

Variant: *NM_001323289.2(CDKL5):c.1612A>G (p.Thr538Ala)*

Version: 1.0

[CA412361958](#)

[3343996 \(ClinVar\)](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: ba323547-c9a0-4c76-ba58-36ec24d41002

Approved on: 2025-06-25

Published on: 2025-08-01

HGVS expressions

NM_001323289.2:c.1612A>G

NM_001323289.2(CDKL5):c.1612A>G (p.Thr538Ala)

NC_000023.11:g.18604536A>G

CM000685.2:g.18604536A>G

NC_000023.10:g.18622656A>G

CM000685.1:g.18622656A>G

NC_000023.9:g.18532577A>G

NG_008475.1:g.183932A>G

ENST00000623535.2:c.1612A>G

ENST00000635828.1:c.1612A>G

ENST00000674046.1:c.1612A>G

ENST00000379989.6:c.1612A>G

ENST00000379996.7:c.1612A>G

ENST00000463994.4:c.1612A>G

ENST00000623535.1:c.1612A>G

NM_001037343.1:c.1612A>G

NM_003159.2:c.1612A>G

NM_001323289.1:c.1612A>G

NM_001037343.2:c.1612A>G

NM_003159.3:c.1612A>G

Likely Benign

Met criteria codes **2**

BS2_Supporting **BP4**

Not Met criteria codes **4**

BS1 **PS4** **PP4** **PM2**

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](#)








Rett and Angelman-like Disorders VCEP

The highest population minor allele frequency of the p.Thr538Ala variant in CDKL5 in gnomAD v4.1 is 0.000004468 in the Non-Finnish European population (not sufficient to meet BS1 criteria). The p.Thr538Ala variant is observed in at least 1 unaffected individual (Internal database - Ambry Genetics) (BS2_Supporting). The computational predictor REVEL gives a score of 0.214, which is below the threshold of 0.290, evidence that does not predict a damaging effect on CDKL5 function (BP4). In summary, the p.Thr538Ala variant in CDKL5 is classified as likely benign based on the ACMG/AMP criteria (BS2_Supporting, BP4). (CDKL5 Specifications v.4.1; curation approved on 06/25/2025)

Met criteria codes

- | | | | |
|-----------------------|---|---|--|
| BS2_Supporting |  |  | The p.Thr538Ala variant is observed in at least 1 unaffected individual (Internal database - Ambry Genetics). |
| BP4 |  |  | The computational predictor REVEL gives a score of 0.214, which is below the threshold of 0.290, evidence that does not predict a damaging effect on CDKL5 function (BP4). |

Not Met criteria codes

- | | | | |
|------------|---|---|---|
| BS1 |  |  | The highest population minor allele frequency of the p.Thr538Ala variant in CDKL5 in gnomAD v4.1 is 0.000004468 in Non-Finnish European population (not sufficient to meet BS1 criteria). |
| PS4 |  |  | PM2 not met. |
| PP4 |  |  | Computational prediction analysis tools are inconclusive for this variant. |
| PM2 | |  | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

Curation History [↗](#)

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