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_001323289.2(CDKL5):c.2500C>T (p.Gln834Ter)

Version: 1.0

CA121519

11500 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: 88fe8ef5-c6a1-44f0-8176-fce1e98c77c7
Approved on: 2024/10/30
Published on: 2024/12/4

HGVS expressions

NM_001323289.2(CDKL5):c.2500C>T (p.Gln834Ter)
NM_001323289.2:c.2500C>T
NC_000023.11:g.18628374C>T
CM000685.2:g.18628374C>T
NC_000023.10:g.18646494C>T
CM000685.1:g.18646494C>T
NC_000023.9:g.18556415C>T
NG_008475.1:g.207770C>T
ENST00000623535.2:c.2500C>T
ENST00000674046.1:c.2623C>T
ENST00000379989.6:c.2500C>T
ENST00000379996.7:c.2500C>T
ENST00000623535.1:c.2500C>T
NM_001037343.1:c.2500C>T
NM_003159.2:c.2500C>T
NM_001323289.1:c.2500C>T
NM_001037343.2:c.2500C>T
NM_003159.3:c.2500C>T

Pathogenic

Met criteria codes 4

PVS1 PM6 PP4 PM2_Supporting

Evidence Links 0

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Rett and Angelman-like Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CDKL5 Version 3.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Gln834Ter variant in CDKL5 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism. There is significant evidence that loss of this region of the gene is pathogenic (PVS1). The p.Gln834Ter variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting). The p.Gln834Ter variant in CDKL5 has been reported in an individual with a clinical phenotype suggestive of CDKL5 disorder (PMID: 16813600) (PP4). The p.Gln834Ter variant in CDKL5 occurs in the de novo state (biological parentage unconfirmed) in this individual (PM6). In summary, the p.Gln834Ter variant in CDKL5 is classified as Pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PVS1, PM2_Supporting, PP4, PM6).

Met criteria codes

PVS1	✔	PVS1 is applicable, variant is upstream of p.R948. The p.Gln834Ter variant in CDKL5 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism. There is significant evidence that loss of this region of the gene is pathogenic.
PM6	✔	PM6: The p.Gln834Ter variant in CDKL5 occurs in the de novo state (biological parentage unconfirmed) in this individual.
PP4	✔	The p.Gln834Ter variant in CDKL5 has been reported in an individual with a clinical phenotype suggestive of CDKL5 disorder (PMID: 16813600).
PM2_Supporting	✔	The p.Gln834Ter variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting).

Curation History

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