CNGA3 gene

cyclic nucleotide gated channel subunit alpha 3

Normal Function

The *CNGA3* gene provides instructions for making one part (the alpha subunit) of the cone photoreceptor cyclic nucleotide-gated (CNG) channel. These channels are found exclusively in light-detecting (photoreceptor) cells called cones, which are located in a specialized tissue at the back of the eye known as the retina. Cones provide vision in bright light (daylight vision), including color vision. Other photoreceptor cells, called rods, provide vision in low light (night vision).

CNG channels are openings in the cell membrane that transport positively charged atoms (cations) into cells. In cones, CNG channels remain open under dark conditions, allowing cations to flow in. When light enters the eye, it triggers the closure of these channels, stopping the inward flow of cations. This change in cation transport alters the cone's electrical charge, which ultimately generates a signal that is interpreted by the brain as vision. This process of translating light into an electrical signal is called phototransduction.

Health Conditions Related to Genetic Changes

Achromatopsia

More than 100 mutations in the *CNGA3* gene have been found to cause the vision disorder achromatopsia. These mutations underlie about 25 percent of cases of complete achromatopsia, a form of the disorder characterized by a total lack of color vision and other vision problems that are present from early infancy. *CNGA3* gene mutations have also been identified in a few individuals with incomplete achromatopsia, a milder form of the disorder associated with limited color vision.

The *CNGA3* gene mutations that underlie complete achromatopsia affect the production or function of the alpha subunit. In some cases, no protein is produced. In others, the protein is altered and does not function normally. CNG channels assembled without the alpha subunit or with an abnormal subunit are nonfunctional; they prevent cones from carrying out phototransduction. Researchers speculate that some defective channels allow a huge influx of cations into cones, which ultimately causes these cells to self-destruct (undergo apoptosis). A loss of cone function underlies the lack of color vision and other vision problems in people with complete achromatopsia.

A few mutations in the *CNGA3* gene reduce but do not eliminate the function of CNG channels in cones. These mutations cause incomplete achromatopsia because the partially functioning cones can transmit some visual information to the brain.

Because these CNG channels are specific to cones, rods are generally unaffected by this disorder.

Cone-rod dystrophy

MedlinePlus Genetics provides information about Cone-rod dystrophy

Other disorders

Mutations in the *CNGA3* gene have also been identified in a small percentage of cases of progressive cone dystrophy. Like achromatopsia (described above), this condition affects the function of cones in the retina. However, unlike achromatopsia, progressive cone dystrophy is associated with cones that work normally at birth but begin to malfunction in childhood or adolescence. Over time, people with progressive cone dystrophy develop increasing blurriness and loss of color vision. It is unclear why some *CNGA3* gene mutations cause achromatopsia and others result in progressive cone dystrophy.

Other Names for This Gene

- ACHM2
- CCNC1
- CCNCa
- CCNCalpha
- CNCG3
- CNG3
- CNGA3_HUMAN
- cone photoreceptor cGMP-gated channel alpha subunit

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CNGA3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=1261[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CNGA3%5BTIAB%5D%29+OR+%28cyclic+nucleotide+gated+channel+alpha+3%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%2

9%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- CYCLIC NUCLEOTIDE-GATED CHANNEL, ALPHA-3; CNGA3 (https://omim.org/entry/600053)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/1261)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=CNGA3[gene])

References

- Johnson S, Michaelides M, Aligianis IA, Ainsworth JR, Mollon JD, Maher ER,Moore AT, Hunt DM. Achromatopsia caused by novel mutations in both CNGA3 andCNGB3. J Med Genet. 2004 Feb;41(2):e20. doi: 10.1136/jmg.2003.011437. No abstractavailable. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14757870) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1735666/)
- Koeppen K, Reuter P, Ladewig T, Kohl S, Baumann B, Jacobson SG, Plomp AS, Hamel CP, Janecke AR, Wissinger B. Dissecting the pathogenic mechanisms ofmutations in the pore region of the human cone photoreceptor cyclicnucleotide-gated channel. Hum Mutat. 2010 Jul;31(7):830-9. doi:10.1002/humu.21283. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20506298)
- Kohl S, Jagle H, Wissinger B, Zobor D. Achromatopsia. 2004 Jun 24 [updated2018 Sep 20]. In: Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews(R) [Internet]. Seattle (WA):University of Washington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK1418/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20301591)
- Kohl S, Marx T, Giddings I, Jagle H, Jacobson SG, Apfelstedt-Sylla E, ZrennerE, Sharpe LT, Wissinger B. Total colourblindness is caused by mutations in thegene encoding the alpha-subunit of the cone photoreceptor cGMP-gated cationchannel. Nat Genet. 1998 Jul;19(3):257-9. doi: 10.1038/935. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/9662398)
- Patel KA, Bartoli KM, Fandino RA, Ngatchou AN, Woch G, Carey J, Tanaka JC. Transmembrane S1 mutations in CNGA3 from achromatopsia 2 patients cause loss offunction and impaired cellular trafficking of the cone CNG channel. InvestOphthalmol Vis Sci. 2005 Jul;46(7):2282-90. doi: 10.1167/iovs.05-0179. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15980212)
- Reuter P, Koeppen K, Ladewig T, Kohl S, Baumann B, Wissinger B; AchromatopsiaClinical Study Group. Mutations in CNGA3 impair trafficking or

function of conecyclic nucleotide-gated channels, resulting in achromatopsia. Hum Mutat. 2008Oct;29(10):1228-36. doi: 10.1002/humu.20790. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18521937)

- Thiadens AA, Roosing S, Collin RW, van Moll-Ramirez N, van Lith-Verhoeven JJ, van Schooneveld MJ, den Hollander AI, van den Born LI, Hoyng CB, Cremers FP, Klaver CC. Comprehensive analysis of the achromatopsia genes CNGA3 and CNGB3 inprogressive cone dystrophy. Ophthalmology. 2010 Apr;117(4):825-30.e1. doi:10.1016/j.ophtha.2009.09.008. Epub 2010 Jan 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20079539)
- Trankner D, Jagle H, Kohl S, Apfelstedt-Sylla E, Sharpe LT, Kaupp UB, ZrennerE, Seifert R, Wissinger B. Molecular basis of an inherited form of incompleteachromatopsia. J Neurosci. 2004 Jan 7;24(1):138-47. doi:10.1523/JNEUROSCI.3883-03.2004. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/14715947)
- Wissinger B, Gamer D, Jagle H, Giorda R, Marx T, Mayer S, Tippmann S, Broghammer M, Jurklies B, Rosenberg T, Jacobson SG, Sener EC, Tatlipinar S, HoyngCB, Castellan C, Bitoun P, Andreasson S, Rudolph G, Kellner U, Lorenz B, Wolff G,Verellen-Dumoulin C, Schwartz M, Cremers FP, Apfelstedt-Sylla E, Zrenner E,Salati R, Sharpe LT, Kohl S. CNGA3 mutations in hereditary cone photoreceptordisorders. Am J Hum Genet. 2001 Oct;69(4):722-37. doi: 10.1086/323613. Epub 2001Aug 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11536077) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1226059/)

Genomic Location

The *CNGA3* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

Last updated January 1, 2015