



## CACNA1F gene

calcium voltage-gated channel subunit alpha1 F

### Normal Function

The *CACNA1F* gene belongs to a family of genes that provide instructions for making calcium channels. These channels, which transport positively charged calcium atoms (calcium ions) across cell membranes, play a key role in a cell's ability to generate and transmit electrical signals.

The *CACNA1F* gene provides instructions for making one part (the alpha-1 subunit) of a calcium channel called CaV1.4. This subunit forms the hole (pore) in the cell membrane through which calcium ions can flow. CaV1.4 channels are found in many types of cells, although they play a particularly important role in a specialized tissue at the back of the eye called the retina. Within the retina, the channels are located in light-detecting cells called photoreceptors. The retina contains two types of photoreceptors: rods and cones. Rods are responsible for vision in low light. Cones provide vision in bright light, including color vision.

CaV1.4 channels appear to play a critical role in normal vision. Studies suggest they help relay visual signals from rods and cones to other retinal cells called bipolar cells. This signaling is an essential step in the transmission of visual information from the eyes to the brain.

### Health Conditions Related to Genetic Changes

#### X-linked congenital stationary night blindness

More than 70 mutations in the *CACNA1F* gene have been identified in people with X-linked congenital stationary night blindness. Mutations in this gene are responsible for the incomplete form of the disorder, which is characterized by vision problems including a loss of sharpness (reduced acuity), nearsightedness (myopia), involuntary movements of the eyes (nystagmus), and eyes that do not look in the same direction (strabismus). Many affected individuals also have difficulty seeing in low light (night blindness).

*CACNA1F* mutations change the structure of the alpha-1 subunit, which alters or eliminates the function of CaV1.4 channels. These changes prevent the normal transport of calcium ions across the cell membrane of photoreceptor cells. A loss of calcium ion transport disrupts the ability of both rods and cones to transmit visual signals, which impairs vision.

#### Cone-rod dystrophy

## Other disorders

Mutations in the *CACNA1F* gene cause several other rare disorders that impair vision. These include Åland Island eye disease, X-linked cone-rod dystrophy, an X-linked retinal disorder in New Zealand, and retinal and optic disc atrophy. Each of these disorders has been reported in only a few individuals or families worldwide. They cause vision problems similar to those of X-linked congenital stationary night blindness.

Researchers have identified at least one *CACNA1F* mutation that can cause Åland Island eye disease (also known as Forsius-Eriksson syndrome). This condition was first described in a family from the Åland Islands, which are in the Baltic Sea off the coast of Sweden. Åland Island eye disease is characterized by reduced visual acuity, nystagmus, an irregular curvature of the front part of the eye (astigmatism), myopia, abnormal color vision, and night blindness. The mutation associated with this disorder deletes a segment of genetic material from the *CACNA1F* gene, which significantly alters the structure of the alpha-1 subunit of CaV1.4 channels. These changes prevent the normal transport of calcium ions across the cell membrane of photoreceptor cells. A loss of calcium ion transport disrupts the ability of both rods and cones to transmit visual signals.

At least one other *CACNA1F* mutation is responsible for X-linked cone-rod dystrophy (also known as CORDX3). The signs and symptoms of this condition include reduced visual acuity, an increased sensitivity to light (photophobia), myopia, and impaired color vision. These vision problems tend to worsen over time. The mutation associated with this disorder deletes part of the alpha-1 subunit, which likely prevents the production of functional CaV1.4 channels. A loss of these channels keeps photoreceptor cells from relaying visual signals normally, which leads to impaired vision.

A *CACNA1F* mutation has also been found to cause an X-linked retinal disorder in a large Maori family from New Zealand. The major features of this disorder include reduced visual acuity, abnormal color vision, photophobia, and mild nystagmus. Some affected individuals have also had intellectual disability. The *CACNA1F* mutation associated with this condition alters a single protein building block (amino acid) in the alpha-1 subunit, which appears to overactivate CaV1.4 channels. The resulting increase in calcium ion transport probably disrupts the transmission of visual signals in the retina.

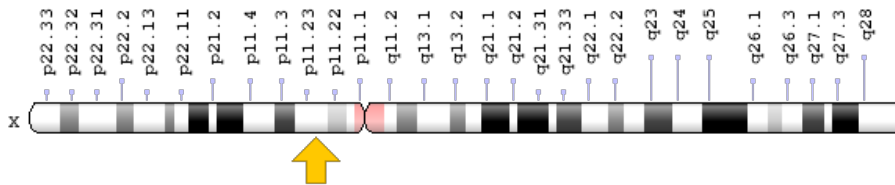
Another eye disorder, known as retinal and optic disc atrophy, has been associated with a *CACNA1F* mutation in two Japanese brothers. The affected individuals experienced a progressive decline in visual acuity and color vision. These vision problems were caused by deterioration of the retina, including an area called the optic disc (which is where the retina connects with the nerve that relays visual information to the brain). The *CACNA1F* mutation responsible for retinal and optic disc atrophy alters the structure of the alpha-1 subunit, which probably leads to the production of nonfunctional CaV1.4 channels. This mutation has also been identified

in at least one Japanese family with X-linked congenital stationary night blindness. It is unclear why this single genetic change can cause different vision abnormalities in different families.

### Chromosomal Location

Cytogenetic Location: Xp11.23, which is the short (p) arm of the X chromosome at position 11.23

Molecular Location: base pairs 49,205,063 to 49,233,404 on the X chromosome (Homo sapiens Annotation Release 109, GRCh38.p12) (NCBI)



Credit: Genome Decoration Page/NCBI

### Other Names for This Gene

- AIED
- CAC1F\_HUMAN
- calcium channel, voltage-dependent, L type, alpha 1F subunit
- Cav1.4
- Cav1.4alpha1
- COD3
- COD4
- CORDX
- CORDX3
- CSNB2
- CSNB2A
- CSNBX2
- JM8
- JMC8
- OA2

## **Additional Information & Resources**

### Educational Resources

- Madame Curie Bioscience Database:  $\alpha$ 1F/ CaV1.4  
<https://www.ncbi.nlm.nih.gov/books/NBK6181/#A30881>
- Neuromuscular Disease Center, Washington University: Calcium channels  
<https://neuromuscular.wustl.edu/mother/chan.html#ca>

### Clinical Information from GeneReviews

- X-Linked Congenital Stationary Night Blindness  
<https://www.ncbi.nlm.nih.gov/books/NBK1245>

### Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28CACNA1F%5BTIAB%5D%29+OR+%28Cav1.4%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+2160+days%22%5Bdp%5D>

### Catalog of Genes and Diseases from OMIM

- ALAND ISLAND EYE DISEASE  
<http://omim.org/entry/300600>
- CALCIUM CHANNEL, VOLTAGE-DEPENDENT, ALPHA-1F SUBUNIT  
<http://omim.org/entry/300110>
- CONE-ROD DYSTROPHY, X-LINKED, 3  
<http://omim.org/entry/300476>

### Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology  
[http://atlasgeneticsoncology.org/Genes/GC\\_CACNA1F.html](http://atlasgeneticsoncology.org/Genes/GC_CACNA1F.html)
- ClinVar  
<https://www.ncbi.nlm.nih.gov/clinvar?term=CACNA1F%5Bgene%5D>
- HGNC Gene Symbol Report  
[https://www.genenames.org/data/gene-symbol-report/#!/hgnc\\_id/HGNC:1393](https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:1393)
- Monarch Initiative  
<https://monarchinitiative.org/gene/NCBIGene:778>
- NCBI Gene  
<https://www.ncbi.nlm.nih.gov/gene/778>
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