

Oligodendrocytes are glial cells that are the source of myelin in the vertebrate central nervous system. Myelin provides an electrically insulating layer along the axons and is indispensable for the conduction of nerve impulses and neuronal survival. The myelin sheath formed by oligodendrocytes can be destroyed as a consequence of various insults to the nervous tissue, such as spinal cord injury (SCI), or as a result of inflammatory-demyelinating neurological disorders such as multiple sclerosis (MS). The primary injury to the myelin sheath is followed by degeneration and loss of demyelinated axons leading to progressive neurological disability. In Poland MS affects approximately 40 000 young individuals. Also, each year over 2500 people in Poland suffer from a traumatic SCI and a recent estimate puts the number of people living with paralysis at 4 million worldwide. In all these patients the restoration of the myelin sheath (remyelination) is largely inefficient which gives rise to serious health and social problems.

Mature oligodendrocytes, which can produce myelin, derive as a result of differentiation of oligodendrocyte precursor cells. Oligodendrocyte precursor cells and intracellular mechanisms involved in their differentiation have been extensively studied but, up to now, the reasons of remyelination failure are poorly understood. Our preliminary data show that transient inhibition of ribosome biogenesis, which gives rise to nucleolar stress, can trigger oligodendrocyte differentiation. Thus, in our studies we plan to establish the influence of inhibitors of ribosome biogenesis and of nucleolar proteins on oligodendrocyte differentiation and myelination processes. We plan to conduct our experiments on rat primary oligodendrocyte precursor cells and on human oligodendrocyte MO3.13 cell line. We will analyze cell morphology, estimate the level of oligodendrocyte differentiation markers and of nucleolar proteins after inhibition of ribosome biogenesis.

We believe that our studies will make us better understand the mechanism involved in differentiation of oligodendrocyte precursor cells and in the process of myelination. Also, we are convinced that results obtained during realization of this project will create sufficient basis for development of new drugs/therapies enhancing oligodendrocyte differentiation and myelination processes that can be used in treatment of spinal cord injury (SCI) and multiple sclerosis (MS).