

Variant: *NM\_001323289.2(CDKL5):c.863C>G (p.Thr288Arg)*

Version: 1.0

CA412355847 [↗](#)

1879751 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** X-linked inheritance

**UUID:** 18e3e3c3-2b62-4a8c-9bb7-eed9a840b51a

**Approved on:** 2025/10/28

**Published on:** 2025/12/23

### HGVS expressions

**NM\_001323289.2:c.863C>G**

**NM\_001323289.2(CDKL5):c.863C>G (p.Thr288Arg)**

NC\_000023.11:g.18598499C>G

CM000685.2:g.18598499C>G

NC\_000023.10:g.18616619C>G

CM000685.1:g.18616619C>G

NC\_000023.9:g.18526540C>G

NG\_008475.1:g.177895C>G

ENST00000623535.2:c.863C>G

ENST00000635828.1:c.863C>G

ENST00000637881.1:c.863C>G

ENST00000674046.1:c.863C>G

ENST00000379989.6:c.863C>G

ENST00000379996.7:c.863C>G

ENST00000463994.4:c.863C>G

ENST00000623535.1:c.863C>G

NM\_001037343.1:c.863C>G

NM\_003159.2:c.863C>G

NM\_001323289.1:c.863C>G

NM\_001037343.2:c.863C>G

NM\_003159.3:c.863C>G

**Likely Pathogenic**

Met criteria codes **4**

PS2 PS4\_Supporting

PM2\_Supporting PP3

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.Thr288Arg variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with early onset epilepsy (internal database - CeGaT Center for Human Genetics Tuebingen) (PS2). The p.Thr288Arg variant has been observed in at least 1 other individual with features of CDKL5 disorder (internal database - LabCorp (formerly Invitae)) (PS4\_Supporting). The p.Thr288Arg 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.Thr288Arg variant in CDKL5 is classified as Likely Pathogenic for CDKL5 disorder based on the ACMG/AMP criteria (PS2, PS4\_Supporting, PM2\_Supporting, PP3). (CDKL5 Specifications v5.0; curation approved on 10/28/2025)

**Met criteria codes**

|                       |                                                                                    |                                                                                    |                                                                                                                                                                                                                               |
|-----------------------|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>PS2</b>            |   |   | The p.Thr288Arg variant in CDKL5 has been reported as a de novo occurrence (biological parentage confirmed) in an individual with early onset epilepsy (internal database - CeGaT Center for Human Genetics Tuebingen) (PS2). |
| <b>PS4_Supporting</b> |   |   | The p.Thr288Arg variant has been observed in at least 1 other individual with features of CDKL5 disorder (internal database - LabCorp (formerly Invitae)) (PS4_Supporting).                                                   |
| <b>PM2_Supporting</b> |   |   | The p.Thr288Arg variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting).                                                                                                                                                 |
| <b>PP3</b>            |  |  | Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).                                                                     |

Curation History 



 

 

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