



DLD gene

dihydrolipoamide dehydrogenase

Normal Function

The *DLD* gene provides instructions for making an enzyme called dihydrolipoamide dehydrogenase. This enzyme forms one part (subunit), called the E3 component, of several groups of enzymes that work together (enzyme complexes). These complexes are essential for the breakdown of certain molecules to produce energy in cells.

Branched-chain alpha-keto acid dehydrogenase, or BCKD, is one of the enzyme complexes that include dihydrolipoamide dehydrogenase. The BCKD enzyme complex performs one step in the breakdown of three protein building blocks (amino acids). These amino acids—leucine, isoleucine, and valine—are obtained from the diet. They are present in many kinds of food, particularly protein-rich foods such as milk, meat, and eggs. The breakdown of these amino acids produces molecules that can be used for energy.

Dihydrolipoamide dehydrogenase is also part of the pyruvate dehydrogenase (PDH) complex. This enzyme complex plays an important role in the production of energy for cells. It converts a molecule called pyruvate, which is formed from the breakdown of carbohydrates, into another molecule called acetyl-CoA. Dihydrolipoamide dehydrogenase performs one step of this chemical reaction. The conversion of pyruvate is essential to begin the series of chemical reactions that ultimately produces adenosine triphosphate (ATP), the cell's main energy source.

Dihydrolipoamide dehydrogenase is part of a third enzyme complex involved in cellular energy production. This complex, called alpha-ketoglutarate dehydrogenase (α KGDH), converts a molecule called α -ketoglutarate to another molecule called succinyl-CoA. Further steps in this process generate ATP for cells to use as energy.

Health Conditions Related to Genetic Changes

Dihydrolipoamide dehydrogenase deficiency

At least 17 mutations in the *DLD* gene have been found to cause dihydrolipoamide dehydrogenase deficiency. The signs and symptoms of this severe condition vary widely, but they most commonly include a potentially life-threatening buildup of lactic acid in the tissues (lactic acidosis), neurological problems, and liver disease.

Most *DLD* mutations change single amino acids in dihydrolipoamide dehydrogenase, which prevents the BCKD, PDH, and α KGDH enzyme complexes from functioning normally. Impairment of BCKD function leads to a buildup of valine, isoleucine,

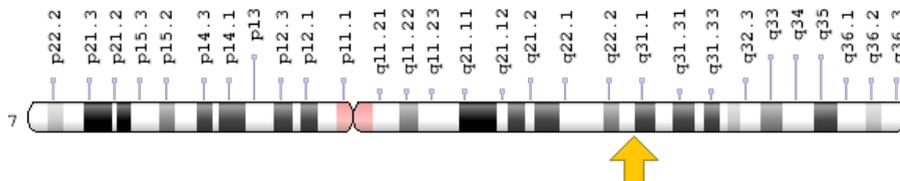
and leucine and their byproducts in the body. This accumulation is toxic to cells and tissues, particularly in the nervous system, and contributes to neurological problems in people with dihydrolipoamide dehydrogenase deficiency. A reduction in pyruvate dehydrogenase function results in buildup of pyruvate, which is converted in another chemical reaction to lactic acid, contributing to lactic acidosis in affected individuals. Impairment of α KGDH leads to the accumulation of alpha-ketoglutarate and likely also contributes to lactic acidosis. Reduced function of these three enzyme complexes also diminishes the production of cellular energy. The brain, which requires especially large amounts of energy, is severely affected, resulting in the neurological problems associated with dihydrolipoamide dehydrogenase deficiency. Liver problems are likely also related to decreased energy production in cells. The degree of impairment of each complex contributes to the variability in the features of this condition.

Leigh syndrome

Chromosomal Location

Cytogenetic Location: 7q31.1, which is the long (q) arm of chromosome 7 at position 31.1

Molecular Location: base pairs 107,891,107 to 107,921,198 on chromosome 7 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DIA1
- diaphorase
- dihydrolipoamide dehydrogenase (E3 component of pyruvate dehydrogenase complex, 2-oxo-glutarate complex, branched chain keto acid dehydrogenase complex)
- dihydrolipoyl dehydrogenase
- DLDH
- DLDH_HUMAN

- E3 component of pyruvate dehydrogenase
- GCSL
- glycine cleavage system L protein
- LAD
- lipoamide dehydrogenase
- lipoamide reductase
- lipoamide reductase (NADH)
- lipoyl dehydrogenase
- PHE3
- pyruvate dehydrogenase component E3

Additional Information & Resources

Educational Resources

- Basic Neurochemistry (sixth edition, 1998): Major Pathways of Branched-Chain Amino Acid Metabolism (figure)
<https://www.ncbi.nlm.nih.gov/books/NBK20436/figure/A3097/>
- Biochemistry (fifth edition, 2002): Succinyl Coenzyme A Is Formed by the Oxidative Decarboxylation of α -Ketoglutarate
https://www.ncbi.nlm.nih.gov/books/NBK22427/#_A2397_
- Biochemistry (fifth edition, 2002): The Formation of Acetyl Coenzyme A from Pyruvate
<https://www.ncbi.nlm.nih.gov/books/NBK22427/#A2376>
- Biochemistry (fifth edition, 2002): The Pyruvate Dehydrogenase Complex Is Regulated Allosterically and by Reversible Phosphorylation
<https://www.ncbi.nlm.nih.gov/books/NBK22347/#A2410>
- Molecular Biology of the Cell (fourth edition, 2002): Sugars and Fats Are Both Degraded to Acetyl CoA in Mitochondria
<https://www.ncbi.nlm.nih.gov/books/NBK26882/#A300>
- Molecular Cell Biology (fourth edition, 2000): Mitochondrial Oxidation of Pyruvate Begins with the Formation of Acetyl CoA
<https://www.ncbi.nlm.nih.gov/books/NBK21624/#A4352>

Clinical Information from GeneReviews

- Dihydrolipoamide Dehydrogenase Deficiency
<https://www.ncbi.nlm.nih.gov/books/NBK220444>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28DLD%5BTIAB%5D%29+AND+%28maple+syrup+urine+disease%5BTIAB%5D%29%29+OR+%28Dihydrolipoamide+dehydrogenase%5BMAJR%5D%29+OR+%28%28Dihydrolipoamide+dehydrogenase%5BMH%5D%29+AND+%28DLD+%5Btiab%5D+OR+DLDH+%5Btiab%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D>

Catalog of Genes and Diseases from OMIM

- DIHYDROLIPOAMIDE DEHYDROGENASE
<http://omim.org/entry/238331>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_DLD.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=DLD%5Bgene%5D>
- HGNC Gene Symbol Report
https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:2898
- Monarch Initiative
<https://monarchinitiative.org/gene/NCBIGene:1738>
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/1738>
- UniProt
<https://www.uniprot.org/uniprot/P09622>

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