor functions lost as a result of peripheral nerve injury. Research tasks focus on modulating of expression of selected microenvironmental factors produced in the damaged peripheral nerves that may support axonal regeneration and reconstruction of neuromuscular connections, and ultimately restoration of lost motor functions.

Methodically, the project utilizes both traditional neuroanatomical (immunofluorescence, fluorescent and confocal microscopy) and neurophysiological methods as well as in vitro cell culture techniques and modern high-throughput molecular biology techniques such as RNA-Seq and gene expression analysis.

Key responsibilities of Ph.D. candidate will include:

1. participation in planning and conducting experimental work
2. conducting experiments using in vitro cell cultures
3. analysis of gene expression using RNA-Seq, RT-PCR and in situ hybridization
4. participation in experiments conducted in vivo in animal models (rodents)
5. data analysis and reporting the results
6. manuscript preparation

Aim:

The project aim is to understand the role of experimentally selected inhibitors of regeneration of the damaged nerve by silencing their production and determining whether it will trigger functional improvement. In addition, we will identify the specific profiles of gene expression in motor neurons at an early stage of their reaction to the nerve damage in the presence of pro-regenerative signals or their absence.

Requirements:

- M.Sc. degree (or equivalent) in biology, molecular biology, biochemistry, biotechnology, medical or veterinary sciences,
- exceptional motivation for scientific research. Strong interest in neuroscience,
- ability to perform experiments and analyze their results independently,
- hands-on experience in basic molecular biology and/or biochemistry techniques, fluorescent and confocal microscopy as well as in vitro cell culture,
- prior experience in working with animal models will be of advantage but is not mandatory – training will be provided,
- proficiency in spoken and written English,
- previous experience with animal models will be of advantage but is not mandatory,
- general abilities: good work organization, creative thinking, ability to cooperate well as a part of a team,
- A list of scientific publications and/or references of the candidate's thesis tutor will be of advantage but is not mandatory.