

Variant: NM_001323289.2(CDKL5):c.2152G>A
(p.Val718Met)

Version: 1.0

CA199279 [↗](#)

143796 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 285d3afa-2703-4819-af6e-ee9e40fc0071

Approved on: 2025/5/7

Published on: 2025/6/30

HGVS expressions

NM_001323289.2(CDKL5):c.2152G>A (p.Val718Met)

NM_001323289.2:c.2152G>A

NC_000023.11:g.18609570G>A

CM000685.2:g.18609570G>A

NC_000023.10:g.18627690G>A

CM000685.1:g.18627690G>A

NC_000023.9:g.18537611G>A

NG_008475.1:g.188966G>A

ENST00000623535.2:c.2152G>A

ENST00000635828.1:c.2152G>A

ENST00000674046.1:c.2152G>A

ENST00000379989.6:c.2152G>A

ENST00000379996.7:c.2152G>A

ENST00000463994.4:c.2152G>A

ENST00000623535.1:c.2152G>A

NM_001037343.1:c.2152G>A

NM_003159.2:c.2152G>A

NM_001323289.1:c.2152G>A

NM_001037343.2:c.2152G>A

NM_003159.3:c.2152G>A

Pathogenic

Met criteria codes **5**

PM2_Supporting

PM6_Strong

PS3_Supporting

PP4

PS4

Not Met criteria codes **1**

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 4.1.0

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

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

Rett and Angelman-like Disorders VCEP

The p.Val718Met variant in CDKL5 has been reported in at least 2 de novo occurrences (biological parentage unconfirmed) in individuals with a CDKL5-related disorder (PMID 18790821, 27599155) (PM6_strong). The p.Val718Met variant has been observed at least 5 individuals with CDKL5-related disorders (PMID 31313283, 18790821, 27599155, GeneDx internal database) (PS4), including in an individual with a clinical phenotype very specific to a CDKL5-related disorder (PMID 27599155) (PP4). Additionally, an in vitro study using a minigene splicing assay showed that splicing is disrupted, resulting in exon 14 being omitted from the transcript (PMID: 29264392) (PS3_supporting). The p.Val718Met variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting). In summary, the p.Val718Met variant in CDKL5 is classified as pathogenic for CDKL5-related disorders based on the ACMG/AMP criteria (PM6_strong, PS4, PP4, PS3_supporting, PM2_supporting). (CDKL5 Specifications v.4.1; curation approved on [5/7/2025])

Met criteria codes

PM2_Supporting			The p.Val718Met variant in CDKL5 is absent from gnomAD v4.1 (PM2_Supporting).
PM6_Strong			The p.Val718Met variant in CDKL5 has been reported in at least 2 de novo occurrences (biological parentage unconfirmed) in individuals with a CDKL5-related disorder. (PMID 18790821, 27599155).
PS3_Supporting			An in vitro study using a minigene splicing assay showed that splicing is disrupted, resulting in exon 14 being omitted from the transcript (PMID: 29264392).
PP4			The p.Val718Met variant in CDKL5 has been reported in an individual with a clinical phenotype suggestive of a CDKL5-related disorder (PMID 27599155)
PS4			The p.Val718Met variant has been observed at least 5 individuals with CDKL5-related disorders (PMID 31313283, 18790821, 27599155, GeneDx internal database) (PS4).

Not Met criteria codes

PP3			Computational prediction analysis tools are inconclusive for this variant.
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