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Variant: NM_001110792.2(MECP2):c.400G>A (p.Val134Met)

Version: 1.0

CA270366

143546 (ClinVar)

Gene: MECP2 (HGNC:4204)
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 524c0c15-0c45-4f53-a9b3-ab6d2536879f
Approved on: 2021/10/26
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HGVS expressions

NM_001110792.2(MECP2):c.400G>A (p.Val134Met)
NM_001110792.2:c.400G>A
NC_000023.11:g.154032220C>T
CM000685.2:g.154032220C>T
NC_000023.10:g.153297671C>T
CM000685.1:g.153297671C>T
NC_000023.9:g.152950865C>T
NG_007107.2:g.109908G>A
NG_007107.3:g.109884G>A
ENST00000303391.11:c.364G>A
ENST00000453960.7:c.400G>A
ENST00000303391.10:c.364G>A
ENST00000369957.5:c.*418G>A
ENST00000407218.5:c.400G>A
ENST00000453960.6:c.400G>A
ENST00000486506.5:n.2712G>A
ENST00000611468.1:c.352G>A
ENST00000619732.4:c.364G>A
ENST00000622433.4:c.352G>A
ENST00000628176.2:c.364G>A
NM_001110792.1:c.400G>A
NM_001316337.1:c.85G>A
NM_004992.3:c.364G>A
NM_001316337.2:c.85G>A
NM_001369391.2:c.85G>A
NM_001369392.2:c.85G>A
NM_001369393.2:c.85G>A
NM_001369394.1:c.85G>A
NM_001369394.2:c.85G>A
NM_001386137.1:c.-197G>A
NM_001386138.1:c.-197G>A
NM_001386139.1:c.-197G>A
NM_004992.4:c.364G>A

Met criteria codes 6

Expert Panel

Pathogenic

PM2_Supporting PS4_Supporting PS2 PM1 PP3 PP4

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 p.Val122Met variant in MECP2 (NM_004992.3) has been reported in an individual with a clinical phenotype suggestive of Rett syndrome (PMID: 17089071) (PP4). The p.Val122Met variant in MECP2 occurs in the de novo state (biological parentage unconfirmed) in this individual. It is also reported in the mosaic state in a male patient with clinical features of Rett syndrome (PMID 28837158, internal database - GeneDx) and therefore confirmed to be de novo (PS2, PS4_supporting). The p.Val122Met variant occurs in the well-characterized methyl-DNA binding (MDB) functional domain of MECP2 (PM1). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). The p.Val122Met variant in MECP2 is absent from gnomAD (PM2_supporting). In summary, the p.Val122Met variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PS2, PM1, PS4_supporting, PM2_supporting, PP3, PP4).

Met criteria codes

PM2_Supporting	✔	The p.Val122Met variant in MECP2 is absent from gnomAD (PM2_supporting).
PS4_Supporting	✔	The p.Val122Met variant has been observed in at least 1 other individual with clinical features of Rett syndrome (PMID 28837158) (PS4_supporting).
PS2	✔	The p.Val122Met variant in MECP2 occurs in the de novo state (biological parentage unconfirmed) in this individual. It is also reported in the mosaic state in a male patient with clinical features of Rett syndrome (PMID 28837158, internal database - GeneDx) and therefore confirmed to be de novo (PS2).
PM1	✔	The p.Val122Met variant occurs in the well-characterized methyl-DNA binding (MDB) functional domain of MECP2 (PM1).
PP3	✔	Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PP4	✔	The p.Val122Me variant in MECP2 has been reported in an individual with a clinical phenotype suggestive of Rett syndrome (PMID: 17089071) (PP4).

Curation History

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