

Variant: NM_001042723.2(RYR1):c.2654G>A (p.Arg885His)

CA063661 [↗](#)

212100 (ClinVar) [↗](#)

Gene: RYR1 ([HGNC:6261](#))

Condition: malignant hyperthermia, susceptibility to, 1 ([MONDO:0007783](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 75f6a216-0fff-441e-a01f-0c9a73ffa399

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HGVS expressions

NM_001042723.2(RYR1):c.2654G>A (p.Arg885His)

NM_001042723.2:c.2654G>A

NC_000019.10:g.38463499G>A

CM000681.2:g.38463499G>A

NC_000019.9:g.38954139G>A

CM000681.1:g.38954139G>A

NC_000019.8:g.43645979G>A

NG_008866.1:g.34800G>A

ENST00000599547.6:n.2654G>A

ENST00000359596.8:c.2654G>A

ENST00000355481.8:c.2654G>A

ENST00000359596.7:n.2654G>A

ENST00000360985.7:c.2654G>A

NM_000540.2:c.2654G>A

NM_001042723.1:c.2654G>A

NM_000540.3:c.2654G>A

NM_000540.3(RYR1):c.2654G>A (p.Arg885His)

Uncertain Significance

The Expert Panel has overridden the computationally generated classification - "[unknown]"

Not Met criteria codes 4

BP4

PS4_Supporting

PP3

PM1

Evidence Links 0

Expert Panel

[Malignant Hyperthermia Susceptibility VCEP](#) [↗](#)

Criteria Specification Information !

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Malignant Hyperthermia Susceptibility VCEP

This pathogenicity assessment is relevant only for malignant hyperthermia susceptibility (MHS) inherited in an autosomal dominant pattern. Variants in RYR1 can also cause other myopathies inherited in an autosomal dominant pattern or in an autosomal recessive pattern. Some of these disorders may predispose individuals to malignant hyperthermia. RYR1 variants may also contribute to a malignant hyperthermia reaction in combination with other genetic and non-genetic factors and the clinician needs to consider such factors in making management decisions. This sequence variant predicts a substitution of arginine with histidine at codon 885 of the RYR1 protein (p.Arg885His). The maximum allele frequency for this variant among the six major gnomAD populations is SAS: 0.00042, a frequency

consistent with pathogenicity for MHS. This variant has been reported in an individual with a personal or family history of an MH episode and a positive in vitro contracture test (IVCT) or caffeine halothane contracture test (CHCT) result (if the proband was unavailable for testing, a positive diagnostic test result in a mutation-positive relative was counted), however, the MAF in the SAS population in gnomAD does not allow PS4 to be utilized (PMID:30236257). No functional studies were identified for this variant.This variant does not reside in a hotspot for pathogenic variants that contribute to MHS. A REVEL score of 0.609 supports neither a pathogenic nor a benign status for this variant. This variant has been classified as a Variant of Unknown Significance. Criteria implemented: none.

Not Met criteria codes

BP4			A REVEL score of 0.609 supports neither a pathogenic nor a benign status for this variant.
PS4_Supporting			This variant has been reported in an individual with a personal or family history of an MH episode and a positive in vitro contracture test (IVCT) or caffeine halothane contracture test (CHCT) result (if the proband was unavailable for testing, a positive diagnostic test result in a mutation-positive relative was counted), however, the MAF in the SAS population in gnomAD does not allow PS4 to be utilized (PMID:30236257).
PP3			A REVEL score of 0.609 supports neither a pathogenic nor a benign status for this variant.
PM1			This variant does not reside in a hotspot for pathogenic variants that contribute to MHS.

Curation History



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[See Report](#)  Preferred Variant Title  Classification   Condition  Published Date  Version  Criteria Specification  Gene

No matching records found

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.