

Variant: *NM\_000540.3(RYR1):c.577T>A (p.Ser193Thr)*

Version: 1.0

[CA10642702](#)

[328993 \(ClinVar\)](#)

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

**Condition:** RYR1-related myopathy ([MONDO:0100150](#))

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 72d5c8c2-18b7-479a-b37a-6925d3c3c152

**Approved on:** 2024-08-27

**Published on:** 2025-01-03

### *HGVS expressions*

**NM\_000540.3:c.577T>A**

NM\_000540.3(RYR1):c.577T>A (p.Ser193Thr)

NC\_000019.10:g.38444623T>A

CM000681.2:g.38444623T>A

NC\_000019.9:g.38935263T>A

CM000681.1:g.38935263T>A

NC\_000019.8:g.43627103T>A

NG\_008866.1:g.15924T>A

ENST00000599547.6:c.577T>A

ENST00000359596.8:c.577T>A

ENST00000355481.8:c.577T>A

ENST00000359596.7:c.577T>A

ENST00000360985.7:c.577T>A

NM\_000540.2:c.577T>A

NM\_001042723.1:c.577T>A

NM\_001042723.2:c.577T>A

Uncertain Significance

Met criteria codes **1**

PP3

Not Met criteria codes **4**

BS1

BP4

BA1

PM2

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 2.0.0*

**Criteria Specification Approval History**

**Criteria Specifications for this VCEP**


Evidence submitted by expert panel

#### ***Congenital Myopathies VCEP***



The c.577T>A variant in RYR1 is a missense variant predicted to cause substitution of serine by threonine at amino acid 193 (p.Ser193Thr). The highest population minor allele frequency in gnomAD v4.1 is 0.00002712 (32/1179992) in the European (non-Finnish) population


(PM2\_Supporting, BS1, and BA1 are not met). The REVEL score is 0.78, which is greater than the threshold of  $\geq 0.7$  set by the CM VCEP (PP3). In summary, this variant meets the criteria to be classified as uncertain significance for AD/AR RYR1-related myopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen Congenital Myopathies VCEP: PP3. (ClinGen Congenital Myopathies VCEP specifications version 2; 08/27/2024)



#### Met criteria codes


**PP3**   The REVEL score is 0.78, which is greater than the threshold of  $\geq 0.7$  set by the CM VCEP (PP3).

#### Not Met criteria codes

**BS1**   The highest population minor allele frequency in gnomAD v4.1 is 0.00002712 (32/1179992) in the European (non-Finnish) population (PM2\_Supporting, BS1, and BA1 are not met).

**BP4**   The REVEL score is 0.78, which is greater than the threshold of  $\geq 0.7$  set by the CM VCEP (PP3).



**BA1**   The highest population minor allele frequency in gnomAD v4.1 is 0.00002712 (32/1179992) in the European (non-Finnish) population (PM2\_Supporting, BS1, and BA1 are not met).

**PM2**  The highest population minor allele frequency in gnomAD v4.1 is 0.00002712 (32/1179992) in the European (non-Finnish) population (PM2\_Supporting, BS1, and BA1 are not met).

#### Curation History [↗](#)



Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification 	Condition	Published Date	Version 	Criteria Specification	Gene
<a href="#">View</a>	NM_000540.3(RYR1):c.577T>A (p.Ser1...	<span style="background-color: #00a0e3; color: white; padding: 2px;">Uncertain Significance</span>	RYR1-Related Myopathy <a href="#">↗</a>	2025-01-03	1.0	ClinGen Congenital Myopathies Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RYR1 Version 2.0.0 <a href="#">↗</a>	<a href="#">RYR1</a> <a href="#">↗</a>

Showing 1 to 1 of 1 rows

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.

---

[ClinGen Terms of Use.](#)  
⌘ Powered by BCM's Genboree.