SUCLG1 gene

succinate-CoA ligase GDP/ADP-forming subunit alpha

Normal Function

The *SUCLG1* gene provides instructions for making one part, the alpha subunit, of an enzyme called succinate-CoA ligase. Two slightly different versions of this enzyme are made with the alpha subunit: ADP-forming succinate-CoA ligase (A-SUCL) and GDP-forming succinate-CoA ligase (G-SUCL). A-SUCL is most active in tissues that require a large amount of energy, such as those of the brain and muscles. G-SUCL is most active in other tissues, particularly in the liver and kidneys.

Both versions of succinate-CoA ligase play a critical role in mitochondria, which are structures inside cells that convert the energy from food into a form that cells can use. Within mitochondria, these enzymes are likely involved in a series of chemical reactions known as the citric acid cycle or Krebs cycle. These reactions allow cells to use oxygen and generate energy.

Mitochondria each contain a small amount of DNA, known as mitochondrial DNA or mtDNA. Studies suggest that succinate-CoA ligase interacts with another enzyme, nucleoside diphosphate kinase, to produce and maintain the building blocks of mitochondrial DNA. Having an adequate amount of mitochondrial DNA is essential for normal energy production within cells.

Health Conditions Related to Genetic Changes

Succinate-CoA ligase deficiency

At least two mutations in the *SUCLG1* gene have been identified in people with succinate-CoA ligase deficiency. One mutation has been found to cause a very severe form of the condition known as fatal infantile lactic acidosis. Children with this condition usually live only a few days after birth. The mutation responsible for fatal infantile lactic acidosis deletes a small amount of genetic material from the *SUCLG1* gene, which completely eliminates the activity of both versions of succinate-CoA ligase.

At least one other *SUCLG1* gene mutation results in a somewhat less severe form of succinate-CoA ligase deficiency that is characterized by very weak muscle tone (severe hypotonia), uncontrolled movements, hearing loss, and delayed development. This mutation changes a single protein building block (amino acid) in succinate-CoA ligase,

which reduces but does not eliminate the activity of both A-SUCL and G-SUCL.

A shortage (deficiency) of succinate-CoA ligase leads to problems with the production and maintenance of mitochondrial DNA. A reduction in the amount of mitochondrial DNA (known as mitochondrial DNA depletion) impairs mitochondrial function in many of the body's cells and tissues. A total loss of succinate-CoA ligase activity appears to have more severe effects than a partial loss of enzyme activity.

Leigh syndrome

MedlinePlus Genetics provides information about Leigh syndrome

Other Names for This Gene

- FLJ21114
- G-ALPHA
- SUCA_HUMAN
- succinate-CoA ligase, alpha subunit
- succinate-CoA ligase, GDP-forming alpha subunit
- SUCLA1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of SUCLG1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=8802[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28SUCLG1%5BALL%5D%29+OR+%28succinate-CoA+ligase%5BALL%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- SUCCINATE-CoA LIGASE, GDP/ADP-FORMING, SUBUNIT ALPHA; SUCLG1 (https://omim.org/entry/611224)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/8802)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=SUCLG1[gene])

References

- El-Hattab AW, Scaglia F. SUCLG1-Related Mitochondrial DNA DepletionSyndrome, Encephalomyopathic Form with Methylmalonic Aciduria. 2017 Mar 30. In:Adam MP, Feldman J, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, AmemiyaA, editors. GeneReviews(R) [Internet]. Seattle (WA): University ofWashington, Seattle; 1993-2024. Available fromhttp://www.ncbi.nlm.nih.gov/books/NBK425223/ Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/28358460)
- Kowluru A, Tannous M, Chen HQ. Localization and characterization of themitochondrial isoform of the nucleoside diphosphate kinase in the pancreatic betacell: evidence for its complexation with mitochondrial succinyl-CoA synthetase. Arch Biochem Biophys. 2002 Feb 15;398(2):160-9. doi: 10.1006/abbi.2001.2710. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/11831846)
- Lambeth DO, Tews KN, Adkins S, Frohlich D, Milavetz BI. Expression of twosuccinyl-CoA synthetases with different nucleotide specificities in mammaliantissues. J Biol Chem. 2004 Aug 27;279(35):36621-4. doi: 10.1074/jbc. M406884200.Epub 2004 Jul 2. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov /15234968)
- Ostergaard E, Christensen E, Kristensen E, Mogensen B, Duno M, Shoubridge EA, Wibrand F. Deficiency of the alpha subunit of succinate-coenzyme A ligase causesfatal infantile lactic acidosis with mitochondrial DNA depletion. Am J Hum Genet.2007 Aug;81(2):383-7. doi: 10.1086/519222. Epub 2007 Jun 4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17668387) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1950792/)
- Ostergaard E, Schwartz M, Batbayli M, Christensen E, Hjalmarson O, Kollberg G, Holme E. A novel missense mutation in SUCLG1 associated with mitochondrial DNAdepletion, encephalomyopathic form, with methylmalonic aciduria. Eur J Pediatr. 2010 Feb;169(2):201-5. doi: 10.1007/s00431-009-1007-z. Epub 2009 Jun 14. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19526370)
- Ostergaard E. Disorders caused by deficiency of succinate-CoA ligase. JInherit Metab Dis. 2008 Apr;31(2):226-9. doi: 10.1007/s10545-008-0828-7. Epub2008 Apr 4. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/18392745)

Genomic Location

The *SUCLG1* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chrom osome/2/).

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