BCKDHA gene
branched chain keto acid dehydrogenase E1, alpha polypeptide

Normal Function

The *BCKDHA* gene provides instructions for making one part, the alpha subunit, of a group of enzymes called the branched-chain alpha-keto acid dehydrogenase (BCKD) enzyme complex. Two alpha subunits connect with two beta subunits, which are produced from the *BCKDHB* gene, to form a critical piece of the enzyme complex called the E1 component.

The BCKD enzyme complex is responsible for one step in the normal 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 BCKD enzyme complex is active in mitochondria, which are specialized structures inside cells that serve as energy-producing centers. The breakdown of leucine, isoleucine, and valine produces molecules that can be used for energy.

Health Conditions Related to Genetic Changes

**Maple syrup urine disease**

More than 80 mutations in the *BCKDHA* gene have been identified in people with maple syrup urine disease. These mutations most often cause the severe, classic form of the disorder, which becomes apparent soon after birth. Maple syrup urine disease gets its name from the distinctive sweet odor of affected infants’ urine. It is also characterized by poor feeding, vomiting, lack of energy (lethargy), abnormal movements, and delayed development.

Most *BCKDHA* mutations change single amino acids in the alpha subunit of the BCKD enzyme complex. In the Old Order Mennonite population, where maple syrup urine disease occurs frequently, the most common mutation replaces the amino acid tyrosine with the amino acid asparagine at position 438 (written as Tyr438Asn or Y438N).

Mutations in the *BCKDHA* gene disrupt the normal function of the BCKD enzyme complex, preventing it from effectively breaking down leucine, isoleucine, and valine. As a result, these amino acids and their byproducts build up in the body. This accumulation is toxic to cells and tissues, particularly in the nervous system. The buildup of these substances can lead to seizures, developmental delay, and the other health problems associated with maple syrup urine disease.
Chromosomal Location

Cytogenetic Location: 19q13.2, which is the long (q) arm of chromosome 19 at position 13.2

Molecular Location: base pairs 41,397,818 to 41,425,002 on chromosome 19 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)

Credit: Genome Decoration Page/NCBI

Other Names for This Gene

• BCKDE1A
• BCKDH E1-alpha
• branched chain keto acid dehydrogenase E1, alpha polypeptide (maple syrup urine disease)
• MSUD1
• ODBA_HUMAN

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/

• Basic Neurochemistry (sixth edition, 1998): Maple syrup urine disease was the first congenital defect of branched-chain amino acid catabolism to be described
  https://www.ncbi.nlm.nih.gov/books/NBK28225/#A3107

Clinical Information from GeneReviews

• Maple Syrup Urine Disease
  https://www.ncbi.nlm.nih.gov/books/NBK1319
Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28BCKDHA%5BTIAB%5D%29+OR+%28%28BCKD%5BTIAB%5D%29+AND+%28E1%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D

Catalog of Genes and Diseases from OMIM

- BRANCHED-CHAIN KETO ACID DEHYDROGENASE E1, ALPHA POLYPEPTIDE
  http://omim.org/entry/608348

Research Resources

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

- HGNC Gene Symbol Report

- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:593

- NCBI Gene

- UniProt
  https://www.uniprot.org/uniprot/P12694

Sources for This Summary

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/17922217

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/14517957

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/12888983

  Citation on PubMed: https://www.ncbi.nlm.nih.gov/pubmed/18378174

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