ACAT1 gene

acetyl-CoA acetyltransferase 1

Normal Function

The *ACAT1* gene provides instructions for making an enzyme that is found in the energy-producing centers within cells (mitochondria). This enzyme plays an essential role in breaking down proteins and fats from the diet. Specifically, it helps process isoleucine, an amino acid that is a building block of many proteins. This enzyme is also involved in processing ketones, which are molecules that are produced when fats are broken down in the body.

During the breakdown of proteins, the ACAT1 enzyme is responsible for a step in processing isoleucine. It converts a molecule called 2-methyl-acetoacetyl-CoA into two smaller molecules, propionyl-CoA and acetyl-CoA, that can be used to produce energy.

The ACAT1 enzyme carries out the last step in ketone breakdown (ketolysis) during the processing of fats. The enzyme converts a molecule called acetoacetyl-CoA into two molecules of acetyl-CoA, which can be used to produce energy. In the liver, the enzyme also carries out this chemical reaction in reverse, which is a step in building new ketones (ketogenesis).

Health Conditions Related to Genetic Changes

Beta-ketothiolase deficiency

More than 100 mutations in the *ACAT1* gene have been identified in people with beta-ketothiolase deficiency. The condition usually appears before age 2 and causes episodes (called ketoacidotic attacks) of vomiting, dehydration and other health problems, which can lead to coma. Some of the genetic changes that cause beta-ketothiolase deficiency disrupt the normal function of the enzyme, while other mutations prevent cells from producing any functional enzyme.

A shortage of the ACAT1 enzyme prevents the body from processing proteins and fats properly. As a result, chemical byproducts called organic acids can build up to toxic levels in the blood. These substances may cause the blood to become too acidic (ketoacidosis) and can damage the body's tissues and organs, particularly in the nervous system. This damage likely underlies the episodes associated with beta-ketothiolase deficiency.

Other Names for This Gene

- ACAT
- acetoacetyl Coenzyme A thiolase
- acetyl-Coenzyme A acetyltransferase 1
- acetyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase)
- MAT
- methylacetoacetyl-Coenzyme A thiolase
- T2
- THIL
- THIL_HUMAN

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of ACAT1 (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=38[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ACAT1%5BTIAB%5D%29+OR+%28acetyl-Coenzyme+A+acetyltransferase+1%5BTIAB%5D%29+OR+%28acetoacetyl+Coenzyme+A+thiolase%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- ACETYL-CoA ACETYLTRANSFERASE 1; ACAT1 (https://omim.org/entry/607809)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/38)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=ACAT1[gene])

References

- Abdelkreem E, Harijan RK, Yamaguchi S, Wierenga RK, Fukao T. Mutation updateon ACAT1 variants associated with mitochondrial acetoacetyl-CoA thiolase (T2)deficiency. Hum Mutat. 2019 Oct;40(10):1641-1663. doi: 10.1002/humu.23831. Epub2019 Jul 3. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/31268215) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC679

0690/)

- Fukao T, Yamaguchi S, Orii T, Hashimoto T. Molecular basis ofbeta-ketothiolase deficiency: mutations and polymorphisms in the humanmitochondrial acetoacetyl-coenzyme A thiolase gene. Hum Mutat. 1995;5(2):113-20.doi: 10.1002/humu.1380050203. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/7749408)
- Grunert SC, Sass JO. 2-methylacetoacetyl-coenzyme A thiolase(beta-ketothiolase) deficiency: one disease - two pathways. Orphanet J Rare Dis.2020 Apr 28;15(1):106. doi: 10.1186/s13023-020-01357-0. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/32345314) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7187484/)
- Kano M, Fukao T, Yamaguchi S, Orii T, Osumi T, Hashimoto T. Structure andexpression of the human mitochondrial acetoacetyl-CoA thiolase-encoding gene. Gene. 1991 Dec 30;109(2):285-90. doi: 10.1016/0378-1119(91)90623-j. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/1684944)

Genomic Location

The *ACAT1* gene is found on chromosome 11 (https://medlineplus.gov/genetics/chromosome/11/).

Last updated June 1, 2020