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_001482.3(GATM):c.1269C>G (p.Asp423Glu)

Version: 1.1

CA392254551

589915 (ClinVar)

Gene: GATM (HGNC:2628)
Condition: AGAT deficiency (MONDO:0012996)
Inheritance Mode: Autosomal recessive inheritance
UUID: 59922c1f-f11d-4a37-947e-cbd65fe16ee8
Approved on: 2025-04-11
Published on: 2025-04-11

HGVS expressions

NM_001482.3:c.1269C>G
NM_001482.3(GATM):c.1269C>G (p.Asp423Glu)
NC_000015.10:g.45362112G>C
CM000677.2:g.45362112G>C
NC_000015.9:g.45654310G>C
CM000677.1:g.45654310G>C
NC_000015.8:g.43441602G>C
NG_011674.1:g.21671C>G
NG_011674.2:g.45206C>G
ENST00000396659.8:c.1269C>G
ENST00000674905.1:c.*231C>G
ENST00000675158.1:c.*169C>G
ENST00000675323.1:c.*1771C>G
ENST00000675701.1:c.1209C>G
ENST00000675974.1:n.3818C>G
ENST00000676090.1:c.*2000C>G
ENST00000396659.7:c.1269C>G
ENST00000558362.5:n.2925C>G
NM_001482.2:c.1269C>G
NM_001321015.1:c.882C>G
NM_001321015.2:c.882C>G

Uncertain Significance

Met criteria codes 2

BP4 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 GATM 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_001482.3: c.1269C>G variant in GATM is a missense variant predicted to cause substitution of aspartate by glutamate at amino acid 423 (p.Asp423Glu). To our knowledge, this variant has not been reported in the literature in an individual with features of AGAT deficiency. This variant is absent in gnomAD v4.1.0. (PM2_Supporting). The computational predictor REVEL gives a score of 0.092 which is below the threshold of 0.29, evidence that does not predict a damaging effect on AGAT function, and SpliceAI does not predict any impact in splicing (BP4). There is a ClinVar entry for this variant (Variation ID: 58991). In summary, this variant meets the criteria to be classified as a variant of uncertain significance for AGAT deficiency based on the ACMG/AMP criteria applied, as specified by the ClinGen Cerebral Creatine Deficiency Syndromes Variant Curation Expert Panel (Specifications Version 2.0.0): PM2_Supporting, BP4. (Classification approved by the ClinGen CCDS VCEP on April 11, 2025).

Met criteria codes

BP4	✔	The computational predictor REVEL gives a score of 0.092 which is below the threshold of 0.29, evidence that does not predict a damaging effect on AGAT function, and SpliceAI does not predict any impact on splicing (BP4).
PM2_Supporting	✔	Absent from gnomAD v4.1.0. (PM2_Supporting).

Curation History

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