

Variant: *NM_000260.4(MYO7A):c.3827C>T (p.Ser1276Leu)*

Version: 1.1

CA278732 [↗](#)

178283 (ClinVar) [↗](#)

Gene: MYO7A ([HGNC:4647](#))

Condition: Usher syndrome ([MONDO:0019501](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 0e2cad56-a84e-46aa-b94f-6652a04eb450

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HGVS expressions

NM_000260.4:c.3827C>T

NM_000260.4(MYO7A):c.3827C>T (p.Ser1276Leu)

NC_000011.10:g.77190773C>T

CM000673.2:g.77190773C>T

NC_000011.9:g.76901818C>T

CM000673.1:g.76901818C>T

NC_000011.8:g.76579466C>T

NG_009086.1:g.67509C>T

NG_009086.2:g.67528C>T

ENST00000409709.9:c.3827C>T

ENST00000670577.1:c.1668C>T

ENST00000409619.6:c.3794C>T

ENST00000409709.7:c.3827C>T

ENST00000458169.2:c.1370C>T

ENST00000458637.6:c.3827C>T

ENST00000467137.1:n.354C>T

ENST00000481328.7:n.1370C>T

NM_000260.3:c.3827C>T

NM_001127180.1:c.3827C>T

NM_001127180.2:c.3827C>T

NM_001369365.1:c.3794C>T

Uncertain Significance

Met criteria codes **2**

PM3 PP3

Not Met criteria codes **2**

PM2 PP4

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 NM_000260.4:c.3827C>T variant in the MYO7A gene is a missense variant predicted to cause substitution of serine to leucine at amino acid 1276 (p.Ser1276Leu). The highest population minor allele frequency in gnomAD v2.1.1 is 0.0078% (1/12706) in African/African American population (PM2_Supporting, BS1, and BA1 are not met). This variant has been detected in 1 patient with hearing loss in trans with a likely pathogenic variant (PM3; Partners LMM internal data SCV000204707.4). The computational predictor REVEL gives a score of 0.769, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3). In summary, due to limited evidence, this variant is classified as a variant of uncertain significance based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss Variant Curation Expert Panel: PM3, PP3. (VCEP specifications version 2.0.0; Dec 21, 2022)

Met criteria codes

PM3			The variant was identified in an individual with mild hearing loss and retinal pigmentary changes. It was confirmed in trans with the p.Leu366Pro variant in MYO7A (LMM internal data SCV000204707.4). This variant is classified as LP with 2 star concordance by two clinical labs in ClinVar. This scores 1 point for PM3.
PP3			The REVEL score is 0.769, which is above the HL cutoff for pathogenicity 0.7. The residue is entirely conserved in UCSC and no species harbor the variant amino acid. Maxentscan does not predict any splicing differences.

Not Met criteria codes

PM2			[12.21.2022] 1/12706 in African/African American chromosomes, 0.000078, criteria is ≤0.00007 agreed on call it is not met. [PREVIOUS] This variant was identified in 1/12706 African alleles in gnomAD (0.008%) which meets the cutoff for PM2_Supporting for AR disease.
PP4			The patient's phenotype (mild hearing loss with retinal pigment changes) is not necessarily consistent with Usher syndrome Type 1.

Curation History



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