# CLN8 Gene

Subjects: Genetics & Heredity
Contributor: Vicky Zhou

CLN8, transmembrane ER and ERGIC protein

genes

## 1. Normal Function

The *CLN8* gene provides instructions for making a protein whose precise function is not known but that is thought to play a transport role within cells. Specifically, the CLN8 protein likely helps to move materials in and out of a cell structure called the endoplasmic reticulum, which is involved in protein production, processing, and transport. The CLN8 protein may also play a role in helping the endoplasmic reticulum regulate levels of fats (lipids) in cells. In certain cells, including nerve cells, the CLN8 protein is thought to be active outside of the endoplasmic reticulum, but its function is unknown.

## 2. Health Conditions Related to Genetic Changes

### CLN8 Disease

At least 25 mutations in the *CLN8* gene have been found to cause CLN8 disease. CLN8 disease is an inherited disorder that varies in severity and primarily affects the nervous system. The less-severe form of CLN8 disease is characterized by recurrent seizures (epilepsy) and a decline in intellectual function that begins between ages 5 and 10. Individuals with the less-severe form of CLN8 disease often live into late adulthood. People with the more-severe form of CLN8 disease experience a gradual worsening of motor and cognitive skills, epilepsy, and vision loss. In this form, signs and symptoms typically appear between ages 2 and 7. Individuals with the more-severe form of CLN8 disease usually survive only into late childhood or adolescence.

A specific mutation that replaces the protein building block (amino acid) arginine with the amino acid glycine at position 26 in the CLN8 protein (written as Arg26Gly or R26G) is found in all individuals from a northern region of Finland who have the less-severe form of CLN8 disease. This mutation probably leads to production of a protein with reduced function. Because there is likely still some normal function of the CLN8 protein, features of this form are less severe compared to other cases of CLN8 disease. Affected individuals have a reduction in the levels of certain lipids in the brain, likely due to a decrease in CLN8 protein activity, but the effects of this reduction are unclear. Individuals with this form of CLN8 disease have mild brain abnormalities resulting from nerve cell death in the brain, but the cause of this cell death is unknown.

Some *CLN8* gene mutations that cause the more-severe form of CLN8 disease likely drastically reduce the function of the CLN8 protein. Other mutations likely impair transport of the protein to the endoplasmic reticulum, so that it cannot perform its function. It is unclear how a loss or reduction of CLN8 protein leads to the signs and symptoms of CLN8 disease. In the more-severe form of CLN8 disease, proteins and other substances accumulate in cell structures called lysosomes. While accumulations of these substances occur in cells throughout the body, nerve cells appear to be particularly vulnerable to damage caused by the abnormal cell materials; however, it is unclear how mutations in the *CLN8* gene are involved in this buildup. Widespread loss of nerve cells in CLN8 disease leads to the neurological signs and symptoms and, in the case of the more-severe form, early death.

## 3. Other Names for This Gene

- C8orf61
- ceroid-lipofuscinosis, neuronal 8
- ceroid-lipofuscinosis, neuronal 8 (epilepsy, progressive with mental retardation)
- CLN8_HUMAN
- EPMR
- FLJ39417

## References

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