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# *Variant: NM_000232.5(SGCB):c.699_702del (p.Phe233fs)*

Version: 1.0

*CA16040953*

*370474 (ClinVar)*

**Gene**: SGCB (HGNC:6443)
**Condition**: autosomal recessive limb-girdle muscular dystrophy (MONDO:0015152)
**Inheritance Mode**: Autosomal recessive inheritance
**UUID:** be814538-bc09-4bef-99d5-429d40398430
**Approved on**: 2025/1/8
**Published on**: 2025/1/8

## *HGVS expressions*

**NM_000232.5:c.699_702del**
**NM_000232.5(SGCB):c.699_702del (p.Phe233fs)**
NC_000004.12:g.52028022_52028025del
CM000666.2:g.52028022_52028025del
NC_000004.11:g.52894188_52894191del
CM000666.1:g.52894188_52894191del
NC_000004.10:g.52588945_52588948del
NG_008891.1:g.15298_15301del
ENST00000381431.10:c.699_702del
ENST00000381431.9:c.699_702del
NM_000232.4:c.699_702del

**Likely Pathogenic**

**Met criteria codes** 5

PVS1_Strong PP1 PP4 PM3 PM2_Supporting

**Not Met criteria codes** 21

PP2 PP3 PM6 BA1 PM1 PM5 PM4 BS1 BS4 BS3 BS2 PS1 PS2 PS3 PS4 BP5 BP7 BP4 BP3 BP1 BP2

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 SGCB 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_000232.5: c.699_702del p.(Phe233LeufsTer16) variant in SGCB is a frameshift variant that may cause loss of function of the protein; the resulting transcript is predicted to escape nonsense mediated decay but remove >10% of the protein (PVS1_Strong). This variant has been detected in at least two unrelated individuals with autosomal recessive limb girdle muscular dystrophy, including confirmed in trans with a likely pathogenic or pathogenic variant (c.377_384dup, 1 pt, PMID: 25862795) and in a homozygous state (0.25 pts, PMID: 25862795) (PM3). At least one patient with this variant and a second SGCB variant displayed progressive limb girdle muscle weakness as well as absent expression of beta-sarcoglycan protein, which is highly specific for SGCB-related LGMD; however, the presence**

**of potentially diagnostic variants in all of the other sarcoglycan genes was not ruled out (PP4; PMID: 12868499, 25862795, 9032047). The variant has also been reported to segregate with autosomal recessive limb girdle muscular dystrophy in one affected family member (PP1; PMID: 25862795) and is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting). 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; 01/08/2025): PVS1_Strong, PM3, PP4, PP1, PM2_Supporting.**

**Met criteria codes**

| | | |
|---|---|---|
| **PVS1_Strong** | ✔ | The NM_000232.5: c.699_702del p.(Phe233LeufsTer16) variant in SGCB is a frameshift variant that may cause loss of function of the protein; the resulting transcript is predicted to escape nonsense mediated decay but remove >10% of the protein (PVS1_Strong). |
| **PP1** | ✔ | The variant has been reported to segregate with autosomal recessive limb girdle muscular dystrophy in one affected family member (PP1_Supporting; PMID: 25862795). |
| **PP4** | ✔ | At least one patient with this variant and a second SGCB variant displayed progressive limb girdle muscle weakness as well as absent expression of beta-sarcoglycan protein, which is highly specific for SGCB-related LGMD; however, the presence of potentially diagnostic variants in all of the other sarcoglycan genes was not ruled out (PP4; PMID: 12868499, 25862795, 9032047). |
| **PM3** | ✔ | This variant has been detected in at least two unrelated individuals with autosomal recessive limb girdle muscular dystrophy, including confirmed in trans with a likely pathogenic or pathogenic variant (c.377_384dup, 1 pt, PMID: 25862795) and in a homozygous state (0.25 pts, PMID: 25862795) (PM3). |
| **PM2_Supporting** | ✔ | This variant is absent from gnomAD v2.1.1 and v3.1.2 (PM2_Supporting). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PP2** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **PP3** | ✖ | 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 |
| **BA1** | ✖ | 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** | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |

| | | | |
|---|---|---|---|
| **PM4** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS1** | ℹ | ✖ | No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline |
| **BS4** | ℹ | ✖ | 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 |
| **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 |

## Curation History

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