# PLP1 Gene

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Contributor: Lily Guo

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## 1. Introduction

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 nerves in the brain and spinal cord (the central nervous system) and DM20 is produced mainly in 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, where they make up a large proportion of myelin and help myelin stay anchored to the cells. Myelin is the fatty covering that insulates nerve fibers and promotes the rapid transmission of nerve impulses.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Pelizaeus-Merzbacher disease

There are more than 280 mutations in the *PLP1* gene that have been found to cause Pelizaeus-Merzbacher disease. Pelizaeus-Merzbacher disease is an inherited condition involving the central nervous system that primarily affects males. Individuals with Pelizaeus-Merzbacher disease have neurological problems including abnormal eye movements (nystagmus) and other movement abnormalities. In addition, these individuals have difficulty walking or cannot walk.

An extra copy (duplication) of the *PLP1* gene accounts for 50 to 70 percent of all Pelizaeus-Merzbacher disease mutations. 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, mutations change single protein building blocks (amino acids) in the proteolipid protein 1 and DM20 proteins and lead to excess or abnormal proteins that are often misfolded. Excess or abnormal proteins become trapped within cell structures and cannot travel to the cell membrane. The accumulation of excess proteins leads to swelling and breakdown of nerve fibers. In less than 2 percent of cases, a mutation that deletes the entire *PLP1* gene causes Pelizaeus-Merzbacher disease. Such a deletion prevents production of proteolipid protein 1 and DM20 protein.

All of these *PLP1* gene mutations 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 fiber damage and the loss of nerve fibers that are covered by myelin (leukodystrophy), leading to impairment of nervous system function and the signs and symptoms of Pelizaeus-Merzbacher disease.

### 2.2. Spastic paraplegia type 2

More than 20 mutations in the *PLP1* gene that cause spastic paraplegia type 2 have been identified. Spastic paraplegia type 2 is characterized by movement problems, particularly muscle stiffness (spasticity) in the lower limbs that worsens over time. Generally, *PLP1* gene mutations 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. It is thought that because there is some remaining myelin production, the signs and symptoms of spastic paraplegia type 2 are milder than those of Pelizaeus-Merzbacher disease (described above).

## 3. Other Names for This Gene

- lipophilin
- major myelin proteolipid protein

- MMPL
- MYPR_HUMAN
- PLP
- PLP/DM20

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