The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000156.6(GAMT):c.134G>A (p.Trp45Ter)

Version: 1.0

CA402998096

2419155 (ClinVar)

Gene: GAMT (HGNC:2593)
Condition: guanidinoacetate methyltransferase deficiency (MONDO:0012999)
Inheritance Mode: Autosomal recessive inheritance
UUID: 683bc758-d93c-4fd6-a8f9-f9c5cd7a5bfa
Approved on: 2023/10/12
Published on: 2023/11/8

HGVS expressions

NM_000156.6(GAMT):c.134G>A (p.Trp45Ter)
NM_000156.6:c.134G>A
NC_000019.10:g.1401343C>T
CM000681.2:g.1401343C>T
NC_000019.9:g.1401342C>T
CM000681.1:g.1401342C>T
NC_000019.8:g.1352342C>T
NG_009785.1:g.5211G>A
ENST00000252288.8:c.134G>A
ENST00000447102.8:c.134G>A
ENST00000640762.1:c.112+22G>A
ENST00000252288.6:c.134G>A
ENST00000447102.7:c.134G>A
NM_000156.5:c.134G>A
NM_138924.2:c.134G>A
NM_138924.3:c.134G>A

Pathogenic

Met criteria codes 4

PVS1 PM3 PP4 PM2_Supporting

Not Met criteria codes 2

BA1 BS1

Evidence Links 0

Expert Panel

Cerebral Creatine Deficiency Syndromes VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Cerebral Creatine Deficiency Syndromes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GAMT Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_000156.6:c.134G>A (p.Trp45Ter) variant in GAMT is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 1/6 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been detected in at least two probands with GAMT deficiency. Of those probands, both were homozygous for the variant (PMIDs 31222513, 33996490) (PM3). At least one proband (two siblings) with this variant had elevated GAA and low creatine in plasma (PP4). This variant is absent in gnomAD v2.1.1 (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 2419155). In summary, this variant meets the criteria to be classified as pathogenic for GAMT deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (Specifications Version 1.1.0): PVS1, PM3, PP4, PM2_Supporting. (Classification approved by the ClinGen CCDS VCEP on Oct 12, 2023)

Met criteria codes

PVS1	✔	Nonsense variant in exon 1
PM3	✔	Variant observed in the homozygous state in two probands with clinical features of GAMT deficiency
PP4	✔	Variant found homozygous in two affected siblings with elevated plasma GAA and low creatine levels.
PM2_Supporting	✔	Absent from gnomAD

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.