

ACSF3 gene

acyl-CoA synthetase family member 3

Normal Function

The ACSF3 gene provides instructions for making an enzyme involved in the formation (synthesis) of fatty acids, which are building blocks used to make fats (lipids). The ACSF3 enzyme performs a chemical reaction that converts malonic acid to malonyl-CoA, which is the first step of fatty acid synthesis. Based on this activity, the enzyme is classified as a malonyl-CoA synthetase. The ACSF3 enzyme also converts methylmalonic acid to methylmalonyl-CoA, making it a methylmalonyl-CoA synthetase as well.

Fatty acid synthesis occurs through two pathways, one of which takes place in cellular structures called mitochondria. Mitochondria convert the energy from food into a form that cells can use, and fatty acid synthesis in these structures is thought to be important for their proper functioning. The ACSF3 enzyme is found only in mitochondria and is involved in mitochondrial fatty acid synthesis.

Health Conditions Related to Genetic Changes

Combined malonic and methylmalonic aciduria

About a dozen mutations in the *ACSF3* gene have been found in people with combined malonic and methylmalonic aciduria (CMAMMA), a condition characterized by elevated levels of chemicals known as malonic acid and methylmalonic acid in the body. This condition can cause development and growth problems beginning in childhood or neurological problems beginning in adulthood.

Most *ACSF3* gene mutations involved in CMAMMA change single protein building blocks (amino acids) in the ACSF3 enzyme. The altered enzyme likely has little or no function. Because the enzyme cannot convert malonic and methylmalonic acids, they build up in the body. Damage to organs and tissues caused by accumulation of malonic and methylmalonic acids may be responsible for the signs and symptoms of CMAMMA, although the mechanisms are unclear.

Other Names for This Gene

ACSF3_HUMAN

- acyl-CoA synthetase family member 3, mitochondrial
- acyl-CoA synthetase family member 3, mitochondrial precursor

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

Tests of ACSF3 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=197322[geneid])

Scientific Articles on PubMed

 PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28ACSF3%5BTIAB%5D%29+A ND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22% 5Bdp%5D)

Catalog of Genes and Diseases from OMIM

 ACYL-CoA SYNTHETASE FAMILY, MEMBER 3; ACSF3 (https://omim.org/entry/61 4245)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/197322)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ACSF3[gene])

References

- Alfares A, Nunez LD, Al-Thihli K, Mitchell J, Melancon S, Anastasio N, Ha KC, Majewski J, Rosenblatt DS, Braverman N. Combined malonic and methylmalonicaciduria: exome sequencing reveals mutations in the ACSF3 gene in patients with anon-classic phenotype. J Med Genet. 2011 Sep;48(9):602-5. doi:10. 1136/jmedgenet-2011-100230. Epub 2011 Jul 23. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21785126)
- Sloan JL, Johnston JJ, Manoli I, Chandler RJ, Krause C, Carrillo-Carrasco N, Chandrasekaran SD, Sysol JR, O'Brien K, Hauser NS, Sapp JC, Dorward HM, HuizingM; NIH Intramural Sequencing Center Group; Barshop BA, Berry SA, James PM, Champaigne NL, de Lonlay P, Valayannopoulos V, Geschwind MD, Gavrilov DK, NyhanWL, Biesecker LG, Venditti CP. Exome sequencing identifies ACSF3 as a cause ofcombined malonic and methylmalonic aciduria. Nat Genet. 2011 Aug 14;43(9):883-6.doi: 10.1038/ng.908. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21841779) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3163731/)

- Watkins PA, Maiguel D, Jia Z, Pevsner J. Evidence for 26 distinctacyl-coenzyme A synthetase genes in the human genome. J Lipid Res. 2007Dec;48(12):2736-50. doi: 10.1194/jlr.M700378-JLR200. Epub 2007 Aug 30. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17762044)
- Witkowski A, Thweatt J, Smith S. Mammalian ACSF3 protein is a malonyl-CoAsynthetase that supplies the chain extender units for mitochondrial fatty acidsynthesis. J Biol Chem. 2011 Sep 30;286(39):33729-36. doi:10.1074/jbc.M111. 291591. Epub 2011 Aug 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/2 1846720) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3190830/)

Genomic Location

The ACSF3 gene is found on chromosome 16 (https://medlineplus.gov/genetics/chromosome/16/).

Last updated January 1, 2013