

Variant: NM_001110792.2(MECP2):c.503A>G (p.Asp168Gly)

Version: 1.0

CA270431 [↗](#)

143583 (ClinVar) [↗](#)

Gene: MECP2 ([HGNC:4204](#))
Condition: Rett syndrome ([MONDO:0010726](#))
Inheritance Mode: X-linked inheritance
UUID: 1cb2470d-8a34-48e7-a854-6aae0154359d
Approved on: 2021/10/26
Published on: 2021/12/27

HGVS expressions

NM_001110792.2:c.503A>G
NM_001110792.2(MECP2):c.503A>G (p.Asp168Gly)
NC_000023.11:g.154031361T>C
CM000685.2:g.154031361T>C
NC_000023.10:g.153296812T>C
CM000685.1:g.153296812T>C
NC_000023.9:g.152950006T>C
NG_007107.2:g.110767A>G
NG_007107.3:g.110743A>G
ENST00000303391.11:c.467A>G
ENST00000453960.7:c.503A>G
ENST00000637917.1:c.65+35A>G
ENST00000303391.10:c.467A>G
ENST00000407218.5:c.468+35A>G
ENST00000453960.6:c.503A>G
ENST00000486506.5:n.2815A>G
ENST00000611468.1:c.455A>G
ENST00000619732.4:c.467A>G
ENST00000622433.4:c.455A>G
ENST00000628176.2:c.432+35A>G
NM_001110792.1:c.503A>G
NM_001316337.1:c.188A>G
NM_004992.3:c.467A>G
NM_001316337.2:c.188A>G
NM_001369391.2:c.188A>G
NM_001369392.2:c.188A>G
NM_001369393.2:c.188A>G
NM_001369394.1:c.188A>G
NM_001369394.2:c.188A>G
NM_001386137.1:c.-129+35A>G
NM_001386138.1:c.-129+35A>G
NM_001386139.1:c.-129+35A>G
NM_004992.4:c.467A>G

Pathogenic

- PP3
- PM2
- PM1
- PM5
- PS4_Moderate
- PM6_Strong
- PS3_Supporting

Not Met criteria codes 1

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.Asp156Gly variant in MECP2 (NM_004992.3) has been reported in at least 2 de novo occurrences (biological parentage unconfirmed) in individuals with phenotype consistent with Rett syndrome (PMID 11309679, 11241840) (PM6_strong). The p.Asp156Gly variant in MECP2 has been observed in at least 2 other individuals with clinical features of Rett syndrome (PMID 11309679, 11241840) (PS4_moderate). The p.Asp156Gly variant occurs in the well-characterized methyl-binding domain (MBD) functional domain of MECP2 (PMID 1326358, 23770565) (PM1). A pathogenic missense variant (p.Asp156Glu) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID 11524741, 15737703, 26984561, 27354166, 12843318, 26418480, internal database - Invitae) (PM5). The p.Asp156Gly variant in MECP2 is absent from gnomAD (PM2_supporting). Chromatin binding and in vitro transcription repression assays have shown that this variant impacts protein function (PMID 12843318) (PS3_supporting). Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3). In summary, the p.Asp156Gly variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PM6_strong, PS4_moderate, PM1, PM5, PS3_supporting, PM2_supporting, PP3).

Met criteria codes

PP3			Computational prediction analysis tools suggests a deleterious impact; however, this information does not predict clinical significance on its own (PP3).
PM2			The p.Asp156Gly variant in MECP2 is absent from gnomAD (PM2_supporting).
PM1			The p.Asp156Gly variant occurs in the well-characterized methyl-binding domain (MBD) functional domain of MECP2 (PMID 1326358, 23770565) (PM1).
PM5			A pathogenic missense variant (p.Asp156Glu) has been previously identified within this codon which indicates that this residue is critical to the function of the protein (PMID 11524741, 15737703, 26984561, 27354166, 12843318, 26418480, internal database - Invitae) (PM5).
PS4_Moderate			The p.Asp156Gly variant in MECP2 has been observed in at least 2 other individual2 with clinical features of Rett syndrome (PMID 11309679, 11241840) (PS4_moderate).
PM6_Strong			The p.Asp156Gly variant in MECP2 has been reported in at least 2 de novo occurrences (biological parentage unconfirmed) in individuals with Rett syndrome (PMID 11309679, 11241840) (PM6_strong, PP4).
PS3_Supporting			Chromatin binding and in vitro transcription repression assays have shown that this variant impacts protein function (PMID 12843318).

Not Met criteria codes

PP4			In PMID 11241840 the patient cohort was given a tentative diagnosis of Rett syndrome.
------------	---	---	---

▼

▼

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.