



SLC25A13 gene

solute carrier family 25 member 13

Normal Function

The *SLC25A13* gene provides instructions for making a protein called citrin. This protein is active chiefly in the liver, kidneys, and heart. Within the cells of these organs, citrin is involved in transporting molecules into and out of energy-producing structures called mitochondria. Specifically, citrin carries a protein building block (amino acid) called glutamate into mitochondria and transports the amino acid aspartate out of mitochondria as part of a process called the malate-aspartate shuttle.

An adequate supply of aspartate must be transported out of mitochondria to participate in a process called the urea cycle. The urea cycle is a sequence of chemical reactions that takes place in liver cells. These reactions process excess nitrogen that is generated as the body uses proteins. The excess nitrogen is used to make a compound called urea, which is excreted from the body in urine.

Citrin participates in several other important cellular functions as part of the malate-aspartate shuttle. This protein plays a role in producing and breaking down simple sugars and making proteins. It is also involved in the production of nucleotides, which are the building blocks of DNA and its chemical cousin, RNA.

Health Conditions Related to Genetic Changes

Citrullinemia

More than 20 mutations in the *SLC25A13* gene have been identified in people with adult-onset type II citrullinemia. This condition causes neurological problems, such as confusion, restlessness, irritability, and seizures, usually beginning in adulthood. Almost all of the identified mutations lead to the production of an unstable citrin protein that is quickly broken down or an abnormally short, nonfunctional version of the protein.

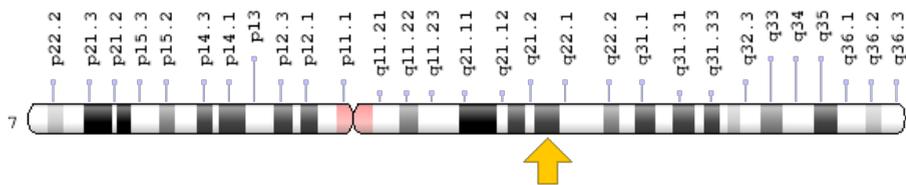
A lack of functional citrin blocks the malate-aspartate shuttle, including the transport of aspartate out of mitochondria. This loss of citrin inhibits the normal production of proteins and nucleotides. It also reduces the amount of aspartate available to take part in the urea cycle. As a result, the liver cannot effectively process excess nitrogen into urea. A disruption in the urea cycle allows nitrogen (in the form of ammonia) and other byproducts of the urea cycle (such as citrulline) to build up in the bloodstream. Ammonia is toxic, especially to the nervous system, which helps explain the development of abnormal behaviors and other neurological problems in people with adult-onset type II citrullinemia.

Mutations in the *SLC25A13* gene also have been found in infants with a liver disorder called neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD). This liver disorder is also known as neonatal-onset type II citrullinemia. NICCD blocks the flow of bile (a digestive fluid produced by the liver) and prevents the body from processing certain nutrients properly. Ammonia does not build up in the bloodstream of infants with NICCD, and the signs and symptoms typically go away within a year. In rare cases, these individuals develop signs and symptoms of another condition called failure to thrive and dyslipidemia caused by citrin deficiency (FTTDCD) after recovering from NICCD. Many individuals with NICCD or FTTDCD have the same mutations in the *SLC25A13* gene as people with adult-onset type II citrullinemia. Years or even decades later, some people who had NICCD or FTTDCD develop the features of adult-onset type II citrullinemia.

Chromosomal Location

Cytogenetic Location: 7q21.3, which is the long (q) arm of chromosome 7 at position 21.3

Molecular Location: base pairs 96,120,220 to 96,322,147 on chromosome 7 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ARALAR2
- calcium-binding mitochondrial carrier protein Aralar2
- CITRIN
- CMC2_HUMAN
- CTLN2
- mitochondrial aspartate glutamate carrier 2
- solute carrier family 25 (aspartate/glutamate carrier), member 13

Additional Information & Resources

Educational Resources

- Chapter 23.4: Ammonium Ion Is Converted Into Urea in Most Terrestrial Vertebrates (Biochemistry, fifth edition, 2002)
<https://www.ncbi.nlm.nih.gov/books/NBK22450/>

Clinical Information from GeneReviews

- Citrin Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK1181>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28SLC25A13%5BTIAB%5D%29+OR+%28solute+carrier+family+25,+member+13%5BTIAB%5D%29%29+OR+%28%28ARALAR2%5BTIAB%5D%29+OR+%28CITRIN%5BTIAB%5D%29+OR+%28CTLN2%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+2160+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- CITRULLINEMIA, TYPE II, NEONATAL-ONSET
<http://omim.org/entry/605814>
- SOLUTE CARRIER FAMILY 25 (CITRIN), MEMBER 13
<http://omim.org/entry/603859>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_SLC25A13.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=SLC25A13%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report#!/hgnc_id/HGNC:10983
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:10165>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/10165>
- UniProt
<https://www.uniprot.org/uniprot/Q9UJS0>

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