GAMT gene

guanidinoacetate N-methyltransferase

Normal Function

The *GAMT* gene provides instructions for making the enzyme guanidinoacetate methyltransferase, which is active (expressed) mainly in the liver. This enzyme participates in the two-step production (synthesis) of the compound creatine from the protein building blocks (amino acids) glycine, arginine, and methionine. Specifically, guanidinoacetate methyltransferase controls the second step of this process. In this step, creatine is produced from another compound called guanidinoacetate. Creatine is needed for the body to store and use energy properly. It is involved in providing energy for muscle contraction, and is also important in nervous system functioning.

In addition to its role in creatine synthesis, the guanidinoacetate methyltransferase enzyme is thought to help activate a process called fatty acid oxidation. This process provides an energy source for cells during times of stress when their normal fuel, the simple sugar glucose, is scarce.

Health Conditions Related to Genetic Changes

Guanidinoacetate methyltransferase deficiency

At least 49 mutations in the *GAMT* gene cause guanidinoacetate methyltransferase deficiency, a disorder that involves intellectual disability and seizures. Most affected individuals of Portuguese ancestry have a particular mutation in which the amino acid tryptophan is replaced by the amino acid serine at position 20 in the enzyme (written as Trp20Ser or W20S).

GAMT gene mutations impair the ability of the guanidinoacetate methyltransferase enzyme to participate in creatine synthesis, resulting in a shortage of creatine. The effects of guanidinoacetate methyltransferase deficiency are most severe in organs and tissues that require large amounts of energy, especially the brain.

Other Names for This Gene

- GAMT_HUMAN
- PIG2
- TP53I2

Additional Information & Resources

Tests Listed in the Genetic Testing Registry

- Tests of GAMT (https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=2593[geneid])

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28GAMT%5BTIAB%5D%29+OR+%28guanidinoacetate+N-methyltransferase%5BTIAB%5D%29%29+OR+%28PIG2%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D)

Catalog of Genes and Diseases from OMIM

- GUANIDINOACETATE METHYLTRANSFERASE; GAMT (https://omim.org/entry/601240)

Gene and Variant Databases

- NCBI Gene (https://www.ncbi.nlm.nih.gov/gene/2593)
- ClinVar (https://www.ncbi.nlm.nih.gov/clinvar?term=GAMT[gene])

References

- Almeida LS, Vilarinho L, Darmin PS, Rosenberg EH, Martinez-Munoz C, Jakobs C, Salomons GS. A prevalent pathogenic GAMT mutation (c.59G>C) in Portugal. MolGenet Metab. 2007 May;91(1):1-6. doi: 10.1016/j.ymgme.2007.01.005. Epub 2007 Mar1. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/17336114)
- Beard E, Braissant O. Synthesis and transport of creatine in the CNS:importance for cerebral functions. J Neurochem. 2010 Oct;115(2):297-313. doi:10.1111/j.1471-4159.2010.06935.x. Epub 2010 Aug 25. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20796169)
- Braissant O, Henry H, Beard E, Uldry J. Creatine deficiency syndromes and theimportance of creatine synthesis in the brain. Amino Acids. 2011May;40(5):1315-24. doi: 10.1007/s00726-011-0852-z. Epub 2011 Mar 10. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/21390529)
- Dhar SU, Scaglia F, Li FY, Smith L, Barshop BA, Eng CM, Haas RH, Hunter JV, Lotze T, Maranda B, Willis M, Abdenur JE, Chen E, O'Brien W, Wong LJ. Expandedclinical and molecular spectrum of guanidinoacetate methyltransferase (GAMT)deficiency. Mol Genet Metab. 2009 Jan;96(1):38-43. doi:10.1016/j.ymgme.2008.10.008. Epub 2008 Nov 21. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19027335)

- Gordon N. Guanidinoacetate methyltransferase deficiency (GAMT). Brain Dev.2010 Feb;32(2):79-81. doi: 10.1016/j.braindev.2009.01.008. Epub 2009 Mar 16. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19289269)
- Ide T, Brown-Endres L, Chu K, Ongusaha PP, Ohtsuka T, El-Deiry WS, AaronsonSA, Lee SW. GAMT, a p53-inducible modulator of apoptosis, is critical for theadaptive response to nutrient stress. Mol Cell. 2009 Nov 13;36(3):379-92. doi:10.1016/j.molcel.2009.09.031. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/19917247) or Free article on PubMed Central (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2779531/)
- Leuzzi V, Carducci C, Carducci C, Matricardi M, Bianchi MC, Di Sabato ML,Artiola C, Antonozzi I. A mutation on exon 6 of guanidinoacetatemethyltransferase (GAMT) gene supports a different function for isoform a and bof GAMT enzyme. Mol Genet Metab. 2006 Jan;87(1):88-90. doi:10.1016/j.ymgme.2005.09.017. Epub 2005 Nov 15. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/16293431)
- Mercimek-Mahmutoglu S, Ndika J, Kanhai W, de Villemeur TB, Cheillan D, Christensen E, Dorison N, Hannig V, Hendriks Y, Hofstede FC, Lion-Francois L, Lund AM, Mundy H, Pitelet G, Raspall-Chaure M, Scott-Schwoerer JA, Szakszon K, Valayannopoulos V, Williams M, Salomons GS. Thirteen new patients withguanidinoacetate methyltransferase deficiency and functional characterization ofnineteen novel missense variants in the GAMT gene. Hum Mutat. 2014Apr;35(4):462-9. doi: 10.1002/humu.22511. Epub 2014 Mar 6. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/24415674)
- Nasrallah F, Feki M, Kaabachi N. Creatine and creatine deficiency syndromes: biochemical and clinical aspects. Pediatr Neurol. 2010 Mar;42(3):163-71. doi:10.1016/j.pediatrneurol.2009.07.015. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/20159424)
- Schulze A. Creatine deficiency syndromes. Mol Cell Biochem. 2003Feb;244(1-2):143-50. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/12701824)
- Stockler S, Holzbach U, Hanefeld F, Marquardt I, Helms G, Requart M, HanickeW, Frahm J. Creatine deficiency in the brain: a new, treatable inborn error ofmetabolism. Pediatr Res. 1994 Sep;36(3):409-13. doi:10.1203/00006450-199409000-00023. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/7808840)
- Sykut-Cegielska J, Gradowska W, Mercimek-Mahmutoglu S, Stockler-Ipsiroglu S. Biochemical and clinical characteristics of creatine deficiency syndromes. ActaBiochim Pol. 2004;51(4):875-82. Citation on PubMed (https://pubmed.ncbi.nlm.nih.gov/15625559)

Genomic Location

The *GAMT* gene is found on chromosome 19 (https://medlineplus.gov/genetics/chromosome/19/).

Last updated June 1, 2015