The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_004992.3(MECP2):c.806delG (p.Gly269Alafs)

Version: 1.0

CA199475

95202 (ClinVar)

Gene: MECP2
Condition: Rett syndrome (MONDO:0010726)
Inheritance Mode: X-linked inheritance
UUID: 1e897fde-76a7-45dc-8f7f-6e1191668335
Approved on: 2021-03-09
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HGVS expressions

NM_004992.3:c.806del
NM_004992.3:c.806delG
NM_004992.3(MECP2):c.806delG (p.Gly269Alafs)
NC_000023.11:g.154031025del
CM000685.2:g.154031025del
NC_000023.10:g.153296476del
CM000685.1:g.153296476del
NC_000023.9:g.152949670del
NG_007107.2:g.111106del
NG_007107.3:g.111082del
ENST00000303391.11:c.806del
ENST00000453960.7:c.842del
ENST00000637917.1:c.66-86del
ENST00000303391.10:c.806del
ENST00000407218.5:c.*178del
ENST00000453960.6:c.842del
ENST00000619732.4:c.806del
ENST00000622433.4:c.794del
ENST00000628176.2:c.*178del
NM_001110792.1:c.842del
NM_001316337.1:c.527del
NM_001110792.2:c.842del
NM_001316337.2:c.527del
NM_001369391.2:c.527del
NM_001369392.2:c.527del
NM_001369393.2:c.527del
NM_001369394.1:c.527del
NM_001369394.2:c.527del
NM_001386137.1:c.137del
NM_001386138.1:c.137del
NM_001386139.1:c.137del
NM_004992.4:c.806del

Pathogenic

Met criteria codes 3

PM2_Supporting | PS2_Very Strong | PVS1

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

The p.Gly269Alafs*20 variant in MECP2 is predicted to cause a premature stop codon that leads to a truncated or absent protein in a gene where loss-of-function is an established mechanism. There is significant evidence that loss of this region of the gene is pathogenic (PVS1). This variant has been reported as a de novo occurrence (biological parentage confirmed) in at least 2 individuals with Rett syndrome (PMID 26984561, 10854091) (PS2_VS). The p.Gly269Alafs*20 variant in MECP2 is absent from gnomAD (PM2_supporting). In summary, the p.Gly269Alafs*20 variant in MECP2 is classified as Pathogenic for Rett syndrome based on the ACMG/AMP criteria (PVS1, PS2_VS, PM2_supporting).

Met criteria codes

PM2_Supporting	✔	Met- variant is absent in gnomAD
PS2_Very Strong	✔	≥2 independent occurrences of De novo (both maternity and paternity confirmed) in patients with the Rett syndrome and no family history,(PMID 26984561,10854091)
PVS1	✔	Met- Null variant (frame-shift) affecting gene MECP2, which is a known mechanism of disease, PMID: 12481990

Curation History

Showing 1 to 1 of 1 rows

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