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.220G>T (p.Glu74Ter)

Version: 1.0

CA294584

156592 (ClinVar)

Gene: CDKL5 (HGNC:6792)
Condition: CDKL5 disorder (MONDO:0100039)
Inheritance Mode: X-linked inheritance
UUID: bbfab30d-9fcb-40a0-ab5c-fb65234c123b
Approved on: 2025/5/7
Published on: 2025/6/30

HGVS expressions

NM_001323289.2(CDKL5):c.220G>T (p.Glu74Ter)
NM_001323289.2:c.220G>T
NC_000023.11:g.18575428G>T
CM000685.2:g.18575428G>T
NC_000023.10:g.18593548G>T
CM000685.1:g.18593548G>T
NC_000023.9:g.18503469G>T
NG_008475.1:g.154824G>T
ENST00000623535.2:c.220G>T
ENST00000635828.1:c.220G>T
ENST00000637881.1:c.220G>T
ENST00000674046.1:c.220G>T
ENST00000379989.6:c.220G>T
ENST00000379996.7:c.220G>T
ENST00000463994.4:c.220G>T
ENST00000623535.1:c.220G>T
NM_001037343.1:c.220G>T
NM_003159.2:c.220G>T
NM_001323289.1:c.220G>T
NM_001037343.2:c.220G>T
NM_003159.3:c.220G>T

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PS4_Moderate

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 4.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Glu74Ter 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.Glu74Ter variant has been observed in 3 individuals with CDKL5-related disorders (PMID 3131328, PMID 25657822, GeneDx internal database) (PS4_moderate). The p.Glu74Ter variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting). In summary, the p.Glu74Ter variant in CDKL5 is classified as pathogenic for CDKL5-related disorders based on the ACMG/AMP criteria (PVS1, PS4_moderate, PM2_supporting). (CDKL5 Specifications v4.1; curation approved on [5/7/2025])

Met criteria codes

PVS1	✔	The p.Glu74Ter 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.Glu74Ter variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting).
PS4_Moderate	✔	The p.Glu74Ter variant has been observed in 3 individuals with CDKL5-related disorders (PMID 3131328, 25657822, GeneDx internal database) (PS4_moderate).

Curation History

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