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Variant: NM_000023.4(SGCA):c.402C>G (p.Tyr134Ter)

Version: 1.0

CA8643795

284945 (ClinVar)

Gene: SGCA (HGNC:6442)
Condition: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
Inheritance Mode: Autosomal recessive inheritance
UUID: ee176100-4e90-4f89-b1bf-d48998ca8c7b
Approved on: 2025/11/11
Published on: 2026/1/12

HGVS expressions

NM_000023.4:c.402C>G
NM_000023.4(SGCA):c.402C>G (p.Tyr134Ter)
NC_000017.11:g.50168390C>G
CM000679.2:g.50168390C>G
NC_000017.10:g.48245751C>G
CM000679.1:g.48245751C>G
NC_000017.9:g.45600750C>G
NG_008889.1:g.7386C>G
ENST00000504073.2:c.402C>G
ENST00000511303.6:n.127C>G
ENST00000512526.2:c.393C>G
ENST00000682109.1:c.282C>G
ENST00000683226.1:n.112C>G
ENST00000683294.1:c.402C>G
ENST00000262018.8:c.402C>G
ENST00000262018.7:c.402C>G
ENST00000344627.10:c.402C>G
ENST00000502555.5:c.*61C>G
ENST00000511303.5:c.123C>G
ENST00000512526.1:c.237C>G
ENST00000513821.5:c.402C>G
ENST00000513942.5:n.193C>G
ENST00000514934.1:c.*108C>G
NM_000023.2:c.402C>G
NM_001135697.1:c.402C>G
NM_000023.3:c.402C>G
NM_001135697.2:c.402C>G
NR_135553.1:n.458C>G
NM_001135697.3:c.402C>G
NR_135553.2:n.438C>G

Pathogenic

Met criteria codes 4

PP4 PM3 PVS1 PM2_Supporting

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 2.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Limb Girdle Muscular Dystrophy VCEP

The NM_000023.4: c.402C>G p.(Tyr134Ter) variant in SGCA is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 5/10, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1). This variant has been detected in a heterozygous state in at least four individuals with limb girdle muscular dystrophy (PMID: 37526466, 38876406, 30919934). Of those individuals, three were also heterozygous for a pathogenic SGCA variant in unconfirmed phase (c.739G>A p.(Val247Met), 0.5 pts, PMID: 37526466; c.229C>T p.(Arg77Cys), 0.5 pts, PMID: 38876406; c.850C>T p.(Arg284Cys), 0.5 pts, PMID: 38876406) (PM3). At least one individual with this variant and a second presumed diagnostic SGCA variant displayed progressive limb girdle muscle weakness or had a clinical suspicion of LGMD (PP4, PMID: 38876406). The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000009028 (5/1164486 European (non-Finnish) alleles), which is lower than the ClinGen LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting). In summary, this variant meets the criteria to be classified as 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 2.0.0; 11/11/2025): PVS1, PM3, PP4, PM2_Supporting.

Met criteria codes

PP4	✔	At least one individual with this variant and a second presumed diagnostic SGCA variant displayed progressive limb girdle muscle weakness or had a clinical suspicion of LGMD (PP4, PMID: 38876406).
PM3	✔	This variant has been detected in a heterozygous state in at least four individuals with limb girdle muscular dystrophy (PMID: 37526466, 38876406, 30919934). Of those individuals, three were also heterozygous for a pathogenic SGCA variant in unconfirmed phase (c.739G>A p.(Val247Met), 0.5 pts, PMID: 37526466; c.229C>T p.(Arg77Cys), 0.5 pts, PMID: 38876406; c.850C>T p.(Arg284Cys), 0.5 pts, PMID: 38876406) (PM3). Co-occurrence predictions checked for all variants in unconfirmed phase
PVS1	✔	The NM_000023.4: c.402C>G p.(Tyr134Ter) variant in SGCA is a nonsense variant predicted to cause a premature stop codon in biologically relevant exon 5/10, leading to nonsense mediated decay in a gene in which loss of function is an established disease mechanism (PVS1).
PM2_Supporting	✔	The upper bound of the 95% confidence interval of the Grpmax variant allele frequency in gnomAD v4.1.0 is 0.000009028 (5/1164486 European (non-Finnish) alleles), which is lower than the ClinGen LGMD VCEP threshold (<0.00009) for PM2_Supporting, and therefore meets this criterion (PM2_Supporting).

Curation History

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