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Variant: NM_000156.6(GAMT):c.432G>A (p.Trp144Ter)

Version: 1.0

CA402995151

1391239 (ClinVar)

Gene: GAMT (HGNC:2593)
Condition: guanidinoacetate methyltransferase deficiency (MONDO:0012999)
Inheritance Mode: Autosomal recessive inheritance
UUID: 81f58b0c-e8be-4b55-80d9-c3b4231e7873
Approved on: 2024/4/26
Published on: 2024/7/2

HGVS expressions

NM_000156.6:c.432G>A
NM_000156.6(GAMT):c.432G>A (p.Trp144Ter)
NC_000019.10:g.1399155C>T
CM000681.2:g.1399155C>T
NC_000019.9:g.1399154C>T
CM000681.1:g.1399154C>T
NC_000019.8:g.1350154C>T
NG_009785.1:g.7399G>A
ENST00000252288.8:c.432G>A
ENST00000447102.8:c.432G>A
ENST00000591788.3:c.115G>A
ENST00000640164.1:n.265G>A
ENST00000640762.1:c.363G>A
ENST00000252288.6:c.432G>A
ENST00000447102.7:c.432G>A
ENST00000591788.2:c.117G>A
NM_000156.5:c.432G>A
NM_138924.2:c.432G>A
NM_138924.3:c.432G>A

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PP4_Moderate PM3_Supporting

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.432G>A variant in GAMT is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 4 out of 6, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been previously reported in one individual with GAMT deficiency (PMID: 36911476). This individual was homozygous for the variant (PM3_Supporting). This individual had significantly decreased creatine peak on brain MRS (PP4_Moderate). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 1391239). In summary, this variant meets the criteria to be classified as pathogenic for GAMT deficiency based on the GAMT-specific ACMG/AMP criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (Specifications Version 1.1.0): PVS1, PM2_Supporting, PM3_Supporting, PP4_Moderate. (Classification approved by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel on April 26, 2024)

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1	✔	The NM_000156.6:c.432G>A variant in GAMT is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 4 out of 6, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PP4_Moderate	✔	This individual had significantly decreased creatine peak on brain MRS (PP4_Moderate)
PM3_Supporting	✔	This variant has been previously reported in one individual with GAMT deficiency (PMID: 36911476). This individual was homozygous for the variant (PM3_Supporting).

Curation History

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