

CA5A gene

carbonic anhydrase 5A

Normal Function

The *CA5A* gene provides instructions for making an enzyme called carbonic anhydrase VA. This enzyme helps convert carbon dioxide to a substance called bicarbonate. Bicarbonate is necessary to maintain the proper acid-base balance in the body, which is necessary for most biological reactions to proceed properly.

The carbonic anhydrase VA enzyme is particularly important in the liver, where it provides bicarbonate needed by four enzymes in the energy-producing centers of cells (mitochondria): carbomoyl phosphate synthetase-1, pyruvate carboxylase, propionyl-CoA carboxylase, and 3-methylcrotonyl-CoA carboxylase. These enzymes help control the amount of certain other substances in the body. Carbomoyl phosphate synthetase-1 is involved in the urea cycle, which processes excess nitrogen and prevents it from accumulating as ammonia, a substance that is toxic to the brain. Pyruvate carboxylase is involved in the production of the simple sugar glucose (gluconeogenesis) in the liver. Propionyl-CoA carboxylase and 3-methylcrotonyl-CoA carboxylase help break down certain protein building blocks (amino acids).

Health Conditions Related to Genetic Changes

Carbonic anhydrase VA deficiency

At least three *CA5A* gene mutations have been identified in people with carbonic anhydrase VA deficiency. This inherited disorder is characterized by potentially life-threatening episodes of poor feeding, vomiting, weight loss, tiredness (lethargy), rapid breathing (tachypnea), seizures, or coma. The risk of these episodes is thought to decline after childhood.

Mutations in the *CA5A* gene result in absent or impaired carbonic anhydrase VA enzyme function, leading to reduced bicarbonate production. Insufficient bicarbonate results in impaired control of acid-base balance and reduces the activity of the four affected mitochondrial enzymes, leading to various biochemical abnormalities that are associated with carbonic anhydrase VA deficiency and that cause the episodes that occur in this disorder. Studies suggest that a related enzyme produced from the *CA5B* gene may increasingly compensate for the lack of carbonic anhydrase VA as affected individuals mature, which may result in a reduced risk of disease episodes after

childhood.

Other Names for This Gene

- CA-VA
- CA5
- CA5AD
- carbonate dehydratase VA
- carbonic anhydrase 5A, mitochondrial precursor
- carbonic anhydrase V, mitochondrial
- carbonic anhydrase VA, mitochondrial
- carbonic dehydratase
- CAV
- CAVA
- GS1-21A4.1

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of CA5A ([https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=763\[geneid\]](https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=763[geneid]))

Scientific Articles on PubMed

- PubMed (<https://pubmed.ncbi.nlm.nih.gov/?term=%28%28CA5A%5BTIAB%5D%29+OR+%28carbonic+anhydrase+5A%5BTIAB%5D%29%29+OR+%28%28CA-VA%5BTIAB%5D%29+OR+%28carbonate+dehydratase+VA%5BTIAB%5D%29+OR+%28carbonic+anhydrase+5A,+mitochondrial+precursor%5BTIAB%5D%29+OR+%28carbonic+anhydrase+V,+mitochondrial%5BTIAB%5D%29+OR+%28carbonic+anhydrase+VA,+mitochondrial%5BTIAB%5D%29+OR+%28carbonic+dehydratase%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D%29%29>)

Catalog of Genes and Diseases from OMIM

- CARBONIC ANHYDRASE VA; CA5A (<https://omim.org/entry/114761>)

Gene and Variant Databases

- NCBI Gene (<https://www.ncbi.nlm.nih.gov/gene/763>)
- ClinVar ([https://www.ncbi.nlm.nih.gov/clinvar?term=CA5A\[gene\]](https://www.ncbi.nlm.nih.gov/clinvar?term=CA5A[gene]))

References

- Diez-Fernandez C, Rufenacht V, Santra S, Lund AM, Santer R, Lindner M, Tangeraas T, Unsinn C, de Lonlay P, Burlina A, van Karnebeek CD, Haberle J. Defective hepatic bicarbonate production due to carbonic anhydrase VA deficiency leads to early-onset life-threatening metabolic crisis. *Genet Med*. 2016 Oct; 18(10):991-1000. doi: 10.1038/gim.2015.201. Epub 2016 Feb 25. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/26913920>)
- Nagao Y, Batanian JR, Clemente MF, Sly WS. Genomic organization of the human gene (CA5) and pseudogene for mitochondrial carbonic anhydrase V and their localization to chromosomes 16q and 16p. *Genomics*. 1995 Aug 10; 28(3):477-84. doi:10.1006/geno.1995.1177. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/7490083>)
- Pastorekova S, Parkkila S, Pastorek J, Supuran CT. Carbonic anhydrases: current state of the art, therapeutic applications and future prospects. *J Enzyme Inhib Med Chem*. 2004 Jun; 19(3):199-229. doi: 10.1080/14756360410001689540. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/15499993>)
- Shah GN, Rubbelke TS, Hendin J, Nguyen H, Waheed A, Shoemaker JD, Sly WS. Targeted mutagenesis of mitochondrial carbonic anhydrases VA and VB implicates both enzymes in ammonia detoxification and glucose metabolism. *Proc Natl Acad Sci U S A*. 2013 Apr 30; 110(18):7423-8. doi: 10.1073/pnas.1305805110. Epub 2013 Apr 15. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/23589845>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3645511/>)
- Sly WS, Hu PY. Human carbonic anhydrases and carbonic anhydrase deficiencies. *Annu Rev Biochem*. 1995; 64:375-401. doi: 10.1146/annurev.bi.64.070195.002111. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/7574487>)
- van Karnebeek C, Haberle J. Carbonic Anhydrase VA Deficiency. 2015 Apr 2 [updated 2021 Aug 26]. In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A, editors. *GeneReviews*(R) [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from <http://www.ncbi.nlm.nih.gov/books/NBK284774/> Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/25834911>)
- van Karnebeek CD, Sly WS, Ross CJ, Salvarinova R, Yapliito-Lee J, Santra S, Shyr C, Horvath GA, Eydoux P, Lehman AM, Bernard V, Newlove T, Ukpeh H, Chakrapani A, Preece MA, Ball S, Pitt J, Vallance HD, Coulter-Mackie M, Nguyen H, Zhang LH, Bhavsar AP, Sinclair G, Waheed A, Wasserman WW, Stockler-Ipsiroglu S. Mitochondrial carbonic anhydrase VA deficiency resulting from CA5A alterations presents with hyperammonemia in early childhood. *Am J Hum Genet*. 2014 Mar 6; 94(3):453-61. doi: 10.1016/j.ajhg.2014.01.006. Epub 2014 Feb 13. Citation on PubMed (<https://pubmed.ncbi.nlm.nih.gov/24530203>) or Free article on PubMed Central (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3951944/>)

Genomic Location

The CA5A gene is found on chromosome 16 (<https://medlineplus.gov/genetics/chromos>

ome/16/).

Last updated September 1, 2016