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Variant: NM_004958.4(MTOR):c.1249A>G (p.Met417Val)

Version: 2.1

CA590769

1296996 (ClinVar)

Gene: MTOR (HGNC:2475)
Condition: overgrowth syndrome and/or cerebral malformations due to abnormalities in MTOR pathway genes (MONDO:0100283)
Inheritance Mode: Autosomal dominant inheritance (mosaic)
UUID: d905c8f8-e589-45f8-bf70-1f3919e30c53
Approved on: 2025/6/6
Published on: 2025/6/30

HGVS expressions

NM_004958.4(MTOR):c.1249A>G (p.Met417Val)
NM_004958.4:c.1249A>G
NC_000001.11:g.11243277T>C
CM000663.2:g.11243277T>C
NC_000001.10:g.11303334T>C
CM000663.1:g.11303334T>C
NC_000001.9:g.11225921T>C
NG_033239.1:g.24275A>G
ENST00000703118.1:c.1249A>G
ENST00000703132.1:n.1121A>G
ENST00000703140.1:c.1249A>G
ENST00000703141.1:c.1249A>G
ENST00000703142.1:c.1249A>G
ENST00000703143.1:c.1249A>G
ENST00000361445.9:c.1249A>G
ENST00000361445.8:c.1249A>G
NM_004958.3:c.1249A>G
NM_001386500.1:c.1249A>G
NM_001386501.1:c.1A>G

Uncertain Significance

Met criteria codes 1

PP2

Not Met criteria codes 2

PM2 BS1

Evidence Links 0

Expert Panel

Brain Malformations VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Brain Malformations Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Brain Malformations VCEP

The NM_004958.4:c.1249A>G variant in the MTOR gene is a missense variant predicted to cause substitution of methionine by valine at amino acid 417. In gnomAD v4.1.0, this variant has a filtering allele frequency of 0.001567% in the European (non-Finnish) population and a minor allele frequency of 0.002288% (27/1180014), also in the European (non-Finnish) population (PM2_Supporting, BS1, and BS1_Supporting not met). MTOR, in which the variant was identified, is defined by the ClinGen Brain Malformations Variant Curation Expert Panel (BM VCEP) as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of disease (PP2). In summary, this variant meets the criteria to be classified as uncertain significance for overgrowth syndrome and/or cerebral malformations due to abnormalities in MTOR pathway genes based on the ACMG/AMP criteria applied, as specified by the ClinGen BM VCEP: PP2 (ClinGen Brain Malformations VCEP Specifications Version 1.1).

Met criteria codes

PP2	✔	MTOR is defined by the BM VCEP as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of disease

Not Met criteria codes

PM2	✖	In gnomAD v4.1.0, this variant has a filtering allele frequency of 0.001567% and a minor allele frequency of 0.002288% (27/1180014) n the European (non-Finnish) population.
BS1	✖	In gnomAD v4.1.0, this variant has a filtering allele frequency of 0.001567% and a minor allele frequency of 0.002288% (27/1180014) n the European (non-Finnish) population.

Curation History

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