NAGS gene

N-acetylglutamate synthase

Normal Function

The *NAGS* gene provides instructions for making the enzyme N-acetylglutamate synthase. This enzyme is needed for the urea cycle, a series of reactions that occurs in liver cells. The urea cycle breaks down excess nitrogen, which is made when protein is used by the body, into a compound called urea. Urea is removed from the body in urine. Removing the excess nitrogen prevents it from accumulating in the form of ammonia, which is toxic at high levels, especially to the brain.

N-acetylglutamate synthase controls the production of a compound called N-acetylglutamate in the mitochondria, the energy-producing centers in cells. N-acetylglutamate is necessary to turn on the enzyme carbamoyl phosphate synthetase I. This enzyme controls the first step of the urea cycle, in which excess nitrogen compounds are incorporated into the cycle to be broken down.

Health Conditions Related to Genetic Changes

N-acetylglutamate synthase deficiency

More than 40 *NAGS* gene mutations have been identified in people with N-acetylglutamate synthase deficiency, which is characterized by abnormally high levels of ammonia in the blood. This condition can cause extreme tiredness (lethargy), difficulty feeding, problems controlling breathing or body temperature, and seizures in infancy. Affected adults can have episodes of vomiting, confusion, headaches, or other neurological problems.

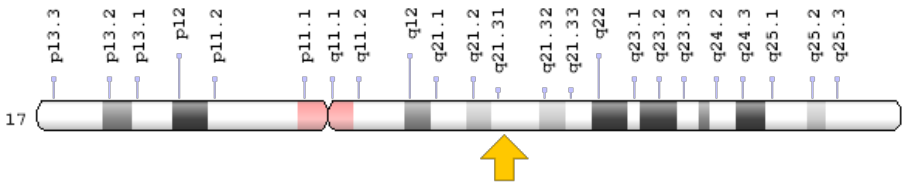
Most *NAGS* gene mutations that cause N-acetylglutamate synthase deficiency change single protein building blocks (amino acids) in the N-acetylglutamate synthase enzyme. It is thought that the abnormal enzyme cannot function properly. Other mutations result in production of an abnormally short N-acetylglutamate synthase enzyme or prevent any enzyme from being produced at all.

When the function of the N-acetylglutamate synthase enzyme is reduced or eliminated, N-acetylglutamate is produced in lower-than-normal amounts, or not at all. This shortage of N-acetylglutamate prevents carbamoyl phosphate synthetase I from being turned on, which prevents the urea cycle from starting. As a result, excess nitrogen is not converted to urea for removal, and ammonia accumulates in the blood. The buildup of ammonia damages tissues in the brain and causes the neurological problems and other signs and symptoms of N-acetylglutamate synthase deficiency.

Chromosomal Location

Cytogenetic Location: 17q21.31, which is the long (q) arm of chromosome 17 at position 21.31

Molecular Location: base pairs 44,004,546 to 44,009,068 on chromosome 17 (Homo sapiens Updated Annotation Release 109.20190905, GRCh38.p13) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- ARGA
- MGC133025
- NAGS_HUMAN

Additional Information & Resources

Educational Resources

- Biochemistry (5th editions, 2002): Ammonium Ion is Converted into Urea in Most Terrestrial Vertebrates
  https://www.ncbi.nlm.nih.gov/books/NBK22450/

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28NAGS%5BTIAB%5D%29+OR+%28N-acetylglutamate+synthase%5BTIAB%5D%29%29+OR+%28%28AGAS%5BTIAB%5D%29+OR+%28ARGA%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+AND+%22last+3600+days%22%5Bdp%5D

Catalog of Genes and Diseases from OMIM

- N-ACETYLGLUTAMATE SYNTHASE
  http://omim.org/entry/608300

Research Resources

- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=NAGS%5Bgene%5D
- HGNC Gene Symbol Report
  https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:17996
- Monarch Initiative
  https://monarchinitiative.org/gene/NCBIGene:162417
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/162417
- UniProt
  https://www.uniprot.org/uniprot/Q8N159

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