GUCY2D gene

guanylate cyclase 2D, retinal

Normal Function

The *GUCY2D* gene provides instructions for making a protein that plays an essential role in normal vision. This protein is found in the retina, which is the specialized tissue at the back of the eye that detects light and color. Within the retina, the GUCY2D protein is located in light-detecting cells called photoreceptors. The retina contains two types of photoreceptor cells: rods and cones. Rods are needed for vision in low light, while cones are needed for vision in bright light, including color vision.

The GUCY2D protein is involved in a process called phototransduction. When light enters the eye, it stimulates specialized pigments called opsins that "hold" a vitamin A molecule in photoreceptor cells. This stimulation triggers a series of chemical reactions that close the open channel in the cell membranes of rod and cone cells. This closure produces an electrical signal, which is then interpreted by the brain as vision.

Once photoreceptors have been stimulated by light, they must return to their resting (or " dark") state before they can be stimulated again. The GUCY2D protein is involved in a chemical reaction that re-opens the cell membrane channels that helps return photoreceptors to their dark state after light exposure.

Health Conditions Related to Genetic Changes

Cone-rod dystrophy

Some variants (also known as mutations) in the *GUCY2D* gene have been identified in people with a vision disorder called cone-rod dystrophy. The problems associated with this condition include a loss of visual sharpness (acuity), an increased sensitivity to light (photophobia), and impaired color vision. These vision problems worsen over time.

The variants that cause cone-rod dystrophy occur in one of the two copies of the *GUCY2D* gene in each cell. These variants are responsible for about one-quarter of the cases of a form of the condition called autosomal dominant cone-rod dystrophy. Most of these variants affect a particular protein building block (amino acid) in the GUCY2D protein, replacing the amino acid arginine at position 838 with one of several other amino acids. These genetic changes impair normal phototransduction, causing the photoreceptor cells to deteriorate over time. The loss of these cells leads to the

progressive vision problems characteristic of cone-rod dystrophy.

Leber congenital amaurosis

Many variants in the *GUCY2D* gene have been found to cause Leber congenital amaurosis. This condition is an eye disorder that primarily affects the retina. People with this disorder typically have severe visual impairment beginning at birth or shortly afterward. Variants in this gene account for 6 to 21 percent of all cases of this condition.

The variants that cause Leber congenital amaurosis occur in both copies of the *GUCY2D* gene in each cell. Most of these genetic changes lead to an abnormally short, nonfunctional version of the GUCY2D protein. A lack of this protein prevents photoreceptor cells from returning to their dark state after they are exposed to light. As a result, the process of phototransduction is almost totally shut down, leading to severe visual impairment beginning very early in life in Leber congenital amaurosis.

Other Names for This Gene

- CORD6
- CYGD
- guanylate cyclase 2D, membrane (retina-specific)
- GUC1A4
- GUC2D
- GUC2D_HUMAN
- LCA1
- RCD2
- retGC
- RETGC-1
- RETGC1
- retinal guanylyl cyclase 1
- rod outer segment membrane guanylate cyclase
- ROS-GC
- ROS-GC1
- ROSGC

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of GUCY2D (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3000[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28GUCY2D%5BTIAB%5D%29+OR+%28RETGC-1%5BTIAB%5D%29+OR+%28RETGC1%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+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- GUANYLATE CYCLASE 2D, RETINAL; GUCY2D (https://omim.org/entry/600179)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3000)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=GUCY2D[gene])

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Genomic Location

The *GUCY2D* gene is found on chromosome 17 (https://medlineplus.gov/genetics/chromosome/17/).

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