

Variant: NM_004992.3(MECP2):c.454C>G (p.Pro152Ala)

Version: 1.0

CA121717 [↗](#)

11844 (ClinVar) [↗](#)

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

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

Inheritance Mode: X-linked inheritance

UUID: 692d4de8-21e1-4102-8ec2-4da4b8d9c892

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HGVS expressions

NM_004992.3(MECP2):c.454C>G (p.Pro152Ala)

NM_004992.3:c.454C>G

NC_000023.11:g.154031374G>C

CM000685.2:g.154031374G>C

NC_000023.10:g.153296825G>C

CM000685.1:g.153296825G>C

NC_000023.9:g.152950019G>C

NG_007107.2:g.110754C>G

NG_007107.3:g.110730C>G

ENST00000303391.11:c.454C>G

ENST00000453960.7:c.490C>G

ENST00000637917.1:c.65+22C>G

ENST00000303391.10:c.454C>G

ENST00000369957.5:c.*508C>G

ENST00000407218.5:c.468+22C>G

ENST00000453960.6:c.490C>G

ENST00000486506.5:n.2802C>G

ENST00000611468.1:c.442C>G

ENST00000619732.4:c.454C>G

ENST00000622433.4:c.442C>G

ENST00000628176.2:c.432+22C>G

NM_001110792.1:c.490C>G

NM_001316337.1:c.175C>G

NM_001110792.2:c.490C>G

NM_001316337.2:c.175C>G

NM_001369391.2:c.175C>G

NM_001369392.2:c.175C>G

NM_001369393.2:c.175C>G

NM_001369394.1:c.175C>G

NM_001369394.2:c.175C>G

NM_001386137.1:c.-129+22C>G

NM_001386138.1:c.-129+22C>G

NM_001386139.1:c.-129+22C>G

NM_004992.4:c.454C>G

Likely Pathogenic

Met criteria codes 5

PP1_ModeratePS3_SupportingPP3PM1PM5

Not Met criteria codes 1

PM2

Evidence Links 0

Expert Panel

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

Functional studies have shown that this variant shows partial reduction in heterochromatin binding (PMID 18989701) (PS3_supporting). The variant has been reported to segregate in three informative meioses (PMID 18989701, internal database) (PP1_Moderate). The p.Pro152Ala variant occurs in the well-characterized Methyl-DNA binding (MDB) functional domain of MECP2 (PM1). A pathogenic missense variant (p.Pro152Arg) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (10767337) (PM5). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). In summary, the p.Pro152Ala variant in MECP2 is classified as likely pathogenic for Rett syndrome based on the ACMG/AMP criteria (PS3_supporting, PP1_moderate, PM1, PM5, PP3).

Met criteria codes

PP1_Moderate		✓	The variant has been reported to segregate in three informative meioses (PMID 18989701, internal database)
PS3_Supporting		✓	Functional studies have shown that this variant shows partial reduction in heterochromatin binding (PMID 18989701)
PP3		✓	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own
PM1		✓	The p.Pro152Ala variant occurs in the well-characterized Methyl-DNA binding (MDB) functional domain of MECP2
PM5		✓	A pathogenic missense variant (p.Pro152Arg) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (10767337)

Not Met criteria codes

PM2		✗	The variant (p.Pro152Ala) is found at extremely low frequency in gnomAD AT 0.001% and absent in ExAC
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Curation History

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