

Variant: *NM_000156.6(GAMT):c.577C>T (p.Gln193Ter)*

Version: 1.0

CA402991043 [↗](#)

2503890 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 69dfad77-097d-47bc-aeb9-67c5f7cf4773

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HGVS expressions

NM_000156.6:c.577C>T

NM_000156.6(GAMT):c.577C>T (p.Gln193Ter)

NC_000019.10:g.1397493G>A

CM000681.2:g.1397493G>A

NC_000019.9:g.1397492G>A

CM000681.1:g.1397492G>A

NC_000019.8:g.1348492G>A

NG_008283.1:g.18610G>A

NG_009785.1:g.9061C>T

ENST00000252288.8:c.577C>T

ENST00000640164.1:n.410C>T

ENST00000640762.1:c.508C>T

ENST00000252288.6:c.577C>T

NM_000156.5:c.577C>T

Likely Pathogenic

Met criteria codes **4**

PVS1_Strong

PP4

PM3

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 2.0.0*

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

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

Evidence submitted by expert panel

Cerebral Creatine Deficiency Syndromes VCEP

The NM_000156.6:c.577C>T (Gln193Ter) variant in GAMT is a nonsense variant predicted to cause a premature stop codon in the last exon of the gene and therefore to escape nonsense mediated decay. More than 10% of the protein is predicted to be removed (PVS1_Strong). This variant has been detected in at least 2 individuals with GAMT deficiency (PMID: 23234264, 31130284), who were both homozygous for

the variant (PM3). One of these patients had elevated urine GAA with low creatine (PMID: 23234264) (PP4). This variant is absent in gnomAD v4.1.0. (PM2_Supporting). There is a ClinVar entry for this variant (Variation ID: 2503890). In summary, this variant meets the criteria to be classified as likely 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 2.0.0): PVS1_Strong, PM2_Supporting, PM3, PP4. (Classification approved by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel on December 10, 2025)

Met criteria codes

PVS1_Strong			The NM_000156.6:c.577C>T (Gln193*) variant in GAMT is a nonsense variant predicted to cause a premature stop codon in the last exon of the gene and therefore to escape nonsense mediated decay. More than than 10% of the protein is predicted to be removed (PVS1_Strong).
PP4			One of these patients had elevated urine GAA with low creatine (PMID: 23234264) (PP4).
PM3			This variant has been detected in at least 2 individuals with GAMT deficiency (PMID: 23234264, 31130284), who were both homozygous for the variant (1pt total) (PM3).
PM2_Supporting			This variant is absent in gnomAD v4.1.0. (PM2_Supporting).

Curation History



 

 

Showing 1 to 1 of 1 rows

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