

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

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HGVS expressions

NM_000260.4:c.397C>A

NM_000260.4(MYO7A):c.397C>A (p.His133Asn)

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**

BA1

PM2

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**

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

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

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