

Variant: *NM_001323289.2(CDKL5):c.545T>C (p.Leu182Pro)*

Version: 1.0

CA412352546 [↗](#)

1700386 (ClinVar) [↗](#)

Gene: CDKL5 ([HGNC:6792](#))

Condition: CDKL5 disorder ([MONDO:0100039](#))

Inheritance Mode: X-linked inheritance

UUID: 6bdfa3c2-2932-40cb-957d-98fa0ae0b77d

Approved on: 2025/8/27

Published on: 2025/9/30

HGVS expressions

NM_001323289.2(CDKL5):c.545T>C (p.Leu182Pro)

NM_001323289.2:c.545T>C

NC_000023.11:g.18584344T>C

CM000685.2:g.18584344T>C

NC_000023.10:g.18602464T>C

CM000685.1:g.18602464T>C

NC_000023.9:g.18512385T>C

NG_008475.1:g.163740T>C

ENST00000623535.2:c.545T>C

ENST00000635828.1:c.545T>C

ENST00000637881.1:c.545T>C

ENST00000674046.1:c.545T>C

ENST00000379989.6:c.545T>C

ENST00000379996.7:c.545T>C

ENST00000463994.4:c.545T>C

ENST00000623535.1:c.545T>C

NM_001037343.1:c.545T>C

NM_003159.2:c.545T>C

NM_001323289.1:c.545T>C

NM_001037343.2:c.545T>C

NM_003159.3:c.545T>C

Likely Pathogenic

Met criteria codes 5

PS2 PP3 PM6 PM2_Supporting

PS4_Supporting

Not Met criteria codes 4

PS1 PS3 PM1 PM5

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**

Rett and Angelman-like Disorders VCEP

The p.Leu182Pro variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with epileptic encephalopathy (PMID 23708187) (PS2). The p.Leu182Pro variant in CDKL5 has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with epileptic encephalopathy (internal database - GeneDx) (PM6). The p.Leu182Pro variant has been observed in at least 2 individuals with epileptic encephalopathy (PMID 23708187, internal database - GeneDx) (PS4_supporting). The p.Leu182Pro variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). In summary, the p.Leu182Pro variant in CDKL5 is classified as likely pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PS2, PS4_supporting, PM6, PM2_Supporting, PP3). (CDKL5 Specifications v.5.0.0; curation approved on 8/27/2025)

Met criteria codes

PS2			The p.Leu182Pro variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with epileptic encephalopathy (PMID 23708187).
PP3			Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own.
PM6			The p.Leu182Pro variant in CDKL5 has been reported as a de novo occurrence (biological parentage unconfirmed) in an individual with epileptic encephalopathy (internal database - GeneDx).
PM2_Supporting			The p.Leu182Pro variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting).
PS4_Supporting			The p.Leu182Pro variant has been observed in at least 2 individuals with epileptic encephalopathy (PMID 23708187, internal database - GeneDx).

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

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