The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000138.5(FBN1):c.5826C>A (p.Cys1942Ter)

Version: 1.0

CA269532860

547334 (ClinVar)

Gene: FBN1 (HGNC:2200)
Condition: Marfan syndrome (MONDO:0007947)
Inheritance Mode: Autosomal dominant inheritance
UUID: 76fe5b55-7709-49dc-b27d-dfa97cef8168
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HGVS expressions

NM_000138.5:c.5826C>A
NM_000138.5(FBN1):c.5826C>A (p.Cys1942Ter)
NC_000015.10:g.48445467G>T
CM000677.2:g.48445467G>T
NC_000015.9:g.48737664G>T
CM000677.1:g.48737664G>T
NC_000015.8:g.46524956G>T
NG_008805.2:g.205322C>A
ENST00000559133.6:c.5826C>A
ENST00000674301.2:c.5826C>A
ENST00000684448.1:n.4500C>A
ENST00000316623.10:c.5826C>A
ENST00000674301.1:c.825C>A
ENST00000316623.9:c.5826C>A
ENST00000537463.6:c.*1589C>A
ENST00000559133.5:c.1133C>A
NM_000138.4:c.5826C>A

Pathogenic

Met criteria codes 6

PVS1 | PM6_Supporting | PP1 | PP4 | PS4_Supporting | PM2_Supporting

Evidence Links 0

Expert Panel

FBN1 VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

FBN1 VCEP

The NM_00138 c.5826C>A, is a nonsense variant in FBN1 expected to cause a premature stop codon and likely results in an absent or disrupted protein product (PVS1). This variant was found in a proband with infantile Marfan syndrome (MFS) and was found to be de novo without confirmation of parental relationships (internal data, PP4, PM6_Supporting). This variant has been reported 7 times in ClinVar, twice as pathogenic and five times as uncertain significance (Variantion ID: 547334). At least three other probands with clinical features of MFS carry the same variant (PMID 12068374, 22772377, Centre for Human Genetics ClinVar entry, PS4_Sup). In one family with features of

MFS, including mitral valve prolapse, striae, pectus carinatum, scoliosis, striae, joint hypermobility, and wrist and thumb sign, this variant was found to segregate with disease in four affected family members (PMID 12068374, PP1). This variant is not present in gnomAD (PM2_sup; https://gnomad.broadinstitute.org/ v2.1.1). In summary, this variant meets criteria to be classified as pathogenic for Marfan syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen FBN1 VCEP: PVS1, PS4_Sup, PM2_Sup, PM6_Sup, PP1, PP4

Met criteria codes

PVS1	✔	PTC at 1942, predicted to undergo NMD
PM6_Supporting	✔	1 de novo with phenotype consistent with gene without confirmation of parental relationships
PP1	✔	3 segregations in 1 family with high systemic score
PP4	✔	one proband with infantile MFS, de novo without confirmation of maternity/paternity
PS4_Supporting	✔	1.5 Pts
PM2_Supporting	✔	Absent in gnomAD

Curation History

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