

ACAD9 gene

acyl-CoA dehydrogenase family member 9

Normal Function

The *ACAD9* gene provides instructions for making an enzyme that is found in mitochondria, the energy-producing structures inside cells. The ACAD9 enzyme is critical in helping assemble a group of proteins known as complex I. Complex I is one of several complexes that carry out a multistep process called oxidative phosphorylation, through which cells derive much of their energy.

The ACAD9 enzyme also plays a role in fatty acid oxidation, a multistep process that occurs within mitochondria to break down (metabolize) fats and convert them into energy. The ACAD9 enzyme helps metabolize two fats called palmitate and oleate, which belong to a certain group of fats called long-chain fatty acids. Fatty acids are a major source of energy for the heart and muscles. During periods without food (fasting), fatty acids are also an important energy source for the liver and other tissues.

Health Conditions Related to Genetic Changes

ACAD9 deficiency

At least 30 *ACAD9* gene mutations have been found to cause ACAD9 deficiency. This condition varies in severity and can cause muscle weakness (myopathy), heart problems, intellectual disability, and other signs and symptoms. Most *ACAD9* gene mutations change single protein building blocks (amino acids) in the ACAD9 enzyme. Some mutations disrupt only complex I assembly. Decreased complex I formation can impair oxidative phosphorylation and reduce the amount of energy available in the cell. Other mutations affect the ACAD9 enzyme's structure or stability and likely disrupt both complex I assembly and long-chain fatty acid oxidation. A reduction in both of these energy production processes tends to be associated with the most severe signs and symptoms of ACAD9 deficiency.

Although the exact mechanism that causes the signs and symptoms of ACAD9 deficiency is unclear, it is likely that cells that are less able to produce energy die off, particularly cells in the brain, skeletal muscle, and other tissues and organs that require a lot of energy. The loss of cells in these tissues is thought to lead to myopathy and other features of ACAD9 deficiency.

MedlinePlus Genetics provides information about Mitochondrial complex I deficiency

- acyl-CoA dehydrogenase family member 9, mitochondrial
- acyl-Coenzyme A dehydrogenase family, member 9
- MGC14452
- NPD002

Tests Listed in the Genetic Testing Registry

- Tests of ACAD9 ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=28976\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=28976[geneid]))

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28ACAD9%5BTIAB%5D%29+OR+%28acyl-CoA+dehydrogenase+family+member+9%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5BIa%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>)

- ACYL-CoA DEHYDROGENASE FAMILY, MEMBER 9; ACAD9 (<https://omim.org/entry/611103>)

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/28976>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=ACAD9\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=ACAD9[gene]))

- Garone C, Donati MA, Sacchini M, Garcia-Diaz B, Bruno C, Calvo S, Mootha VK, Dimauro S. Mitochondrial encephalomyopathy due to a novel mutation in ACAD9. *JAMANeurol*. 2013 Sep 1;70(9):1177-9. doi: 10.1001/jamaneurol.2013.3197. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23836383>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3891824/>)

- Nouws J, Te Brinke H, Nijtmans LG, Houten SM. ACAD9, a complex I assembly factor with a moonlighting function in fatty acid oxidation deficiencies. *Hum Mol Genet.* 2014 Mar 1;23(5):1311-9. doi: 10.1093/hmg/ddt521. Epub 2013 Oct 24. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24158852>)
- Schiff M, Haberberger B, Xia C, Mohsen AW, Goetzman ES, Wang Y, Uppala R, Zhang Y, Karunanidhi A, Prabhu D, Alharbi H, Prochownik EV, Haack T, Haberle J, Munnich A, Rotig A, Taylor RW, Nicholls RD, Kim JJ, Prokisch H, Vockley J. Complex I assembly function and fatty acid oxidation enzyme activity of ACAD9 both contribute to disease severity in ACAD9 deficiency. *Hum Mol Genet.* 2015 Jun 1;24(11):3238-47. doi: 10.1093/hmg/ddv074. Epub 2015 Feb 26. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25721401>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4424958/>)

Genomic Location

The *ACAD9* gene is found on chromosome 3 (<https://medlineplus.gov/genetics/chromosome/3/>).

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