Variant: NM_000023.4(SGCA):c.662G>C (p.Arg221Pro)

Version: 1.0

CA400180670

497670 (ClinVar)

Gene: SGCA (HGNC:6442)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: e203815d-e310-4737-9fca-d20939ca73c3
Approved on: 2025-01-07
Published on: 2025-01-07

HGVS expressions

NM_000023.4:c.662G>C
NM_000023.4(SGCA):c.662G>C (p.Arg221Pro)
NC_000017.11:g.50169169G>C
CM000679.2:g.50169169G>C
NC_000017.10:g.48246530G>C
CM000679.1:g.48246530G>C
NC_000017.9:g.45601529G>C
NG_008889.1:g.8165G>C
ENST00000504073.2:c.597+65G>C
ENST00000511303.6:n.309+597G>C
ENST00000512526.2:c.575+597G>C
ENST00000682109.1:c.542G>C
ENST00000683226.1:n.372G>C
ENST00000683294.1:c.662G>C
ENST00000262018.8:c.662G>C
ENST00000262018.7:c.662G>C
ENST00000344627.10:c.584+597G>C
ENST00000502555.5:c.*321G>C
ENST00000504073.1:c.64+65G>C
ENST00000511303.5:c.305+597G>C
ENST00000512526.1:c.419+597G>C
ENST00000513821.5:c.662G>C
ENST00000513942.5:n.375+597G>C
NM_000023.2:c.662G>C
NM_001135697.1:c.584+597G>C
NM_000023.3:c.662G>C
NM_001135697.2:c.584+597G>C
NR_135553.1:n.718G>C
NM_001135697.3:c.584+597G>C
NR_135553.2:n.698G>C

Likely Pathogenic

Met criteria codes 4

PP4_Strong PM2_Supporting PP3 PM3

Not Met criteria codes 22

PS1 PS2 PS3 PS4 BP5 BP7 BP4 BP3 BP1 BP2 PVS1 BA1 PP1 PP2 PM6 PM1 PM5 PM4 BS1 BS4 BS3 BS2

Evidence Links 0

Expert Panel

Limb Girdle Muscular Dystrophy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Limb Girdle Muscular Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SGCA Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000023.4: c.662G>C variant in SGCA is a missense variant predicted to cause substitution of arginine by proline at amino acid 221 (p.Arg221Pro). This variant has been detected in at least one individual with autosomal recessive limb girdle muscular dystrophy who was compound heterozygous for the variant and a pathogenic variant (c.585-1G>A, 1.0 pt, Washington University internal clinic data communication) (PM3). At least one patient with this variant displayed progressive limb girdle muscle weakness and absent expression of alpha-sarcoglycan protein, which is highly specific for SGCA-related LGMD (PP4_Strong, Washington University internal clinic data communication). This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting). The computational predictor REVEL gives a score of 0.765, which is above the threshold of ≥0.70, evidence that correlates with impact to SGCA function (PP3). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive limb girdle muscular dystrophy based on the ACMG/AMP criteria applied, as specified by the ClinGen LGMD VCEP (LGMD VCEP specifications version 1.0.0; 01/07/2025): PM2_Supporting, PP3, PM3, PP4_Strong.

Met criteria codes

PP4_Strong	ℹ	✓	At least one patient with this variant displayed progressive limb girdle muscle weakness and absent expression of alpha-sarcoglycan protein, which is highly specific for SGCA-related LGMD (PP4_Strong, internal laboratory contributor).
PM2_Supporting	ℹ	✓	This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting).
PP3	ℹ	✓	The computational predictor REVEL gives a score of 0.765, which is above the threshold of ≥0.70, evidence that correlates with impact to SGCA function (PP3).
PM3	ℹ	✓	This variant has been detected in at least one individual with autosomal recessive limb girdle muscular dystrophy who was compound heterozygous for the variant and a pathogenic variant (c.585-1G>A, 1.0 pt, Internal laboratory contributor) (PM3).

Not Met criteria codes

PS1	ℹ	✗	

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

PS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	ⓘ	✖	There are three other ClinVar variants at this codon but at the time of curation they all have a classification of uncertain significance.
PM4	ⓘ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ⓘ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	ⓘ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 1 of 1 rows