

Variant: *NM_001110792.2(MECP2):c.491C>G (p.Pro164Arg)*

Version: 2.0

CA270424 [↗](#)

143579 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 6d7ad90d-38fc-4fab-9db8-b6da72e59655

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HGVS expressions

NM_001110792.2:c.491C>G

NM_001110792.2(MECP2):c.491C>G (p.Pro164Arg)

NC_000023.11:g.154031373G>C

CM000685.2:g.154031373G>C

NC_000023.10:g.153296824G>C

CM000685.1:g.153296824G>C

NC_000023.9:g.152950018G>C

NG_007107.2:g.110755C>G

NG_007107.3:g.110731C>G

ENST00000303391.11:c.455C>G

ENST00000453960.7:c.491C>G

ENST00000637917.1:c.65+23C>G

ENST00000303391.10:c.455C>G

ENST00000369957.5:c.*509C>G

ENST00000407218.5:c.468+23C>G

ENST00000453960.6:c.491C>G

ENST00000486506.5:n.2803C>G

ENST00000611468.1:c.443C>G

ENST00000619732.4:c.455C>G

ENST00000622433.4:c.443C>G

ENST00000628176.2:c.432+23C>G

NM_001110792.1:c.491C>G

NM_001316337.1:c.176C>G

NM_004992.3:c.455C>G

NM_001316337.2:c.176C>G

NM_001369391.2:c.176C>G

NM_001369392.2:c.176C>G

NM_001369393.2:c.176C>G

NM_001369394.1:c.176C>G

NM_001369394.2:c.176C>G

NM_001386137.1:c.-129+23C>G

NM_001386138.1:c.-129+23C>G

NM_001386139.1:c.-129+23C>G

NM_004992.4:c.455C>G

Pathogenic

Met criteria codes 8

PS4

PS3_Supporting

PP3

PP4

PM1

PM5

PM2_Supporting

PM6_Very Strong

Evidence Links 0

Expert Panel

Rett and Angelman-like Disorders VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel			
<i>Rett and Angelman-like Disorders VCEP</i>			
The p.Pro152Arg variant in MECP2 (NM_004992.3) has been reported in at least 6 de novo occurrences (biological parentage unconfirmed) in patients with Rett syndrome (PMID 10767337, 10814718, 11241840) and in at least 4 other individuals with clinical features of Rett syndrome (PMID 11055898, 2385859, RettBASE) (PM6_very strong, PP4, PS4). The p.Pro152Arg variant occurs in the well-characterized methyl-DNA binding (MDB) functional domain of MECP2 (PM1). A pathogenic missense variant (p.Pro152Ala) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID 18989701, 18989701, 27929079, 26842955, ClinVar) (PM5). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). Immunofluorescence assays have shown that the p.Pro152Arg variant in MECP2 impacts heterochromatin clustering (PMID 21831886, 22923521) (PS3_supporting). The p.Pro152Arg variant in MECP2 is absent from gnomAD (PM2_supporting). In summary, the p.Pro152Arg variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PM6_very strong, PS4, PM1, PM5, PS3_supporting, PM2_supporting, PP3, PP4).			
Met criteria codes			
PS4	i	✓	The p.Pro152Arg variant has been observed in at least 4 other individuals with clinical features of Rett syndrome (PMID 11055898, 2385859, 10814718, 11241840, RettBASE) (PS4).
PS3_Supporting	i	✓	Immunofluorescence assays have shown that this variant impacts heterochromatin clustering (PMID 21831886, 22923521) (PS3_supporting).
PP3	i	✓	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PP4	i	✓	The p.Pro152Arg variant in MECP2 has been reported in an individual with a clinical phenotype suggestive of Rett syndrome (PMID: 10767337).
PM1	i	✓	The p.Pro152Arg variant occurs in the well-characterized methyl-DNA binding (MDB) functional domain of MECP2 (PM1).
PM5	i	✓	A pathogenic missense variant (p.Pro152Ala) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID 18989701, 18989701, 27929079, 26842955, ClinVar) (PM5). Grantham score Pro > Ala = 27 Grantham score Pro > Arg = 103
PM2_Supporting	i	✓	The p.Pro152Arg variant in MECP2 is absent from gnomAD (PM2_supporting).
		✓	

PM6_Very
Strong



The p.Pro152Arg variant in MECP2 has been reported in at least 6 de novo occurrences (biological parentage unconfirmed) in patients with Rett syndrome (PMID: 10767337, 10814718, 11241840) (PM6_very strong).

Curation History [↗](#)

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