PLP1 gene

proteolipid protein 1

Normal Function

The *PLP1* gene provides instructions for producing proteolipid protein 1 and a modified version (isoform) of that protein called DM20. Proteolipid protein 1 is found primarily in the brain and spinal cord (the central nervous system). DM20 is produced mainly in the nerves that connect the brain and spinal cord to muscles (the peripheral nervous system). These two proteins are found within the cell membrane of nerve cells called oligodendrocytes, which help coat nerve cells with a protective layer called myelin. Myelin is the fatty sheath that insulates nerve fibers and promotes the rapid transmission of nerve impulses. Proteolipid protein 1 and DM20 make up a large proportion of myelin and help myelin stay anchored to the cells.

Health Conditions Related to Genetic Changes

Pelizaeus-Merzbacher disease

Hundreds of variants (also called mutations) in the *PLP1* gene have been found to cause Pelizaeus-Merzbacher disease. Pelizaeus-Merzbacher disease is an inherited condition that involves the central nervous system and that primarily affects males. Individuals with Pelizaeus-Merzbacher disease have neurological problems including abnormal eye movements (nystagmus) and other movement abnormalities. Some affected individuals have difficulty walking, while others are not able to walk.

An extra copy (duplication) of the *PLP1* gene accounts for 50 to 70 percent of variants that cause Pelizaeus-Merzbacher disease. In many cases, genes near the *PLP1* gene are also duplicated, but having extra copies of these genes does not seem to impact the severity of the condition. In another 10 to 25 percent of cases, variants change single protein building blocks (amino acids) in the proteolipid protein 1 and DM20 proteins. This can cause cells to produce too much protein or to produce abnormal proteins that are often misfolded. Excess or abnormal proteins become trapped within cell structures and cannot travel to the cell membrane. This accumulation of proteins leads to the swelling and breakdown of nerve fibers. In less than 2 percent of cases, a variant that deletes the entire *PLP1* gene causes Pelizaeus-Merzbacher disease. This deletion prevents cells from producing proteolipid protein 1 and DM20 protein.

All of these *PLP1* gene variants prevent proteolipid protein 1 and DM20 from reaching

the nerve cell membrane where they are needed to form myelin. Decreased myelin production leads to nerve damage and the loss of nerve fibers that are covered by myelin (leukodystrophy). As a result, nervous system functions are impaired, which leads to the signs and symptoms of Pelizaeus-Merzbacher disease.

Spastic paraplegia type 2

Several variants in the *PLP1* gene are known to cause spastic paraplegia type 2. Spastic paraplegia type 2 belongs to a group of disorders called hereditary spastic paraplegias, which are characterized by muscle stiffness (spasticity) and weakness that worsens over time and paralysis of the lower limbs (paraplegia). Hereditary spastic paraplegias are divided into two types depending on their signs and symptoms: pure and complex. Spastic paraplegia type 2 can be classified as either pure or complex. The pure type of this condition is more common. The complex type of spastic paraplegia type 2 is sometimes called hypomyelination of early myelinating structures (HEMS). Spastic paraplegia type 2 primarily affects males beginning in early childhood, but females often develop signs and symptoms of the condition in adulthood.

Generally, the *PLP1* gene variants that cause spastic paraplegia type 2 disrupt the production of the proteolipid 1 protein but do not interfere with the production of DM20. Changes in the proteolipid 1 protein appear to impair its function, resulting in reduced myelin production (hypomyelination). People with HEMS typically have more severe hypomyelination than people with the pure type of spastic paraplegia type 2. If nerves are not properly myelinated during development, the nervous system does not function as it should, resulting in the signs and symptoms of spastic paraplegia type 2. It is thought that because people with spastic paraplegia type 2 are able to produce some myelin, their signs and symptoms are milder than those of people with Pelizaeus-Merzbacher disease.

Other Names for This Gene

- lipophilin
- major myelin proteolipid protein
- MMPL
- MYPR_HUMAN
- PLP
- PLP/DM20

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of PLP1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5354[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=((PLP1%5BTIAB%5D)+OR+(proteolipid+protein+1%5BTIAB%5D))+AND+((Genes%5BMH%5D)+OR+(Genetic+Phenomena%5BMH%5D))+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- PROTEOLIPID PROTEIN 1; PLP1 (https://omim.org/entry/300401)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/5354)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=PLP1[gene])

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Genomic Location

The *PLP1* gene is found on the X chromosome (https://medlineplus.gov/genetics/chromosome/x/).

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