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.397C>A (p.His133Asn)

Version: 1.0

CA177366

164656 (ClinVar)

Gene: MYO7A (HGNC:4647)
Condition: Usher syndrome (MONDO:0019501)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6fb982bb-5354-443c-9de4-3efaeacbd10c
Approved on: 2025/3/12
Published on: 2025/3/28

HGVS expressions

NM_000260.4(MYO7A):c.397C>A (p.His133Asn)
NM_000260.4:c.397C>A
NC_000011.10:g.77156018C>A
CM000673.2:g.77156018C>A
NC_000011.9:g.76867064C>A
CM000673.1:g.76867064C>A
NC_000011.8:g.76544712C>A
NG_009086.1:g.32755C>A
NG_009086.2:g.32773C>A
ENST00000409709.9:c.397C>A
ENST00000409619.6:c.364C>A
ENST00000409709.7:c.397C>A
ENST00000409893.5:c.397C>A
ENST00000458637.6:c.397C>A
ENST00000620575.4:c.397C>A
NM_000260.3:c.397C>A
NM_001127179.2:c.397C>A
NM_001127180.1:c.397C>A
NM_001127180.2:c.397C>A
NM_001369365.1:c.364C>A

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM3 PM5

Not Met criteria codes 3

PM2 BA1 BS1

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.397C>A variant in MYO7A is a missense variant predicted to cause substitution of histidine by asparagine at amino acid 133 (p.His133Asn). The filtering allele frequency in gnomAD v4 is 0.01079% (147/1179888) in the European (non-Finnish) population. (PM2_Supporting, BS1, and BA1 are not met). This variant has been reported as compound heterozygous, phase unknown, with a pathogenic variant in three individuals. One individual had a phenotype of Usher syndrome, one individual had congenital, severe to profound hearing loss, and one individual had inherited retinal disease (PM3, PP4; PMID: 36011334, 26969326, 38219857). Two additional individuals with clinical features of Usher syndrome harbored the variant phase unknown with another variant of uncertain significance (PMID: 37466950, SCV001218757.5). The computational predictor REVEL gives a score of 0.937, which is above the threshold necessary to apply PP3 (PP3). Another missense variant, c.397C>T p.His133Tyr, in the same codon has been classified as pathogenic for Usher syndrome by the ClinGen Hearing Loss VCEP (PM5; ClinVar Variation ID: 43228). 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 VCEP: PM3, PP4, PP3, PM5. (ClinGen Hearing Loss VCEP specifications version 2; 03/12/2025).

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.937, which is above the threshold necessary to apply PP3
PP4	✔	One individual had a phenotype of Usher syndrome, one individual had congenital, severe to profound hearing loss, and one individual had inherited retinal disease
PM3	✔	One individual had a phenotype of Usher syndrome, one individual had congenital, severe to profound hearing loss, and one individual had inherited retinal disease
PM5	✔	Another missense variant, c.397C>T p.His133Tyr, in the same codon has been classified as pathogenic for Usher syndrome by the ClinGen Hearing Loss VCEP

Not Met criteria codes

PM2	✖	The filtering allele frequency in gnomAD v4 is 0.01079% (147/1179888) in the European (non-Finnish) population
BA1	✖	The filtering allele frequency in gnomAD v4 is 0.01079% (147/1179888) in the European (non-Finnish) population
BS1	✖	The filtering allele frequency in gnomAD v4 is 0.01079% (147/1179888) in the European (non-Finnish) population

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.397C>A (p.His...	Likely Pathogenic	Usher Syndrome	2025-03-28	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

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