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Variant: NM_000540.3(RYR1):c.10171G>T (p.Glu3391Ter)

Version: 1.0

CA405696104

2710027 (ClinVar)

Gene: RYR1 (HGNC:6261)
Condition: RYR1-related myopathy (MONDO:0100150)
Inheritance Mode: Autosomal recessive inheritance
UUID: e8bcd8b4-302a-4fb6-91e3-c28f30a1d6a5
Approved on: 2024/9/9
Published on: 2024/10/1

HGVS expressions

NM_000540.3(RYR1):c.10171G>T (p.Glu3391Ter)
NM_000540.3:c.10171G>T
NC_000019.10:g.38519366G>T
CM000681.2:g.38519366G>T
NC_000019.9:g.39010006G>T
CM000681.1:g.39010006G>T
NC_000019.8:g.43701846G>T
NG_008866.1:g.90667G>T
ENST00000599547.6:c.10110G>T
ENST00000359596.8:c.10171G>T
ENST00000355481.8:c.10171G>T
ENST00000359596.7:c.10171G>T
ENST00000360985.7:c.10168G>T
ENST00000594335.5:c.3573G>T
ENST00000599547.5:c.978G>T
NM_000540.2:c.10171G>T
NM_001042723.1:c.10171G>T
NM_001042723.2:c.10171G>T

Likely Pathogenic

Met criteria codes 2

PM2_Supporting PVS1

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 NM_000540.3(RYR1):c.10171G>T (p.Glu3391Ter) variant in RYR1 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 67/106 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). The highest population minor allele frequency in gnomAD v4.1.0 is 0.000004243 (5/1178340 alleles) in European (non-Finnish) population, which is lower than the ClinGen Congenital Myopathies VCEP threshold (≤0.00000697) for PM2_Supporting, meeting this criterion (PM2_Supporting). In summary, this variant meets the criteria to be classified as likely pathogenic for RYR1-related myopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen Congenital Myopathies VCEP: PVS1, PM2_P. (Required: ClinGen Congenital Myopathies VCEP specifications version 1; September 9, 2024)

Met criteria codes

PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.0 is 0.000004243 (5/1178340 alleles) in European (non-Finnish) population, which is lower than the ClinGen Congenital Myopathies VCEP threshold (≤0.00000697) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PVS1	✔	The NM_000540.3(RYR1):c.10171G>T (p.Glu3391Ter) variant in RYR1 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 67/106 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Curation History

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