

Variant: *NM_001110792.2(MECP2):c.941C>T (p.Pro314Leu)*

Version: 1.0

CA270574 [↗](#)

143738 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 5440749b-7ac5-4fba-8a4a-70847f234b72

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HGVS expressions

NM_001110792.2:c.941C>T

NM_001110792.2(MECP2):c.941C>T (p.Pro314Leu)

NC_000023.11:g.154030923G>A

CM000685.2:g.154030923G>A

NC_000023.10:g.153296374G>A

CM000685.1:g.153296374G>A

NC_000023.9:g.152949568G>A

NG_007107.2:g.111205C>T

NG_007107.3:g.111181C>T

ENST00000303391.11:c.905C>T

ENST00000453960.7:c.941C>T

ENST00000637917.1:c.79C>T

ENST00000303391.10:c.905C>T

ENST00000407218.5:c.*277C>T

ENST00000453960.6:c.941C>T

ENST00000619732.4:c.905C>T

ENST00000622433.4:c.891C>T

ENST00000628176.2:c.*277C>T

NM_001110792.1:c.941C>T

NM_001316337.1:c.626C>T

NM_004992.3:c.905C>T

NM_001316337.2:c.626C>T

NM_001369391.2:c.626C>T

NM_001369392.2:c.626C>T

NM_001369393.2:c.626C>T

NM_001369394.1:c.626C>T

NM_001369394.2:c.626C>T

NM_001386137.1:c.236C>T

NM_001386138.1:c.236C>T

NM_001386139.1:c.236C>T

NM_004992.4:c.905C>T

Pathogenic

Met criteria codes **7**

PM2_Supporting

PM6_Strong

PS4

PP3

PP4

PM1

PM5

Expert Panel

Rett and Angelman-like Disorders VCEP [↗](#)

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The c.905C>T p.(Pro302Leu) variant in MECP2 (NM_004992.3) is absent from gnomAD (PM2_supporting). The p.(Pro302Leu) variant has been observed in at least 5 individuals with Rett syndrome or severe neonatal encephalopathy (PMID: 10767337, 30377382, 23696494, 11313756, 16473305, 32472557) (PS4, PP4), where it has been reported as a de novo occurrence (biological parentage unconfirmed) in at least 4 of these individuals (PMID: 10767337, 30377382, 23696494, 11313756) (PM6_very strong). The p.(Pro302Leu) variant occurs in the well-characterized transcriptional repression domain (TRD: aa 302-306) of the MECP2 gene (PM1). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). Multiple pathogenic missense variants have been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID: 10814718, 10814719, 10944854, 17387578, 15737703) (PM5). In summary, the c.905C>T p.(Pro302Leu) variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PM6_very strong, PS4, PM1, PM5, PP3, PP4, PM2_supporting).

Met criteria codes

PM2_Supporting	ⓘ	✓	The p.Pro302Leu variant in MECP2 is absent from gnomAD (PM2_supporting).
PM6_Strong	ⓘ	✓	The p.Pro302Leu variant in MECP2 has been reported in at least 4 de novo occurrences (biological parentage unconfirmed) in individuals with Rett syndrome and severe neonatal encephalopathy (PMID: 10767337, 30377382, 23696494, 11313756) (PM6_very strong).
PS4	ⓘ	✓	The p.Pro302Leu variant has been observed in at least 5 individuals with Rett syndrome or severe neonatal encephalopathy (PMID: 10767337, 30377382, 23696494, 11313756, 16473305, 32472557) (PS4).
PP3	ⓘ	✓	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PP4	ⓘ	✓	The p.Pro302Leu variant in MECP2 has been reported in individuals with a clinical phenotype suggestive of Rett syndrome (PMID PMID: 10767337, 30377382, 23696494, 11313756, 16473305) (PP4).
PM1		✓	The p.Pro302Leu variant occurs in the well-characterized transcriptional repression domain (TRD: aa 302-306) of the MECP2 gene (PM1).
PM5	ⓘ	✓	Multiple pathogenic missense variants have been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID: 10814718, 10814719, 10944854, 17387578, 15737703) (PM5).

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