

*Variant: NM_001110792.2(MECP2):c.1001C>T
(p.Pro334Leu)*

Version: 1.0

CA270591 [↗](#)

143754 (ClinVar) [↗](#)

Gene: MECP2 ([HGNC:4204](#))

Condition: Rett syndrome ([MONDO:0010726](#))

Inheritance Mode: X-linked inheritance

UUID: 4e3a5fc4-323d-4a09-8c72-f46d04b0eeb7

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HGVS expressions

NM_001110792.2(MECP2):c.1001C>T (p.Pro334Leu)

NM_001110792.2:c.1001C>T
NC_000023.11:g.154030863G>A
CM000685.2:g.154030863G>A
NC_000023.10:g.153296314G>A
CM000685.1:g.153296314G>A
NC_000023.9:g.152949508G>A
NG_007107.2:g.111265C>T
NG_007107.3:g.111241C>T
ENST00000303391.11:c.965C>T
ENST00000453960.7:c.1001C>T
ENST00000637917.1:c.139C>T
ENST00000303391.10:c.965C>T
ENST00000407218.5:c.*337C>T
ENST00000453960.6:c.1001C>T
ENST00000619732.4:c.965C>T
ENST00000622433.4:c.951C>T
ENST00000628176.2:c.*337C>T
NM_001110792.1:c.1001C>T
NM_001316337.1:c.686C>T
NM_004992.3:c.965C>T
NM_001316337.2:c.686C>T
NM_001369391.2:c.686C>T
NM_001369392.2:c.686C>T
NM_001369393.2:c.686C>T
NM_001369394.1:c.686C>T
NM_001369394.2:c.686C>T
NM_001386137.1:c.296C>T
NM_001386138.1:c.296C>T
NM_001386139.1:c.296C>T
NM_004992.4:c.965C>T

Pathogenic

- PS4
- PP4
- PM5
- PM6_Strong
- PM2_Supporting

Not Met criteria codes 3

- BP4
- PP3
- PM1

Evidence Links 0

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 c.965C>T p.(Pro322Leu) variant in MECP2 (NM_004992.3) is absent from gnomAD (PM2_supporting). The p.(Pro322Leu) variant has been observed in at least 5 individuals with Rett syndrome (PMID: 10814718, 19722030, 17089071, 16672765, 11402105, 16473305) (PS4, PP4), where it has been reported in as de novo occurrences (biological parentage unconfirmed) in at least 2 individuals (PMID 10814718, 11402105) (PM6_strong). Multiple missense variants have been previously identified within this codon, at least one of which is classified as pathogenic; this indicates that this residue is critical to the function of the protein (PMID 10814719, 16966553, 16225173, 32820509) (PM5). In summary, the c.965C>T p.(Pro322Leu) variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PS4, PM6_strong, PP4, PM5).

Met criteria codes

PS4			The p.Pro322Leu variant has been observed in at least 5 individuals with Rett syndrome (PMID: 10814718, 19722030, 17089071, 16672765, 11402105, 16473305) (PS4).
PP4			The p.Pro322Leu variant in MECP2 has been reported in individuals with a clinical phenotype suggestive of Rett syndrome (PMID: 10814718, 19722030, 17089071, 16672765, 11402105, 16473305) (PP4).
PM5			Multiple missense variants have been previously identified within this codon, at least one of which is classified as pathogenic; this indicates that this residue is critical to the function of the protein (PMID 10814719, 16966553, 16225173, 32820509) (PM5).
PM6_Strong			The p.Pro322Leu variant in MECP2 has been reported in at least 2 de novo occurrences (biological parentage unconfirmed) in individuals with Rett syndrome (PMID 10814718, 11402105) (PM6_strong).
PM2_Supporting			The p.Pro322Leu variant in MECP2 is absent from gnomAD (PM2_supporting).

Not Met criteria codes

BP4			Computational prediction analysis tools are inconclusive for this variant.
PP3			Computational prediction analysis tools are inconclusive for this variant.
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 

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