

Variant: *NM_000260.4(MYO7A):c.983T>C (p.Leu328Pro)*

Version: 1.0

CA381933255 [↗](#)

1308583 (ClinVar) [↗](#)

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

Condition: Usher syndrome type 1B ([MONDO:0700087](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 7cdf2c5e-e1ab-4248-b4a4-ff015e04deb2

Approved on: 2024/12/18

Published on: 2025/3/28

HGVS expressions

NM_000260.4(MYO7A):c.983T>C (p.Leu328Pro)

NM_000260.4:c.983T>C

NC_000011.10:g.77158410T>C

CM000673.2:g.77158410T>C

NC_000011.9:g.76869456T>C

CM000673.1:g.76869456T>C

NC_000011.8:g.76547104T>C

NG_009086.1:g.35147T>C

NG_009086.2:g.35165T>C

ENST00000409709.9:c.983T>C

ENST00000409619.6:c.950T>C

ENST00000409709.7:c.983T>C

ENST00000409893.5:c.983T>C

ENST00000458637.6:c.983T>C

ENST00000620575.4:c.983T>C

NM_000260.3:c.983T>C

NM_001127179.2:c.983T>C

NM_001127180.1:c.983T>C

NM_001127180.2:c.983T>C

NM_001369365.1:c.950T>C

Uncertain Significance

Met criteria codes **4**

PP3

PP4

PM2_Supporting

PM3_Supporting

Not Met criteria codes **2**

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

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Hearing Loss VCEP

The variant NM_000260.4:c.983T>C in MYO7A is a missense variant predicted to cause substitution of leucine by proline at amino acid 328 (p.Leu328Pro). The variant is absent from gnomAD v4.1.0 (PM2_Supporting). The variant p.Leu328Pro variant was identified by multigene panel testing in a three year old male proband with congenital bilateral profound sensorineural hearing loss and pigmentary retinopathy, delayed motor milestones, blonde fundus, and a diagnosis of Usher Syndrome 1B (PP4, PMID: 32281467). The proband also harbored a likely pathogenic variant NM_000260(MYO7A):c.471-2A>C, however the phase of the variants was not confirmed (0.5 PM3 points, PM3_Supporting; PMID: 32281467). The computational predictor REVEL gives a score of 0.877, which is above the threshold necessary to apply PP3 (PP3). There is a ClinVar entry for this variant (Variation ID: 1308583, one star review status), with one submitter classifying the variant as uncertain significance. In summary, this variant has been classified as a variant of uncertain significance for autosomal recessive Usher syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PM2_Supporting, PP3, PP4, PM3_Supporting (ClinGen Hearing Loss VCEP specifications version 2; 12/18/2024).

Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.877, which is above the threshold necessary to apply PP3 (PP3).
PP4			The variant p.Leu328Pro variant was identified by multigene panel testing in a three year old male proband with congenital bilateral profound sensorineural hearing loss and pigmentary retinopathy, delayed motor milestones, blonde fundus, and a diagnosis of Usher Syndrome 1B (PP4, PMID: 32281467).
PM2_Supporting			The variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PM3_Supporting			The variant p.Leu328Pro variant was identified by multigene panel testing in a three year old male proband with congenital bilateral profound sensorineural hearing loss and pigmentary retinopathy, delayed motor milestones, blonde fundus, and a diagnosis of Usher Syndrome 1B (PMID: 32281467). The proband also harbored a likely pathogenic variant NM_000260(MYO7A):c.471-2A>C, however the phase of the variants was not confirmed (0.5 PM3 points, PM3_Supporting; PMID: 32281467).

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

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