Variant: NM_000540.3(RYR1):c.1077T>C (p.Ala359=)

Version: 1.0

CA023860

93243 (ClinVar)

Gene: RYR1 (HGNC:6261)
Condition: RYR1-related myopathy (MONDO:0100150)
Inheritance Mode: Undetermined mode of inheritance
UUID: 9afce82c-2e70-4ada-b016-d424b8f60629
Approved on: 2024-08-07
Published on: 2024-10-02

HGVS expressions

NM_000540.3:c.1077T>C
NM_000540.3(RYR1):c.1077T>C (p.Ala359=)
NC_000019.10:g.38448768T>C
CM000681.2:g.38448768T>C
NC_000019.9:g.38939408T>C
CM000681.1:g.38939408T>C
NC_000019.8:g.43631248T>C
NG_008866.1:g.20069T>C
ENST00000599547.6:c.1077T>C
ENST00000359596.8:c.1077T>C
ENST00000355481.8:c.1077T>C
ENST00000359596.7:c.1077T>C
ENST00000360985.7:c.1077T>C
NM_000540.2:c.1077T>C
NM_001042723.1:c.1077T>C
NM_001042723.2:c.1077T>C

Benign

Met criteria codes 3

BA1 **BP7** **BP4**

Not Met criteria codes 2

PM2 **BS1**

Evidence Links 0

Expert Panel

Congenital Myopathies VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Congenital Myopathies Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RYR1 Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Congenital Myopathies VCEP

The variant NM_000540.3:c.1077T>C in RYR1 is a synonymous (silent) variant (p.Ala359=). The filtering allele frequency (the lower threshold of the 95% CI of 19809/19952, 9835 homozygotes) of the c.1077T>C variant in RYR1 is 0.9807 for East Asian chromosomes by

gnomAD v4.1, which is higher than the ClinGen Congenital Myopathies VCEP threshold (≥0.00697) for BA1, and therefore meets this criterion (BA1). The c.1077T>C (p.Ala359=) variant is a synonymous (silent) variant that is not predicted by SpliceAI to impact splicing. In addition, it occurs at a nucleotide that is not conserved as shown by UCSC Genome Browser (BP4, BP7). In summary, the variant meets criteria to be classified as benign. ACMG/AMP criteria met, as specified by the congenital myopathies VCEP: BA1, BP4, BP7 (ClinGen Congenital Myopathies VCEP specifications version 1; 8/7/2024).

Met criteria codes

BA1	ℹ	✓	The filtering allele frequency (the lower threshold of the 95% CI of 19809/19952, 9835 homozygotes) of the c.1077T>C variant in RYR1 is 0.9807 for East Asian chromosomes by gnomAD v4.1, which is higher than the ClinGen Congenital Myopathies VCEP threshold (≥0.00697) for BA1, and therefore meets this criterion (BA1).
BP7	ℹ	✓	SpliceAI predicted no impact on splicing, meeting BP4/BP7 criteria.
BP4	ℹ	✓	SpliceAI predicted no impact on splicing, meeting BP4/BP7 criteria.

Not Met criteria codes

PM2		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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