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Variant: NM_001323289.2(CDKL5):c.351T>A (p.Tyr117Ter)

Version: 1.0

CA294591

156596 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: cb4a2696-b984-42e6-9c0b-ce381dcf5738
Approved on: 2025/10/28
Published on: 2025/12/23

HGVS expressions

NM_001323289.2:c.351T>A
NM_001323289.2(CDKL5):c.351T>A (p.Tyr117Ter)
NC_000023.11:g.18579916T>A
CM000685.2:g.18579916T>A
NC_000023.10:g.18598036T>A
CM000685.1:g.18598036T>A
NC_000023.9:g.18507957T>A
NG_008475.1:g.159312T>A
ENST00000623535.2:c.351T>A
ENST00000635828.1:c.351T>A
ENST00000637881.1:c.351T>A
ENST00000674046.1:c.351T>A
ENST00000379989.6:c.351T>A
ENST00000379996.7:c.351T>A
ENST00000463994.4:c.351T>A
ENST00000623535.1:c.351T>A
NM_001037343.1:c.351T>A
NM_003159.2:c.351T>A
NM_001323289.1:c.351T>A
NM_001037343.2:c.351T>A
NM_003159.3:c.351T>A

Pathogenic

Met criteria codes 4

PS2 PVS1 PM2_Supporting PS4_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 5.0.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Tyr117Ter 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.Tyr117Ter variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with features of CDKL5 disorder (internal database - GeneDx) (PS2). The p.Tyr117Ter variant has been observed in at least 1 additional individual with CDKL5 disorder (PMID: 31313283) (PS4_supporting). The p.Tyr117Ter variant in CDKL5 is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, the p.Tyr117Ter variant in CDKL5 is classified as Pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PVS1, PS2, PS4_supporting, PM2_supporting). (CDKL5 Specifications v5.0; curation approved on 10/28/2025).

Met criteria codes

PS2	✔	The p.Tyr117Ter variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with features of CDKL5 disorder (internal database - GeneDx) (PS2).
PVS1	✔	The p.Tyr117Ter 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).
PM2_Supporting	✔	The p.Tyr117Ter variant in CDKL5 is absent from gnomAD v4.1.0 (PM2_Supporting).
PS4_Supporting	✔	The p.Tyr117Ter variant has been observed in at least 1 additional individual with CDKL5 disorder (PMID: 31313283; internal database - GeneDx) (PS4_supporting).

Curation History

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