Securing balance in tissue homeostasis is one of the major factors to ensuring the proper development of the central nervous system (CNS). In the developing brain, an intense process of neurogenesis is followed by the robust generation of glial cells inherently supporting neurons in their correct functioning. Glial cells perform a vital function in the nervous tissue. Oligodendrocytes are responsible for the myelination in the CNS, due to the process by which the rapid conduction of nerve impulses occur. Microglial cells possess immunomodulatory properties and exert phagocytosis functions, which is the first line of cellular response to tissue injury or the presence of pathogens. According to the most recent studies, they also play an essential role in the development of oligodendrocyte progenitor cells (OPCs) and in myelinogenesis. Two phenotypes of microglia can be distinguished; M1, which are pro-inflammatory and M2, which are anti-inflammatory. Oligodendrocytes, as well as microglia, are extremely sensitive to any changes in the microenvironment, such as a lack of oxygen or trophic support, which may lead to irreversible damage.

Neonatal asphyxia/hypoxic-ischemic (HI) encephalopathy causes brain damage and, as a result, the development of various neurological diseases, which results in a worsening of quality of life. This issue affects 4-6% of full-term births and about 10% of premature babies. According to statistical data, it is also the most common cause of death in children under five. As a result of HI, homeostasis is disturbed in the nervous tissue and, furthermore, the disruption of neuro- and gliogenesis occurs, which leads to, among other things, inhibition in OPCs and the maturation and development of inflammation in the nervous tissue. Currently, only moderate hypothermia is used to alleviate damage, as there is no other available treatment because the mechanism of their formation is not well understood.

Research shows that both oligodendrocytes and microglia secrete a number of substances that can modulate the tissue microenvironment. Preliminary studies strongly suggest that microglia release factors which promote an increase in OPCs proliferation, the process that is inhibited after HI. HI strongly influences the secretory profile of microglia and OPCs. Mutual interactions between these cells may be a key to initiating neurorepair mechanisms due to the secretory activity of both types of glia cells. In addition, the investigation of a neuroprotective factor with immunomodulatory properties such as ghrelin seems promising. Ghrelin is an endocrine peptide that penetrates the blood-brain barrier and reduces HI-induced oxidative stress. However, its effects on oligodendrocyte-microglial interactions have not been studied yet.

The main goal of the proposed project is to examine the interactions between oligodendrocytes and microglia, as well as to analyse the impact of HI on the early stages of CNS development. A key focus of this study will be to identify factors secreted into the culture medium that have a significant effect on oligodendrocyte-microglia interactions and to investigate the neuroprotective potential of ghrelin, thus identifying the handle points for potential regenerative therapies and attempting to understand the hitherto unexplored mechanism of impaired CNS development after HI.

A series of experiments have been planned to investigate the interactions that occur between oligodendrocytes and microglia under physiological normoxia (5% O_2) and under reduced oxygen and trophic support (modelled by the OGD procedure, *oxygen glucose deprivation*), both of which are conditions that imitate HI. We plan to examine the immunomodulatory and neuroprotective potential of ghrelin and secretory activity of oligodendrocytes and microglia (cultivated as monocultures or in co-cultures) in the *in vitro* model of neonatal asphyxia and to analyse a number of cytokines and trophic factors, both in cells and in those released to the culture medium. This will allow the assessment of the effect of changed secretory activity on cell survival, proliferation, differentiation, and their myelinogenic potential. We also plan to study the influence of HI and ghrelin administration to the neonatal rats on the polarization of microglia in the *in vivo* model within the context of the effect of microglia on the myelination efficiency, which will allow an examination into which phenotype of microglia prevails in the developing brain following HI. **The planned experiments will enable the disclosure of basic mechanisms triggered in oligodendroglial and microglial cells by perinatal asphyxia, the evaluation of their mutual interaction, and, finally, indicate potential targets for therapeutic strategies.**