D2HGDH gene

D-2-hydroxyglutarate dehydrogenase

Normal Function

The *D2HGDH* gene provides instructions for making an enzyme called D-2-hydroxyglutarate dehydrogenase. This enzyme is found in mitochondria, which are the energy-producing centers within cells. Within mitochondria, the enzyme participates in reactions that produce energy for cell activities. Specifically, D-2-hydroxyglutarate dehydrogenase converts a compound called D-2-hydroxyglutarate to another compound called 2-ketoglutarate. A series of additional enzymes further process 2-ketoglutarate to produce energy.

Health Conditions Related to Genetic Changes

2-hydroxyglutaric aciduria

Researchers have identified more than 30 *D2HGDH* gene mutations that cause a type of 2-hydroxyglutaric aciduria known as D-2-hydroxyglutaric aciduria (D-2-HGA) type I. This condition has a variety of signs and symptoms that result primarily from progressive damage to the brain beginning early in life.

Some *D2HGDH* gene mutations change single protein building blocks (amino acids) in the D-2-hydroxyglutarate dehydrogenase enzyme, which likely impairs its function. Other mutations lead to the production of an abnormally short, nonfunctional version of the enzyme. With a shortage of functional enzyme, D-2-hydroxyglutarate is not broken down but instead builds up in cells. At high levels, this compound can damage cells and lead to cell death. Brain cells appear to be the most vulnerable to the toxic effects of this compound, which may explain why the signs and symptoms of D-2-HGA type I primarily involve the brain.

Other Names for This Gene

- 2-hydroxypentanedioic acid
- D2HDH_HUMAN
- D2HGD
- FLJ42195
- MGC25181

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of D2HGDH (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=728294[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28D2HGDH%5BTIAB%5D%29+OR+%28D-2-hydroxyglutarate+dehydrogenase%5BTIAB%5D%29+OR+%28D-2-HGDH%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D)

Catalog of Genes and Diseases from OMIM

- D-2-HYDROXYGLUTARATE DEHYDROGENASE; D2HGDH (https://omim.org/entry/609186)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/728294)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=D2HGDH[gene])

References

- Kranendijk M, Struys EA, Gibson KM, Wickenhagen WV, Abdenur JE, Buechner J, Christensen E, de Kremer RD, Errami A, Gissen P, Gradowska W, Hobson E, Islam L,Korman SH, Kurczynski T, Maranda B, Meli C, Rizzo C, Sansaricq C, Trefz FK, Webster R, Jakobs C, Salomons GS. Evidence for genetic heterogeneity inD-2-hydroxyglutaric aciduria. Hum Mutat. 2010 Mar;31(3):279-83. doi:10.1002/humu.21186. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20020533)
- Kranendijk M, Struys EA, Salomons GS, Van der Knaap MS, Jakobs C. Progress inunderstanding 2-hydroxyglutaric acidurias. J Inherit Metab Dis. 2012Jul;35(4):571-87. doi: 10.1007/s10545-012-9462-5. Epub 2012 Mar 6. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/22391998) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3388262/)
- Struys EA, Korman SH, Salomons GS, Darmin PS, Achouri Y, van Schaftingen E, Verhoeven NM, Jakobs C. Mutations in phenotypically mild D-2-hydroxyglutaricaciduria. Ann Neurol. 2005 Oct;58(4):626-30. doi: 10.1002/ana.20559. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16037974)
- Struys EA, Salomons GS, Achouri Y, Van Schaftingen E, Grosso S, Craigen WJ, Verhoeven NM, Jakobs C. Mutations in the D-2-hydroxyglutarate dehydrogenase genecause D-2-hydroxyglutaric aciduria. Am J Hum Genet. 2005 Feb;76(2):358-60.

doi:10.1086/427890. Epub 2004 Dec 17. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15609246) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1196381/)

- Struys EA. D-2-Hydroxyglutaric aciduria: unravelling the biochemical pathwayand the genetic defect. J Inherit Metab Dis. 2006 Feb;29(1):21-9. doi:10.1007/s10545-006-0317-9. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16601864)

Genomic Location

The *D2HGDH* gene is found on chromosome 2 (https://medlineplus.gov/genetics/chromosome/2/).

Last updated August 1, 2013