

GRN gene

granulin precursor

Normal Function

The *GRN* gene provides instructions for making a protein called progranulin. This protein is primarily found in the membrane of cellular structures called lysosomes, which are specialized compartments that digest and recycle materials. Within lysosomes, progranulin can be cut (cleaved) into smaller proteins, known as granulins, which are thought to function similar to progranulin.

Progranulin is found in tissues throughout the body, but it is most active in cells that are dividing rapidly, such as skin cells (fibroblasts), immune system cells, and certain brain cells. This protein helps regulate the growth, division, and survival of these cells. It also plays important roles in early embryonic development, wound healing, and the body's immune response to injury (inflammation). Progranulin is active in several types of brain cells. However, little is known about this protein's role in the brain. It appears to be critical for the survival of nerve cells (neurons).

Health Conditions Related to Genetic Changes

CLN11 disease

At least eight mutations in the *GRN* gene have been found to cause CLN11 disease. This condition is characterized by recurrent seizures (epilepsy), vision loss, problems with balance and coordination (cerebellar ataxia), and a decline in intellectual function that typically begin in adolescence or early adulthood.

Most of the *GRN* gene mutations that cause CLN11 disease disrupt how the gene's information is spliced together to make the blueprint for producing the progranulin protein. As a result, there is a complete loss of functional progranulin protein. This lack of progranulin leads to the death of nerve cells in the brain. Although the exact mechanism is unknown, it is thought to involve impaired function of lysosomes. Unlike in *GRN*-related frontotemporal lobar degeneration (described below), people with CLN11 disease do not appear to have build up of the TDP-43 protein in their brain cells. In CLN11 disease, loss of neurons from many regions of the brain leads to the development of epilepsy, cerebellar ataxia, and other signs and symptoms in adolescence or early adulthood.

GRN-related frontotemporal lobar degeneration

More than 65 mutations in the *GRN* gene have been identified in people with *GRN*-related frontotemporal lobar degeneration. This condition is a progressive brain disorder that can affect behavior, language, and movement. The symptoms of this disorder usually become noticeable in a person's fifties or sixties.

The most common *GRN* gene mutation, which is written as Arg493Ter or R493*, creates a premature stop signal in the instructions for making progranulin. Most of the mutations that cause *GRN*-related frontotemporal lobar degeneration prevent any protein from being produced from one copy of the *GRN* gene in each cell. As a result of these genetic changes, cells make only half the usual amount of progranulin. In rare cases, affected individuals have mutations in both copies of their *GRN* gene. Each of these mutations allow for some functional protein to be produced and when measured, the total amount of progranulin produced amounts to about half of the usual amount.

It is unclear how a shortage of progranulin leads to the features of *GRN*-related frontotemporal lobar degeneration. However, studies have shown that the disorder is characterized by the buildup of a protein called TAR DNA-binding protein 43 (TDP-43) in certain brain cells. The TDP-43 protein forms clumps (aggregates) that may interfere with cell functions and ultimately lead to cell death. Researchers are working to determine how mutations in the *GRN* gene, and the resulting loss of progranulin, are related to a buildup of TDP-43 in the brain.

The features of *GRN*-related frontotemporal lobar degeneration result from the gradual loss of neurons in regions near the front of the brain called the frontal and temporal lobes. The frontal lobes are involved in reasoning, planning, judgment, and problem-solving, while the temporal lobes help process hearing, speech, memory, and emotion. The death of neurons in these areas causes problems with many critical brain functions. However, it is unclear why the loss of neurons occurs in the frontal and temporal lobes more often than other brain regions in people with *GRN*-related frontotemporal lobar degeneration.

Other Names for This Gene

- acrogranin
- CLN11
- GEP
- GP88
- granulin
- granulin-epithelin
- granulins
- granulins precursor
- GRN_HUMAN
- PC cell-derived growth factor

- PCDGF
- PEPI
- PGRN
- proepithelin
- progranulin

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of GRN ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2896\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2896[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28GRN%5BTIAB%5D%29+OR+%28granulin%5BTIAB%5D%29+OR+%28PGRN%5BTIAB%5D%29+OR+%28progranulin%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D%29>)

Catalog of Genes and Diseases from OMIM

- GRANULIN PRECURSOR; GRN (<https://omim.org/entry/138945>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/2896>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=GRN\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=GRN[gene]))

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Genomic Location

The *GRN* gene is found on chromosome 17 (<https://medlineplus.gov/genetics/chromosome/17/>).

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