

Variant: *NM_001323289.2(CDKL5):c.470C>T (p.Ala157Val)*

Version: 1.0

CA279171 [↗](#)

217360 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: c746091d-5bd3-4f1a-a94c-7ce585edbb14

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HGVS expressions

NM_001323289.2(CDKL5):c.470C>T (p.Ala157Val)

NM_001323289.2:c.470C>T

NC_000023.11:g.18584269C>T

CM000685.2:g.18584269C>T

NC_000023.10:g.18602389C>T

CM000685.1:g.18602389C>T

NC_000023.9:g.18512310C>T

NG_008475.1:g.163665C>T

ENST00000623535.2:c.470C>T

ENST00000635828.1:c.470C>T

ENST00000637881.1:c.470C>T

ENST00000674046.1:c.470C>T

ENST00000379989.6:c.470C>T

ENST00000379996.7:c.470C>T

ENST00000463994.4:c.470C>T

ENST00000623535.1:c.470C>T

NM_001037343.1:c.470C>T

NM_003159.2:c.470C>T

NM_001323289.1:c.470C>T

NM_001037343.2:c.470C>T

NM_003159.3:c.470C>T

Likely Pathogenic

Met criteria codes **5**

PS4_Supporting

PS2

PP3

PM2_Supporting

PM5

Not Met criteria codes **1**

PP4

Evidence Links **0**

Expert Panel

[Rett and Angelman-like Disorders VCEP](#) [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The p.Ala157Val variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with infantile epilepsy (GeneDx Internal Database) (PS2). The p.Ala157Val variant in CDKL5 is absent from gnomAD (PM2_supporting). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). The p.Ala157Val variant has been observed in individuals reported to have Rett syndrome or CDKL5 Deficiency disorder, however, additional clinical and segregation information was not provided (PMID: 32472944; 31313283) (PS4_supporting_met, PP4_not met). A pathogenic missense variant (p.Ala157Pro) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (Invitae internal database). In summary, the p.Ala157Val variant in CDKL5 is classified as likely pathogenic for CDKL5-related disorder based on the ACMG/AMP criteria (PS2, PP3, PM2_supporting, PS4_supporting,PM5).

Met criteria codes

PS4_Supporting			The p.Ala157Val variant has been observed in at least 2 individuals with neurological disease (PMID 32472944; 31313283)
PS2			The p.Ala157Val variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual (GeneDx Internal Database)
PP3			Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own
PM2_Supporting			The p.Ala157Val variant in CDKL5 is absent from gnomAD
PM5			A pathogenic missense variant (p.Ala157Pro) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (Invitae internal database)

Not Met criteria codes

PP4			Observed in individuals reported to have Rett syndrome or CDKL5 Deficiency disorder, however, additional clinical and segregation information was not provided (PMID: 32472944; 31313283)
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Curation History



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