PDHA1 gene
pyruvate dehydrogenase E1 alpha 1 subunit

Normal Function

The PDHA1 gene provides instructions for making a protein called E1 alpha. The E1 alpha protein is a piece (a subunit) of a larger protein: two E1 alpha proteins combine with two copies of another protein called E1 beta (produced from the PDHB gene) to form the E1 enzyme. This enzyme, also known as pyruvate dehydrogenase, is a component of a group of proteins called the pyruvate dehydrogenase complex.

The pyruvate dehydrogenase complex plays an important role in the pathways that convert the energy from food into a form that cells can use. This complex converts a molecule called pyruvate, which is formed from the breakdown of carbohydrates, into another molecule called acetyl-CoA. The E1 enzyme performs one part of this chemical reaction. The conversion of pyruvate is essential to begin the series of chemical reactions that produces adenosine triphosphate (ATP), the cell's main energy source.

Health Conditions Related to Genetic Changes

Pyruvate dehydrogenase deficiency

Mutations in the PDHA1 gene are the most common cause of pyruvate dehydrogenase deficiency, accounting for approximately 80 percent of cases of this condition. Pyruvate dehydrogenase deficiency is characterized by a potentially life-threatening buildup of a chemical called lactic acid in the body (lactic acidosis), delayed development, and neurological problems. Dozens of PDHA1 gene mutations have been identified in affected individuals. These mutations have been divided into two groups. One group includes mutations that add or remove DNA building blocks (nucleotides) to the PDHA1 gene (called insertion and deletion mutations, respectively). These types of mutations occur more commonly in affected females than males. The other group includes mutations that change single protein building blocks (amino acids) in the E1 alpha protein or result in a premature stop signal in the instructions for making the protein (called missense and nonsense mutations, respectively). These types of mutations occur in affected males more often than females.

Mutations in the PDHA1 gene associated with pyruvate dehydrogenase deficiency lead to a reduction in the amount of E1 alpha protein or result in an abnormal protein that cannot function properly. The abnormal protein may not be able to interact with E1 beta to form the E1 enzyme or with other factors needed for the E1 enzyme to perform its chemical reaction. A decrease in functional E1 alpha results in reduced pyruvate dehydrogenase complex activity. With decreased function of this complex,
pyruvate builds up and is converted, in another chemical reaction, to lactic acid, causing lactic acidosis. In addition, the production of cellular energy is diminished. The brain, which is especially dependent on this form of energy, is severely affected, resulting in the neurological problems associated with pyruvate dehydrogenase deficiency.

**Leigh syndrome**

**Chromosomal Location**

Cytogenetic Location: Xp22.12, which is the short (p) arm of the X chromosome at position 22.12

Molecular Location: base pairs 19,343,893 to 19,361,718 on the X chromosome (Homo sapiens Updated Annotation Release 109.20190607, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

**Other Names for This Gene**

- ODPA_HUMAN
- PDHA
- PDHCE1A
- PDHE1-A type I
- PHE1A
- pyruvate dehydrogenase (lipoamide) alpha 1
- pyruvate dehydrogenase alpha 1
- pyruvate dehydrogenase complex, E1-alpha polypeptide 1
- pyruvate dehydrogenase E1 component subunit alpha, somatic form, mitochondrial
Additional Information & Resources

Educational Resources

• Biochemistry (fifth edition, 2002): The Formation of Acetyl Coenzyme A from Pyruvate
  https://www.ncbi.nlm.nih.gov/books/NBK22427/#A2376


• 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

Scientific Articles on PubMed

• PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28PDHA1%5BTIAB%5D%29+OR+%28%28PDHA%5BTIAB%5D%29+OR+%28E1+alpha%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

• PYRUVATE DEHYDROGENASE E1-ALPHA DEFICIENCY
  http://omim.org/entry/312170

• PYRUVATE DEHYDROGENASE, ALPHA-1
  http://omim.org/entry/300502

Research Resources

• Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_PDHA1.html

• ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=PDHA1%5Bgene%5D

• HGNC Gene Symbol Report

• Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:5160
NCBI Gene

UniProt
https://www.uniprot.org/uniprot/P08559

Sources for This Summary

  https://www.ncbi.nlm.nih.gov/books/NBK22427/#A2376

  BH. Mutations in the X-linked E1 alpha subunit of pyruvate dehydrogenase: exon skipping,
  insertion of duplicate sequence, and missense mutations leading to the deficiency of the pyruvate
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/7887409
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1801155/

- Imbard A, Boutron A, Vequaud C, Zater M, de Lonlay P, de Baulny HO, Barnerias C, Miné M,
  Marsac C, Saudubray JM, Brivet M. Molecular characterization of 82 patients with pyruvate
  dehydrogenase complex deficiency. Structural implications of novel amino acid substitutions in E1
  Aug 18.
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/21914562

  Y, Kerr DS, Wexler ID, Patel MS, Robinson BH, Seyda A. Mutations in the X-linked pyruvate
  dehydrogenase (E1) alpha subunit gene (PDHA1) in patients with a pyruvate dehydrogenase
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/10679936

- OMIM: PYRUVATE DEHYDROGENASE, ALPHA-1
  http://omim.org/entry/300502

- Patel MS, Korotchkina LG, Sidhu S. Interaction of E1 and E3 components with the core proteins of
  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/20160912
  Free article on PubMed Central: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2770179/

Reprinted from Genetics Home Reference:
https://ghr.nlm.nih.gov/gene/PDHA1

Reviewed: July 2012
Published: August 20, 2019

Lister Hill National Center for Biomedical Communications
U.S. National Library of Medicine
National Institutes of Health
Department of Health & Human Services