Variant: NM_000260.4(MYO7A):c.2558G>A (p.Arg853His)

Version: 1.3

CA132255

43186 (ClinVar)

Gene: MYO7A (HGNC:4647)
Condition: nonsyndromic genetic deafness (MONDO:0019497)
Inheritance Mode: Autosomal dominant inheritance
UUID: c33ae219-757e-4113-a157-ae454a79015c
Approved on: 2022-10-31
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HGVS expressions

NM_000260.4:c.2558G>A
NM_000260.4(MYO7A):c.2558G>A (p.Arg853His)
NC_000011.10:g.77179925G>A
CM000673.2:g.77179925G>A
NC_000011.9:g.76890971G>A
CM000673.1:g.76890971G>A
NC_000011.8:g.76568619G>A
NG_009086.1:g.56662G>A
NG_009086.2:g.56680G>A
ENST00000409709.9:c.2558G>A
ENST00000409893.6:c.623G>A
ENST00000670577.1:c.399G>A
ENST00000409619.6:c.2525G>A
ENST00000409709.7:c.2558G>A
ENST00000409893.5:c.2558G>A
ENST00000458169.2:c.101G>A
ENST00000458637.6:c.2558G>A
ENST00000481328.7:n.101G>A
ENST00000620575.4:c.2558G>A
NM_000260.3:c.2558G>A
NM_001127179.2:c.2558G>A
NM_001127180.1:c.2558G>A
NM_001127180.2:c.2558G>A
NM_001369365.1:c.2525G>A

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PS4_Supporting PP1_Strong PP3

Not Met criteria codes 1

PM5

Evidence Links 0

Expert Panel

Hearing Loss VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Hearing Loss Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for CDH23, COCH, GJB2, KCNQ4, MYO6, MYO7A, SLC26A4, TECTA and USH2A Version 2*
PDF

Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hearing Loss VCEP

The c.2558G>A variant in MYO7A is a missense variant predicted to cause substitution of arginine by histidine at amino acid 853. This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The computational predictor REVEL gives a score of 0.741, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3). This variant has been reported in 3 probands/families with hearing loss (PS4_Supporting; PMIDs: 26969326, 32097363, ClinVar SCV: SCV000059742.6, LMM). The variant has been reported to segregate with nonsyndromic genetic hearing loss in 10 affected family members from 1 family (PP1_Strong; PMID: 32097363). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant nonsyndromic genetic hearing loss based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PP1_S, PS4_P, PM2_P, PP3 (Hearing Loss VCEP specifications version 2; 10/31/2022).

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PS4_Supporting	✔	1 proband from Shearer 2013/Sloan-Heggen 2016 2 probands from LMM internal data (SCV000059742.6) -5mo white female with congenital moderate SNHL, het. for this variant. Also het. for 2 variants in PCDH15, either benign or benign/VUS (ClinVar ID: 46434, 46485) -Not counted: 1yo male with congenital sloping mild-moderate SNHL. Carried another variant in MYO7A (VUS, ClinVar ID: 178990), which unaffected father carried. However, mother carried R853H and was also unaffected.
PP1_Strong	✔	The variant has been reported to segregate with nonsyndromic genetic hearing loss in 10 affected family members from 1 family (PP1_Strong; PMID: 32097363).
PP3	✔	The computational predictor REVEL gives a score of 0.741, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3).

Not Met criteria codes

PM5	✖	2 other variants in this codon: c.2558G>T, VUS in ClinVar, and c.2557C>T (not in ClinVar, and not enough published evidence to reach LP).

Curation History

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