

Variant: *NM_001110792.2(MECP2):c.961C>T (p.Arg321Trp)*

Version: 1.0

CA199325 [↗](#)

143749 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 431d1239-3305-42a4-967d-adad00522f20

Approved on: 2022/7/28

Published on: 2022/9/6

HGVS expressions

NM_001110792.2:c.961C>T

NM_001110792.2(MECP2):c.961C>T (p.Arg321Trp)

NC_000023.11:g.154030903G>A

CM000685.2:g.154030903G>A

NC_000023.10:g.153296354G>A

CM000685.1:g.153296354G>A

NC_000023.9:g.152949548G>A

NG_007107.2:g.111225C>T

NG_007107.3:g.111201C>T

ENST00000303391.11:c.925C>T

ENST00000453960.7:c.961C>T

ENST00000637917.1:c.99C>T

ENST00000303391.10:c.925C>T

ENST00000407218.5:c.*297C>T

ENST00000453960.6:c.961C>T

ENST00000619732.4:c.925C>T

ENST00000622433.4:c.911C>T

ENST00000628176.2:c.*297C>T

NM_001110792.1:c.961C>T

NM_001316337.1:c.646C>T

NM_004992.3:c.925C>T

NM_001316337.2:c.646C>T

NM_001369391.2:c.646C>T

NM_001369392.2:c.646C>T

NM_001369393.2:c.646C>T

NM_001369394.1:c.646C>T

NM_001369394.2:c.646C>T

NM_001386137.1:c.256C>T

NM_001386138.1:c.256C>T

NM_001386139.1:c.256C>T

NM_004992.4:c.925C>T

Pathogenic

Met criteria codes **4**

PP4 PS4 PS2_Very Strong

PM2_Supporting

Expert Panel

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

Not Met criteria codes 3

BP4 PP3 PM1

Evidence Links 0

Criteria Specification Information !

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Rett and Angelman-like Disorders VCEP

The c.925C>T p.(Arg309Trp) variant in MECP2 (NM_004992.3) is absent from gnomAD (PM2_supporting). The p.(Arg309Trp) variant has been observed in at least 5 individuals, including males, with variable neurodevelopmental phenotypes consistent with MECP2-related disease (PMID 26936630, 29655203, 29720203, 28837158, 31178897, 30536762, 32214227) (PS4, PP4). One of the reported individuals with this variant was also found to be heterozygous for a de novo (biological parentage confirmed) SMC3 frameshift variant (PMID 31178897). The p.(Arg309Trp) variant has been reported as a de novo occurrence (biological parentage both confirmed and unconfirmed) in at least 3 of these individuals (PMID 31178897, 26936630) (PS2_very strong). Additional family studies have found the p.(Arg309Trp) variant to be maternally inherited in at least 2 cases (PMID 29720203, 26936630), and inherited from an unaffected mosaic parent in at least 1 case (PMID 28837158). Computational prediction analysis tools are inconclusive for this variant. In summary, the c.925C>T p.(Arg309Trp) variant in MECP2 is classified as Pathogenic for MECP2-related disease based on the ACMG/AMP criteria (PS2_very strong, PS4, PM2_supporting, PP4).

Met criteria codes

PP4			The p.Arg309Trp variant in MECP2 has been reported in individuals with a clinical phenotype suggestive of Rett syndrome (PMID: 26936630, 29655203, 29720203, 28837158, 31178897, 30536762, 32214227) (PP4).
PS4			The p.Arg309Trp variant has been observed in at least 5 individuals with variable neurodevelopmental phenotypes consistent with MECP2-related disease (PMID: 26936630, 29655203, 29720203, 28837158, 31178897, 30536762, 32214227) (PS4).
PS2_Very Strong			The p.Arg309Trp variant in MECP2 has been reported as a de novo occurrence (biological parentage both confirmed and unconfirmed) in at least 3 individuals with clinical features consistent with MECP2-related disease (PMID: 31178897, 26936630) (PS2_very strong).
PM2_Supporting			The p.Arg309Trp variant in MECP2 is absent from gnomAD (PM2_supporting).

Not Met criteria codes

BP4			Computational prediction analysis tools are inconclusive for this variant (REVEL 0.729).
PP3			Computational prediction analysis tools are inconclusive for this variant (REVEL 0.729).
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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