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_000260.4(MYO7A):c.3862G>C (p.Ala1288Pro)

Version: 1.0

CA6198221

866837 (ClinVar)

Gene: MYO7A (HGNC:4647)
Condition: nonsyndromic genetic deafness (MONDO:0019497)
Inheritance Mode: Autosomal recessive inheritance
UUID: 647cd6e5-0b17-415f-9309-9955f27e6ce8
Approved on: 2022/12/21
Published on: 2023/2/6

HGVS expressions

NM_000260.4(MYO7A):c.3862G>C (p.Ala1288Pro)
NM_000260.4:c.3862G>C
NC_000011.10:g.77190808G>C
CM000673.2:g.77190808G>C
NC_000011.9:g.76901853G>C
CM000673.1:g.76901853G>C
NC_000011.8:g.76579501G>C
NG_009086.1:g.67544G>C
NG_009086.2:g.67563G>C
ENST00000409709.9:c.3862G>C
ENST00000670577.1:c.1703G>C
ENST00000409619.6:c.3829G>C
ENST00000409709.7:c.3862G>C
ENST00000458169.2:c.1405G>C
ENST00000458637.6:c.3862G>C
ENST00000467137.1:n.389G>C
ENST00000481328.7:n.1405G>C
NM_000260.3:c.3862G>C
NM_001127180.1:c.3862G>C
NM_001127180.2:c.3862G>C
NM_001369365.1:c.3829G>C

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM2_Supporting PM3_Strong

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 NM_000260.4:c.3862G>C variant in the MYO7A gene is a missense variant predicted to cause substitution of alanine to proline at amino acid 1288 (p.Ala1288Pro). The highest population minor allele frequency in gnomAD v2.1.1 is 0.006% (7/110006 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (<0.007%) for PM2_Supporting. The computational predictor REVEL gives a score of 0.833, evidence that correlates with impact to MYO7A function (PP3). This variant has been detected in five individuals with hearing loss or clinical features of Usher syndrome who were compound heterozygous for the variant and a pathogenic or likely pathogenic variant. However, for each individual phase was unknown (PMID: 10094549, 26969326, SCV001533246.2, 2.5 PM3 points) (PM3_Strong, PP4). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive Usher syndrome, based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss Variant Curation Expert Panel: (PM3_Strong, PM2_Supporting, PP3, PP4). (VCEP specifications version 2.0.0; December 21, 2022)

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.833, evidence that correlates with impact to MYO7A function (PP3).
PP4	✔	Several individuals with features of Usher syndrome, See PM3 for details.
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v2.1.1 is 0.006% (7/110006 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (<0.007%) for PM2_Supporting.
PM3_Strong	✔	This variant has been detected in five individuals with hearing loss or clinical features of Usher syndrome who were compound heterozygous for the variant and a pathogenic or likely pathogenic variant. However, for each individual phase was unknown (PMID: 10094549, 26969326, SCV001533246.2, 2.5 PM3 points) (PM3_Strong, PP4). 1) Invitae internal evidence - Ala1288Pro and p.Tyr403Cys phase unknown in 1 proband with Profound SNHL, prelingual, vestibular dysfunction, RP - 0.5pt PM3, PP4 2) Invitae internal Evidence - Phase unknown with c.2838del p.Met946Ilefs*116 (NMD+, 1/112084 alleles gnomAD, PM2_S met) dx of Usher syndrome (0.5 PM3, PP4) ****AO NOTE: double check the MAF! Which subpopulation? [update 1.01.2023, european non-finnish) 3) PMID:10094549 4 and 5) 26969326

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000260.4(MYO7A):c.3862G>C (p.A...	Likely Pathogenic	Nonsyndromic Genetic Deafness	2023-02-06	1.0	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	MYO7A

Showing 1 to 1 of 1 rows

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