Scientists identify inhibitor of myelin formation in the central nervous system

November 20 2012

Scientists at the Mainz University Medical Center have discovered another molecule that plays an important role in regulating myelin formation in the central nervous system. Myelin promotes the conduction of nerve cell impulses by forming a sheath around their projections, the so-called axons, at specific locations – acting like the plastic insulation around a power cord. The research team, led by Dr. Robin White of the Institute of Physiology and Pathophysiology at the University Medical Center of Johannes Gutenberg University Mainz, recently published their findings in the prestigious journal *EMBO Reports*.

Complex organisms have evolved a technique known as saltatory conduction of impulses to enable nerve cells to transmit information over large distances more efficiently. This is possible because the specialized nerve cell axonal projections involved in conducting impulses are coated at specific intervals with myelin, which acts as an insulating layer. In the central nervous system, myelin develops when oligodendrocytes, which are a type of brain cell, repeatedly wrap their cellular processes around the axons of nerve cells forming a compact stack of cell membranes, a so-called myelin sheath. A myelin sheath not only has a high lipid content but also contains two main proteins, the synthesis of which needs to be carefully regulated.

The current study analyzed the synthesis of myelin basic protein (MBP), a substance which is essential for the formation and stabilization of myelin membranes. In common with all proteins, MBP is generated in a

two-stage process originating from basic genetic material in the form of DNA. First, DNA is converted to mRNA, which, in turn, serves as a template for the actual synthesis of MBP. During myelin formation, the synthesis of MBP in oligodendrocytes is suppressed until distinct signals from nerve cells initiate myelination at specific "production sites". To date, the mechanisms involved in the suppression of MBP synthesis over relatively long periods of time have not been understood. This is where the current work of the Mainz scientists comes in, as they were able to identify a molecule that is responsible for the suppression of MBP synthesis.

"This molecule, called sncRNA715, binds to MBP mRNA, thus preventing MBP synthesis," explains Dr. Robin White. "Our research findings show that levels of sncRNA715 and MBP inversely correlate during myelin formation and that it is possible to influence the extent of MBP production in oligodendrocytes by artificially modifying levels of sncRNA715. This indicates that the recently discovered molecule is a significant factor in the regulation of MBP synthesis."

Understanding the molecular basis for myelin formation is essential with regard to various neurological illnesses that involve a loss of the protective myelin layer. For example, it is still unclear why oligodendrocytes lose their ability to repair the damage to myelin in the progress of multiple sclerosis (MS). "Interestingly, in collaboration with our Dutch colleagues, we have been able to identify a correlation between levels of sncRNA715 and MBP in the brain tissue of MS patients," Robin White continues. "In contrast with unaffected areas of the brain in which the myelin structure appears normal, there are higher levels of sncRNA715 in affected areas in which myelin formation is impaired. Our findings may help to provide a molecular explanation for myelination failures in illnesses such as multiple sclerosis."

More information: Bauer, Nina M. et al., Myelin Basic Protein

synthesis is regulated by small non-coding RNA 715, EMBO Reports 2012:13, 827-834
doi:10.1038/embor.2012.97