

## HMGCL gene

3-hydroxy-3-methylglutaryl-CoA lyase

### Normal Function

The *HMGCL* gene provides instructions for making an enzyme called 3-hydroxymethyl-3-methylglutaryl-CoA lyase (HMG-CoA lyase). This enzyme is found in mitochondria, which are the energy-producing centers inside cells. HMG-CoA lyase plays a critical role in breaking down proteins and fats from the diet. Specifically, it is responsible for processing leucine, a protein building block (amino acid) that is part of many proteins. HMG-CoA lyase also produces ketones during the breakdown of fats. Ketones are compounds that certain organs and tissues, particularly the brain, use for energy when the simple sugar glucose is not available. For example, ketones are important sources of energy during periods of fasting.

### Health Conditions Related to Genetic Changes

#### 3-hydroxy-3-methylglutaryl-CoA lyase deficiency

More than 25 mutations in the *HMGCL* gene have been identified in people with 3-hydroxymethyl-3-methylglutaryl-CoA lyase deficiency (also called HMG-CoA lyase deficiency). Most of these mutations change single amino acids in the HMG-CoA lyase enzyme. For example, the most common mutation in the Saudi Arabian population replaces the amino acid arginine with the amino acid glutamine at position 41 (written as Arg41Gln or R41Q). Other *HMGCL* mutations result in the production of an abnormally short enzyme that is missing critical segments.

If a mutation reduces or eliminates the activity of HMG-CoA lyase, the body is unable to process leucine or make ketones properly. When leucine is not processed normally, chemical byproducts called organic acids can build up and make the blood too acidic (metabolic acidosis). A shortage of ketones can cause blood glucose levels to become dangerously low (hypoglycemia). The effects of metabolic acidosis and hypoglycemia can damage cells, particularly in the brain, resulting in serious illness in children with HMG-CoA lyase deficiency.

### Other Names for This Gene

- 3-hydroxy-3-methylglutarate-CoA lyase
- 3-hydroxy-3-methylglutaryl-Coenzyme A lyase

- 3-hydroxymethyl-3-methylglutaryl-CoA lyase
- 3-hydroxymethyl-3-methylglutaryl-Coenzyme A lyase
- HL
- HMG-CoA lyase
- HMGCL\_HUMAN

## **Additional Information & Resources**

### Tests Listed in the Genetic Testing Registry

- Tests of HMGCL ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3155\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=3155[geneid]))

### Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28HMGCL%5BTIAB%5D%29+OR+%28HMG+CoA+lyase%5BTIAB%5D%29+OR+%283-hydroxy-3-methylglutaryl-Coenzyme+A+lyase%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D%29>)

### Catalog of Genes and Diseases from OMIM

- 3-HYDROXY-3-METHYLGLUTARYL-CoA LYASE; HMGCL (<https://omim.org/entry/613898>)

### Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/3155>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=HMGCL\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=HMGCL[gene]))

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## Genomic Location

The *HMGCL* gene is found on chromosome 1 (<https://medlineplus.gov/genetics/chromosome/1/>).

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