

Variant: *NM_001323289.2(CDKL5):c.1684A>G (p.Thr562Ala)*

Version: 2.0

CA10360405 [↗](#)

434666 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 86cd6c81-4350-4b94-9e7b-7b0ae0934344

Approved on: 2025/2/28

Published on: 2025/3/28

HGVS expressions

NM_001323289.2:c.1684A>G

NM_001323289.2(CDKL5):c.1684A>G (p.Thr562Ala)

NC_000023.11:g.18604608A>G

CM000685.2:g.18604608A>G

NC_000023.10:g.18622728A>G

CM000685.1:g.18622728A>G

NC_000023.9:g.18532649A>G

NG_008475.1:g.184004A>G

ENST00000623535.2:c.1684A>G

ENST00000635828.1:c.1684A>G

ENST00000674046.1:c.1684A>G

ENST00000379989.6:c.1684A>G

ENST00000379996.7:c.1684A>G

ENST00000463994.4:c.1684A>G

ENST00000623535.1:c.1684A>G

NM_001037343.1:c.1684A>G

NM_003159.2:c.1684A>G

NM_001323289.1:c.1684A>G

NM_001037343.2:c.1684A>G

NM_003159.3:c.1684A>G

Likely Benign

Met criteria codes 2

BS2

BP4

Not Met criteria codes 4

PM2

PM1

BS1

PS4

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 3.0.0*

[↗](#) **Criteria Specification Approval History**

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

Rett and Angelman-like Disorders VCEP

The highest population minor allele frequency of the c.1684A>G (p.Thr562Ala) variant in CDKL5 in gnomAD v4.1 is 0.000004 in the European (Non-Finnish) population (not sufficient to meet BS1 criteria). The computational predictor REVEL gives a score of 0.133, evidence that does not predict a damaging effect on CDKL5 function (BP4). The p.Thr562Ala variant is observed in at least 2 unaffected individuals (Ambry Genetics: internal database, Labcorp Genetics Inc. (formerly Invitae): internal database) (BS2). In summary, the p.Thr562Ala variant in CDKL5 is classified as Likely Benign for CDKL5-associated disorder based on the ACMG/AMP criteria (BP4, BS2) (CDKL5 Specifications v.3.0; curation approved on 02/28/2025).

Met criteria codes

BS2			The p.Thr562Ala variant is observed in at least 2 unaffected individuals (internal database - Ambry Genetics, internal database - Labcorp Genetics Inc (formerly Invitae)) (BS2).
BP4			The computational predictor REVEL gives a score of 0.133, evidence that does not predict a damaging effect on CDKL5 function (BP4).

Not Met criteria codes

PM2			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
BS1			The highest population minor allele frequency of the p.Thr562Ala variant in CDKL5 in gnomAD v4.1 is 0.000004 in the European (Non-Finnish) population (not sufficient to meet BS1 criteria).
PS4			The p.Thr562Ala variant is not currently published and is not present in additional databases (internal and publicly available), therefore, no additional criteria are applicable at this time.

Curation History



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