

Variant: NM_001323289.2(CDKL5):c.372_385del
(p.His124fs)

Version: 1.0

CA2580100385 [↗](#)

2105592 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 263fbcc9-4b13-4cbd-b725-fe4674b3aa52

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HGVS expressions

NM_001323289.2(CDKL5):c.372_385del (p.His124fs)

NM_001323289.2:c.372_385del

NC_000023.11:g.18579937_18579950del

CM000685.2:g.18579937_18579950del

NC_000023.10:g.18598057_18598070del

CM000685.1:g.18598057_18598070del

NC_000023.9:g.18507978_18507991del

NG_008475.1:g.159333_159346del

ENST00000623535.2:c.372_385del

ENST00000635828.1:c.372_385del

ENST00000637881.1:c.372_385del

ENST00000674046.1:c.372_385del

ENST00000379989.6:c.372_385del

ENST00000379996.7:c.372_385del

ENST00000463994.4:c.372_385del

ENST00000623535.1:c.372_385del

NM_001037343.1:c.372_385del

NM_003159.2:c.372_385del

NM_001323289.1:c.372_385del

NM_001037343.2:c.372_385del

NM_003159.3:c.372_385del

Pathogenic

Met criteria codes **3**

PM2_Supporting

PVS1

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**

Rett and Angelman-like Disorders VCEP

The p.His124GlnfsTer2 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.His124GlnfsTer2 variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting). The p.His124GlnfsTer2 variant has been observed in at least 2 individuals with CDKL5 disorder (PMID 38539105, internal database - Labcorp (formerly Invitae)) (PS4_Supporting). In summary, the p.His124GlnfsTer2 variant in CDKL5 is classified as pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PVS1, PM2_Supporting, PS4_Supporting). (CDKL5 Specifications v.5.0.0; curation approved on 8/27/2025)

Met criteria codes

PM2_Supporting			The p.His124GlnfsTer2 variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting).
PVS1			The p.His124fs 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).
PS4_Supporting			The p.His124GlnfsTer2 variant has been observed in at least 2 individuals with CDKL5 disorder (PMID 38539105, internal database - Labcorp (formerly Invitae)) (PS4_Supporting).

Curation History



 

 

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