

Variant: *NM_000156.6(GAMT):c.408G>A (p.Thr136=)*

Version: 1.0

CA9043668 [↗](#)

699986 (ClinVar) [↗](#)

Gene: GAMT ([HGNC:2593](#))

Condition: guanidinoacetate methyltransferase deficiency
([MONDO:0012999](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 7b09ba2d-5a29-424b-b5d0-934035626866

Approved on: 2022/6/6

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HGVS expressions

NM_000156.6(GAMT):c.408G>A (p.Thr136=)

NM_000156.6:c.408G>A

NC_000019.10:g.1399179C>T

CM000681.2:g.1399179C>T

NC_000019.9:g.1399178C>T

CM000681.1:g.1399178C>T

NC_000019.8:g.1350178C>T

NG_009785.1:g.7375G>A

ENST00000252288.8:c.408G>A

ENST00000447102.8:c.408G>A

ENST00000591788.3:c.91G>A

ENST00000640164.1:n.241G>A

ENST00000640762.1:c.339G>A

ENST00000252288.6:c.408G>A

ENST00000447102.7:c.408G>A

ENST00000591788.2:c.93G>A

NM_000156.5:c.408G>A

NM_138924.2:c.408G>A

NM_138924.3:c.408G>A

Likely Benign

Met criteria codes **3**

BP4

BP7

PM2_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

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_000156.6:c.408G>A (p.Thr136=) variant in GAMT is a synonymous variant in exon 4. It is predicted to not impact splicing by SpliceAI and VarSeak, and the nucleotide is not highly conserved (BP4, BP7). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00005 (1/ 18390 alleles) in the East Asian population, which is lower than the ClinGen CCDS VCEP’s threshold for PM2_Supporting (<0.0004), meeting this criterion (PM2_Supporting). This variant does not appear to have been previously reported in the published literature. It is noted in ClinVar (Variation ID: 699986). Although this variant is rare (meeting PM2_Supporting), it has been classified as likely benign by the ClinGen Creatine Deficiency Syndromes (CCDS) Variant Curation Expert Panel (VCEP) based on the recommendation of Richards et al (PMID: 25741868) because it is a synonymous variant, the altered nucleotide is not highly conserved, computational prediction suggests no impact on splicing, and there is no additional evidence to suggest that the variant is disease-causing. GAMT-specific ACMG/AMP criteria applied, as specified by the CCDS VCEP (Specifications Version 1.1.0): PM2_Supporting, BP4, BP7. (Classification approved by the ClinGen CCDS VCEP on June 6, 2022).

Met criteria codes

BP4			This variant is predicted to not impact splicing by SpliceAI and VarSeak (BP4).
BP7			It is predicted to not impact splicing by SpliceAI and VarSeak, and the nucleotide is not highly conserved (GERP rejected substitutions (RS) score -6.38) (BP7).
PM2_Supporting			The highest population minor allele frequency in gnomAD v2.1.1 is 0.00005 (1/ 18390 alleles) in the East Asian population, which is lower than the ClinGen CCDS VCEP’s threshold for PM2_Supporting (<0.0004), meeting this criterion (PM2_Supporting).

Curation History







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