Novel mouse model of demyelinating disorder

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In the February 1st issue of G&D, Dr. Brian Popko (The University of Chicago) and colleagues describe how mutation of a gene called ZFP191 leads to disordered CNS myelination in mice -- reminiscent of what is seen in human multiple sclerosis (MS) patients.

MS is a chronic autoimmune disorder, in which the body attacks and destroys the myelin sheath that insulates and protects nerve fibers of the central nervous system (the brain, spinal cord and optic nerves). Demyelination disrupts the conduction of electrical impulses along nerve fibers, and results in regional neural deficits. MS symptoms range from tingling and numbness in limbs, to loss of vision and paralysis.

It is estimated that MS affects 400,000 people in the US and approximately 2.5 million worldwide.

Dr. Popko and colleagues identified a gene called ZFP191 as being necessary for the development of oligodendrocyte cells, which - in their fully mature form - produce myelin. The researchers found that mice harboring a single mutation in ZFP191 display tremors and seizures, caused by a severe deficiency in CNS myelination.

ZFP191 appears to be the first factor identified to be critical for the myelinating function of oligodendrocytes.

The failure of Zfp191-mutant mouse oligodendrocytes to successfully myelinate their targets is reminiscent of human MS lesions, where re-

myelination of damaged tracts fails to occur efficiently even when apparently mature oligodendrocytes are present in the area.

While further research to delineate the precise targets of ZFP191 is needed, this work holds promising clinical value as a potential therapeutic pathway to promote re-myelination, reduce the accumulation of MS lesions and slow disease progression.

More information: The paper will be released online ahead of print at www.genesdev.org.

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