HADH gene

hydroxyacyl-CoA dehydrogenase

Normal Function

The *HADH* gene provides instructions for making an enzyme called 3-hydroxyacyl-CoA dehydrogenase that is important for converting certain fats to energy. This enzyme is involved in a process called fatty acid oxidation, in which several enzymes work in a step-wise fashion to break down (metabolize) fats and convert them to energy. The role of 3-hydroxyacyl-CoA dehydrogenase is to metabolize groups of fats called medium-chain fatty acids and short-chain fatty acids. These fatty acids are found in foods such as milk and certain oils and are produced when larger fatty acids are metabolized.

3-hydroxyacyl-CoA dehydrogenase functions in mitochondria, the energy-producing centers within cells. This enzyme is especially important for the normal functioning of the heart, liver, kidneys, muscles, and pancreas. The pancreas makes enzymes that help digest food, and it also produces insulin, which controls how much sugar is passed from the blood into cells for conversion to energy.

3-hydroxyacyl-CoA dehydrogenase is essential in the process that converts medium-chain and short-chain fatty acids to ketones, the major source of energy used by the heart and muscles. During prolonged periods without food (fasting) or when energy demands are increased, ketones are also important for the liver and other tissues.

Health Conditions Related to Genetic Changes

3-hydroxyacyl-CoA dehydrogenase deficiency

At least three mutations in the *HADH* gene have been found to cause 3-hydroxyacyl-CoA dehydrogenase deficiency. These mutations change single protein building blocks (amino acids) used to make the 3-hydroxyacyl-CoA dehydrogenase enzyme. These changes probably alter the 3-dimensional shape of the enzyme, which impairs its normal function.

With a shortage (deficiency) of functional 3-hydroxyacyl-CoA dehydrogenase, medium-chain and short-chain fatty acids are not metabolized properly. As a result, these fatty acids are not converted to energy, which can lead to signs and symptoms of 3-hydroxyacyl-CoA dehydrogenase deficiency such as lack of energy (lethargy) and low blood sugar (hypoglycemia). Medium-chain and short-chain fatty acids that are not broken down can build up in tissues and damage the liver, heart, and muscles, causing serious complications.

Congenital hyperinsulinism

Other disorders

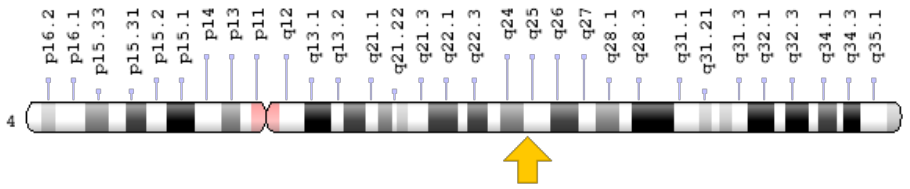
Mutations in the *HADH* gene have been reported in a small number of people with familial hyperinsulinism. This disorder is characterized by abnormally high levels of insulin (hyperinsulinism) and unusually low blood sugar (hypoglycemia).

Researchers have identified at least five *HADH* gene mutations that cause familial hyperinsulinism. These mutations severely reduce 3-hydroxyacyl-CoA dehydrogenase activity, either by impairing the enzyme's function or by decreasing the amount of this enzyme in cells. Researchers believe that inadequate 3-hydroxyacyl-CoA dehydrogenase activity in the pancreas leads to excessive insulin secretion and hypoglycemia in people with familial hyperinsulinism. It is unclear why the *HADH* gene mutations that cause familial hyperinsulinism seem to affect only the pancreas.

Chromosomal Location

Cytogenetic Location: 4q25, which is the long (q) arm of chromosome 4 at position 25

Molecular Location: base pairs 107,989,714 to 108,035,175 on chromosome 4 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- HAD
- HADH1
- HADHSC
- HCDH_HUMAN
- HHF4
- hydroxyacyl-Coenzyme A dehydrogenase
- L-3-hydroxyacyl-Coenzyme A dehydrogenase
- L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain
- M/SCHAD
- medium and short chain L-3-hydroxyacyl-coenzyme A dehydrogenase

- MGC8392
- SCHAD
- short chain 3-hydroxyacyl-CoA dehydrogenase

Additional Information & Resources

Educational Resources

- Biochemistry (fifth edition, 2002): Fatty Acid Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK21173/

Clinical Information from GeneReviews

- Familial Hyperinsulinism
  https://www.ncbi.nlm.nih.gov/books/NBK1375

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28HADH%5BTIAB%5D%29+OR+%28hydroxyacyl-Coenzyme+A+dehydrogenase%5BTIAB%5D%29%29+OR+%28%28SCHAD%5BALL%5D%29+OR+%28HADHSC%5BALL%5D%29+OR+%28M/SCHAD%5BALL%5D%29+NOT+%28Schad%5Bauthor%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+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- 3-HYDROXYACYL-CoA DEHYDROGENASE
  http://omim.org/entry/601609

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=HADH%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:4799
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:3033
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/3033
- UniProt
  https://www.uniprot.org/uniprot/Q16836

Sources for This Summary

- OMIM: 3-HYDROXYACYL-CoA DEHYDROGENASE
  http://omim.org/entry/601609
- Bennett MJ, Russell LK, Tokunaga C, Narayan SB, Tan L, Seegmiller A, Boriack RL, Strauss AW. Reye-like syndrome resulting from novel missense mutations in mitochondrial medium- and short-chain l-3-hydroxy-acyl-CoA dehydrogenase. Mol Genet Metab. 2006 Sep-Oct;89(1-2):74-9. Epub 2006 May 24.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16725361
- Clayton PT, Eaton S, Aynsley-Green A, Edginton M, Hussain K, Krywawych S, Datta V, Malingre HE, Berger R, van den Berg IE. Hyperinsulinism in short-chain L-3-hydroxyacyl-CoA dehydrogenase deficiency reveals the importance of beta-oxidation in insulin secretion. J Clin Invest. 2001 Aug;108(3):457-65.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/11489939
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC209352/
- Hussain K, Clayton PT, Krywawych S, Chatziandreou I, Mills P, Ginbey DW, Geboers AJ, Berger R, van den Berg IE, Eaton S. Hyperinsulinism of infancy associated with a novel splice site mutation in the SCHAD gene. J Pediatr. 2005 May;146(5):706-8.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/15870679
- Kapoor RR, James C, Flanagan SE, Ellard S, Eaton S, Hussain K. 3-Hydroxyacyl-coenzyme A dehydrogenase deficiency and hyperinsulinemic hypoglycemia: characterization of a novel mutation and severe dietary protein sensitivity. J Clin Endocrinol Metab. 2009 Jul;94(7):2221-5. doi: 10.1210/jc.2009-0423. Epub 2009 May 5.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/19417036
- Molven A, Matre GE, Duran M, Wanders RJ, Rishaug U, Njølstad PR, Jellum E, Søvik O. Familial hyperinsulinemic hypoglycemia caused by a defect in the SCHAD enzyme of mitochondrial fatty acid oxidation. Diabetes. 2004 Jan;53(1):221-7.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14693719
- Yang SY, He XY, Schulz H. 3-Hydroxyacyl-CoA dehydrogenase and short chain 3-hydroxyacyl-CoA dehydrogenase in human health and disease. FEBS J. 2005 Oct;272(19):4874-83. Review.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/16176262

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