CISD2 gene
CDGSH iron sulfur domain 2

Normal Function
The CISD2 gene provides instructions for making a protein that is found in the outer membrane of cell structures called mitochondria. Mitochondria are involved in a wide variety of cellular activities, including energy production, chemical signaling, and regulation of cell growth and division. The exact function of the CISD2 protein is unknown, but it is thought to help keep mitochondria functioning normally.

Health Conditions Related to Genetic Changes
Wolfram syndrome
At least one mutation in the CISD2 gene has been found to cause Wolfram syndrome. This condition is characterized by a lack of insulin leading to increased blood sugar (diabetes mellitus), a degeneration of nerves that carry information from the eyes to the brain (optic atrophy), and a number of other features involving the urinary tract, the brain, and hearing. People with this CISD2 gene mutation also experience gastrointestinal ulcers and excessive bleeding after injury.

The CISD2 gene mutation that causes Wolfram syndrome replaces the amino acid glutamic acid with the amino acid glutamine at position 37 in the CISD2 protein (written as Glu37Gln or E37Q). This mutation results in an abnormally small, nonfunctional CISD2 protein. As a result, the function of the mitochondria is impaired and they eventually break down. Since the mitochondria provide energy to cells, the loss of mitochondria leads to decreased energy for cells. Cells that do not have enough energy to function will eventually die. Cells with high energy demands, such as nerve cells in the brain, eyes, or gastrointestinal tract, are most susceptible to cell death due to reduced energy. The gradual loss of cells in various body systems likely causes the signs and symptoms of Wolfram syndrome. When Wolfram syndrome is caused by CISD2 gene mutations, it is sometimes referred to as Wolfram syndrome type 2.
Chromosomal Location

Cytogenetic Location: 4q24, which is the long (q) arm of chromosome 4 at position 24
Molecular Location: base pairs 102,868,992 to 102,892,807 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CDGSH iron-sulfur domain-containing protein 2
- CISD2_HUMAN
- endoplasmic reticulum intermembrane small protein
- ERIS
- Miner1
- NAF-1
- nutrient-deprivation autophagy factor-1
- WFS2
- ZCD2
- zinc finger, CDGSH-type domain 2

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Mitochondria Are Bounded by a Double Membrane
- Madame Curie Bioscience Database: Damage to Mitochondria
  https://www.ncbi.nlm.nih.gov/books/NBK6156/#A76012
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28CISD2%5BTIAB%5D%29+OR+%2828ERIS%5BTIAB%5D%29+OR+%28WFS2%5BTIAB%5D%29+OR+%28ZCD2%5BTIAB%5D%29+AND+%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+human%5Bmh%5D+AND+%22last+3600+days%22

Catalog of Genes and Diseases from OMIM

- CDGSH IRON SULFUR DOMAIN PROTEIN 2
  http://omim.org/entry/611507

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_CISD2.html

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=CISD2%5Bgene%5D

- HGNC Gene Symbol Report

- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:493856

- NCBI Gene

- UniProt
  https://www.uniprot.org/uniprot/Q8N5K1

Sources for This Summary


- OMIM: CDGSH IRON SULFUR DOMAIN PROTEIN 2
  http://omim.org/entry/611507

