In spite of the steady progress in obstetrics and gynecology care, perinatal asphyxia is still the main cause of neonatal brain injury and subsequent development of neurological disorders. Preterm delivery, which accounts for as much as ten percent of newborns, as well as complications during labor are the major causes of birth asphyxia and make it one of the leading causes of under-five child deaths. The limited supply of oxygen and the transiently reduced cerebral blood flow result in the shortage of trophic support and trigger different mechanisms of cell response. The injury affects fragile, developing brains and usually leads to severe neurological deficits, such as cerebral palsy, mental retardation, epilepsy and spastic paresis. One of the major consequences of an experienced episode of hypoxia-ischemia (HI) are alterations in maturation and metabolisms of oligodendrocytes, which are the only specialized cells myelinating nervous fibers within the central nervous system. Process of myelinogenesis requires expression of large quantities of myelin components and elaboration of highly specialized membrane, forming multilammellar, tightly compacted myelin sheath. It is hypothesized that autophagy is one of the major processes regulating oligodendrocyte differentiation and the proper functioning.

Autophagy is a physiological mechanism based on degrading and recycling selected cellular biomolecules and organelles due to forming a multimembrane intermediate compartment. As one of the major mechanisms involved in maintaining tissue homeostasis in response to various forms of stress, autophagy is believed to be modulated by a temporary limitation of glucose and oxygen supply, evoked by an episode of perinatal asphyxia. In fact, intracellular pathways and the intensity of this process are thought to be one of the major mechanisms involved in the initiation of either physiological neuroregeneration or development of neurodegenerative disorders, associated with poor neurodevelopmental outcomes in the survived babies. Therefore the modulation of the autophagy process could be a novel innovative strategy in providing neuroprotection and promoting natural, endogenous reparative processes. However, studies on process of autophagy in oligodendroglial cells are still scarce and to date moderate hypothermia is the only available clinical intervention after perinatal asphyxia. Moreover, as revealed by the latest clinical data, hypothermia actually neither provides complete brain protection nor efficiently stimulates endogenous neuroreparative processes. New treatment options are therefore urgently needed to protect fragile developing brains from the fatal consequences of HI damage and to restore proper physiological functioning of the injured nervous tissue.

To address this issue, **the main aim of the study is to describe way(s) in which oligodendroglial autophagy proceeds and to fill in the gaps in the knowledge concerning mechanisms of the oligodendrocyte involvement in the development of fatal consequences of perinatal, asphyxic injury.** With aim of comprehensively evaluating autophagy processes in oligodendrocyte differentiation and functioning within the nervous tissue, six different working model systems will be used in joint research project of experts from Polish and Swiss laboratories. The intracellular pathways of signal transduction, potentially engaged in oligodendroglial autophagy, will be studied by means of the advanced methods of molecular biology. The proposed approach is also innovative in context of preclinical studies aimed at elaborating effective treatments for neonatal HI and would contribute to identifying potential new therapeutic targets.

The present project aims at **getting insight into previously unexplored aspects of process of autophagy in oligodendroglial cells after perinatal brain damage.** The designed approaches address the issue of elaborating effective therapy dedicated to improve CNS myelination and preventing white matter disorders which are known to have dramatic consequences on neurodevelopment.