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 in photoreceptor cells. This stimulation triggers a series of chemical reactions that produce an electrical signal, which is 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 helps return photoreceptors to their dark state after light exposure.

Health Conditions Related to Genetic Changes

**Cone-rod dystrophy**

At least 10 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 mutations that cause cone-rod dystrophy occur in one of the two copies of the *GUCY2D* gene in each cell. These mutations are responsible for about one-quarter of the cases of a form of the condition called autosomal dominant cone-rod dystrophy. Most of these mutations 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**

More than 160 mutations in the *GUCY2D* gene have been found to cause Leber congenital amaurosis, a condition characterized by vision loss beginning in infancy. Mutations in this gene account for 6 to 21 percent of all cases of this condition.
The mutations that cause Leber congenital amaurosis occur in both copies of the \textit{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.

\textbf{Chromosomal Location}

\begin{itemize}
  \item \textbf{Cytogenetic Location:} 17p13.1, which is the short (p) arm of chromosome 17 at position 13.1
  \item \textbf{Molecular Location:} base pairs 8,002,615 to 8,020,342 on chromosome 17 (Homo sapiens Updated Annotation Release 109.20200522, GRCh38.p13) (NCBI)
\end{itemize}

\textbf{Other Names for This Gene}

\begin{itemize}
  \item CORD6
  \item CYGD
  \item guanylate cyclase 2D, membrane (retina-specific)
  \item GUC1A4
  \item GUC2D
  \item GUC2D\_HUMAN
  \item LCA1
  \item RCD2
  \item retGC
  \item RETGC-1
  \item RETGC1
  \item retinal guanylyl cyclase 1
  \item rod outer segment membrane guanylate cyclase
  \item ROS-GC
\end{itemize}
• ROS-GC1
• ROSGC

Additional Information & Resources

Educational Resources
• Neuroscience (second edition, 2001): Functional Specialization of the Rod and Cone Systems
• Webvision: The Organization of the Retina and Visual System: Structure of Rods and Cones

Clinical Information from GeneReviews
• Leber Congenital Amaurosis / Early-Onset Severe Retinal Dystrophy Overview
  https://www.ncbi.nlm.nih.gov/books/NBK531510

Scientific Articles on PubMed
• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?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, MEMBRANE
  http://omim.org/entry/600179

Research Resources
• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_GUCY2D.html
• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=GUCY2D%5Bgene%5D
• HGNC Gene Symbol Report
• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3000
Sources for This Summary


