

Variant: *NM_000138.5(FBN1):c.6866G>C (p.Cys2289Ser)*

Version: 1.0

CA392331872 [↗](#)

632813 (ClinVar) [↗](#)

Gene: FBN1 ([HGNC:2200](#))

Condition: Marfan syndrome ([MONDO:0007947](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 3b16a9ab-115c-4598-9c85-22f4ebe5eb1c

Approved on: 2024/8/22

Published on: 2024/8/22

HGVS expressions

NM_000138.5:c.6866G>C

NM_000138.5(FBN1):c.6866G>C (p.Cys2289Ser)

NC_000015.10:g.48430676C>G

CM000677.2:g.48430676C>G

NC_000015.9:g.48722873C>G

CM000677.1:g.48722873C>G

NC_000015.8:g.46510165C>G

NG_008805.2:g.220113G>C

ENST00000559133.6:c.6866G>C

ENST00000674301.2:c.*317G>C

ENST00000682170.1:n.475G>C

ENST00000316623.10:c.6866G>C

ENST00000674301.1:c.1970G>C

ENST00000316623.9:c.6866G>C

ENST00000559133.5:c.2173G>C

ENST00000560720.1:n.153G>C

NM_000138.4:c.6866G>C

Likely Pathogenic

Met criteria codes 4

PM1_Strong

PP2

PP3

PM2_Supporting

Not Met criteria codes 1

BS2

Evidence Links 0

Expert Panel

FBN1 VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

FBN1 VCEP

NM_00138 c.6866G>C is a missense variant in **FBN1** predicted to cause a substitution of cysteine by serine at amino acid 2289 (p.Cys2289Ser). This variant is not reported in the literature in any individuals with Marfan syndrome (MFS). This variant has been reported once in ClinVar as Likely pathogenic and once as uncertain significance (Variation ID: 632813). This variant is not present in

gnomAD (PM2_Sup; <https://gnomad.broadinstitute.org/ v4.0.0>). This variant affects a cysteine residue in a calcium binding EGF domain. Cysteine residues are believed to be involved in the formation of disulfide bridges which are essential for the protein structure (PM1_strong). The constraint z-score for missense variants affecting FBN1 is 8.18 (PP2; <https://gnomad.broadinstitute.org/ v4.0.0>). Computational prediction tools and conservation analysis suggest that this variant may impact the protein (REVEL: 0.992, PP3). In summary, this variant meets criteria to be classified as likely pathogenic for Marfan syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen FBN1 VCEP: PM1_Strong, PM2_Sup,PP3, PP2.

Met criteria codes

PM1_Strong			Disrupts a Cysteine residue in cbEGF35
PP2			Missense variant
PP3			REVEL score: 0.992
PM2_Supporting			Absent in gnomAD

Not Met criteria codes

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

--

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.