



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 the last 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 the first step in building new ketones (ketogenesis).

Health Conditions Related to Genetic Changes

Beta-ketothiolase deficiency

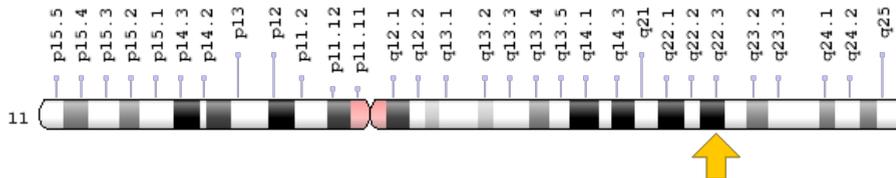
More than 40 mutations in the *ACAT1* gene have been identified in people with beta-ketothiolase deficiency. Some of these genetic changes disrupt the normal function of the enzyme, while other mutations prevent cells from producing any functional enzyme.

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 cause the blood to become too acidic (ketoacidosis), which can damage the body's tissues and organs, particularly in the nervous system. This damage leads to episodes of vomiting, dehydration, and other health problems associated with beta-ketothiolase deficiency.

Chromosomal Location

Cytogenetic Location: 11q22.3, which is the long (q) arm of chromosome 11 at position 22.3

Molecular Location: base pairs 108,116,705 to 108,148,822 on chromosome 11 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

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

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1998): Beta-ketothiolase deficiency syndrome is caused by defects in 2-methylacetoacetyl-CoA thiolase, which mediates the conversion of 2-methylacetoacetyl-CoA to acetyl-CoA and propionyl-CoA
<https://www.ncbi.nlm.nih.gov/books/NBK27945/#A3113>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?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%5BIa%5D+AND+human%5Bmh%5D>

Catalog of Genes and Diseases from OMIM

- ACETYL-CoA ACETYLTRANSFERASE 1
<http://omim.org/entry/607809>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_ACAT1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=ACAT1%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:93
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:38>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/38>
- UniProt
<https://www.uniprot.org/uniprot/P24752>

Sources for This Summary

- Fukao T, Matsuo N, Zhang GX, Urasawa R, Kubo T, Kohno Y, Kondo N. Single base substitutions at the initiator codon in the mitochondrial acetoacetyl-CoA thiolase (ACAT1/T2) gene result in production of varying amounts of wild-type T2 polypeptide. *Hum Mutat.* 2003 Jun;21(6):587-92.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12754704>
- Fukao T, Scriver CR, Kondo N; t2 Collaborative Working Group. The clinical phenotype and outcome of mitochondrial acetoacetyl-CoA thiolase deficiency (beta-ketothiolase or T2 deficiency) in 26 enzymatically proved and mutation-defined patients. *Mol Genet Metab.* 2001 Feb;72(2):109-14.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/11161836>
- Fukao T, Yamaguchi S, Orii T, Hashimoto T. Molecular basis of beta-ketothiolase deficiency: mutations and polymorphisms in the human mitochondrial acetoacetyl-coenzyme A thiolase gene. *Hum Mutat.* 1995;5(2):113-20. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/7749408>
- Kano M, Fukao T, Yamaguchi S, Orii T, Osumi T, Hashimoto T. Structure and expression of the human mitochondrial acetoacetyl-CoA thiolase-encoding gene. *Gene.* 1991 Dec 30;109(2):285-90.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/1684944>

- Korman SH. Inborn errors of isoleucine degradation: a review. *Mol Genet Metab.* 2006 Dec;89(4): 289-99. Epub 2006 Sep 6. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/16950638>
 - Zhang GX, Fukao T, Rolland MO, Zobot MT, Renom G, Touma E, Kondo M, Matsuo N, Kondo N. Mitochondrial acetoacetyl-CoA thiolase (T2) deficiency: T2-deficient patients with "mild" mutation(s) were previously misinterpreted as normal by the coupled assay with tiglyl-CoA. *Pediatr Res.* 2004 Jul;56(1):60-4. Epub 2004 May 5.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/15128923>
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