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 (glucose) 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 glucose (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

MedlinePlus Genetics provides information about 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 glucose (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.

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

Tests Listed in the Genetic Testing Registry

- Tests of HADH (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3033[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?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; HADH (https://omim.org/entry/601609)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/3033)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=HADH[gene])

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Genomic Location

The *HADH* gene is found on chromosome 4 (https://medlineplus.gov/genetics/chromosome/4/).

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