

## PRNP gene

prion protein

### Normal Function

The *PRNP* gene provides instructions for making a protein called prion protein (PrP), which is active in the brain and several other tissues. Although the precise function of this protein is unknown, researchers have proposed roles in several important processes. These include the transport of copper into cells and protection of brain cells (neurons) from injury (neuroprotection). Studies have also suggested a role for PrP in the formation of synapses, which are the junctions between nerve cells (neurons) where cell-to-cell communication occurs.

Different forms of PrP have been identified. The normal version is often designated PrP<sup>C</sup> to distinguish it from abnormal forms of the protein, which are generally designated PrP<sup>Sc</sup>.

### Health Conditions Related to Genetic Changes

#### Huntington's disease-like syndrome

A particular type of variant (also called a mutation) in the *PRNP* gene has been found to cause signs and symptoms that resemble those of Huntington's disease, including uncontrolled movements, emotional problems, and loss of thinking ability. Researchers have proposed that this condition be called Huntington's disease-like 1 (HDL1).

The *PRNP* gene variants associated with HDL1 involve a segment of DNA called an octapeptide repeat. This segment provides instructions for making eight protein building blocks (amino acids) that are linked to form a protein fragment called a peptide. The octapeptide repeat is normally repeated five times in the *PRNP* gene. In people with HDL1, this segment is repeated eleven or thirteen times. An increase in the size of the octapeptide repeat leads to the production of an abnormally long version of PrP. It is unclear how the abnormal protein damages and ultimately destroys neurons, leading to the characteristic features of HDL1.

#### Prion disease

Many variants in the *PRNP* gene have been identified in people with familial forms of prion disease, including Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker syndrome (GSS), and fatal familial insomnia (FFI). The major features of

these diseases include changes in memory, personality, and behavior; a decline in intellectual function (dementia); and abnormal movements, particularly difficulty with coordinating movements (ataxia). The signs and symptoms worsen over time, ultimately leading to death.

Some of the *PRNP* gene variants that cause familial prion disease change single amino acids in PrP. Other variants insert additional amino acids into the protein or result in an unusually short version of the protein. These changes alter the structure of PrP, leading to the production of an abnormally shaped protein, known as PrP<sup>Sc</sup>, from one copy of the *PRNP* gene. In a process that is not fully understood, PrP<sup>Sc</sup> can attach (bind) to PrP<sup>C</sup> and promote its transformation into PrP<sup>Sc</sup>. The abnormal protein builds up in the brain, forming clumps that damage or destroy neurons. The loss of these cells creates microscopic sponge-like holes (vacuoles) in the brain, which leads to the signs and symptoms of prion disease.

Researchers have identified several common variations (polymorphisms) in the *PRNP* gene that affect single amino acids in PrP. These polymorphisms do not cause prion disease, but they may affect a person's risk of developing these disorders. Studies have focused on the effects of a polymorphism at position 129 of PrP. At this position, people can have either the amino acid methionine (Met) or the amino acid valine (Val). This polymorphism is written as Met129Val or M129V. Because people inherit one copy of the *PRNP* gene from each parent, at position 129 an individual can receive methionine from both parents (Met/Met), valine from both parents (Val/Val), or methionine from one parent and valine from the other (Met/Val).

The Met129Val polymorphism appears to influence the risk of developing prion disease. Most affected individuals have the same amino acid at position 129 (Met/Met or Val/Val) instead of different amino acids (Met/Val). Having Met/Met at position 129 is also associated with an earlier age of onset and a more rapid worsening of the disease's signs and symptoms.

### Wilson disease

The Met129Val polymorphism has been reported to influence the onset of Wilson disease, an inherited disorder in which excessive amounts of copper accumulate in the body. Wilson disease is caused by variants in the *ATP7B* gene, but studies suggest that symptoms of Wilson disease begin several years later in people who have Met/Met at position 129 in PrP compared with those who have Met/Val or Val/Val. Other research findings indicate that this polymorphism may also affect the type of symptoms that develop in people with Wilson disease. Having Met/Met at position 129 appears to be associated with an increased occurrence of symptoms that affect the nervous system, particularly tremors.

### Other disorders

The Met129Val variation has been associated with differences in performance on long-term memory tasks among healthy young adults. In one study, people who had either Met/Met or Met/Val at position 129 performed better at long-term memory tasks than

those who had Val/Val. It is unclear how these differences may be related to memory.

### **Other Names for This Gene**

- AltPrP
- ASCR
- CD230 antigen
- CJD
- GSS
- MGC26679
- PRIO\_HUMAN
- prion protein (p27-30) (Creutzfeldt-Jakob disease, Gerstmann-Strausler-Scheinker syndrome, fatal familial insomnia)
- PRIP
- PrP
- PrP27-30
- PrP33-35C
- PrPc
- PrPSc

### **Additional Information & Resources**

#### Tests Listed in the Genetic Testing Registry

- Tests of PRNP ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5621\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=5621[geneid]))

#### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28PRNP%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D%29>)

#### Catalog of Genes and Diseases from OMIM

- PRION PROTEIN; PRNP (<https://omim.org/entry/176640>)

#### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/5621>)

- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=PRNP\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=PRNP[gene]))

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## **Genomic Location**

The *PRNP* gene is found on chromosome 20 (<https://medlineplus.gov/genetics/chromosome/20/>).

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