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.2904G>T (p.Glu968Asp)

Version: 1.1

CA278647

43196 (ClinVar)

Gene: MYO7A (HGNC:4647)
Condition: Usher syndrome type 1B (MONDO:0700087)
Inheritance Mode: Autosomal recessive inheritance
UUID: 19a2a2ac-617d-4a6b-ba5a-d3c5b8766be6
Approved on: 2022/8/3
Published on: 2022/8/3

HGVS expressions

NM_000260.4(MYO7A):c.2904G>T (p.Glu968Asp)
NM_000260.4:c.2904G>T
NC_000011.10:g.77181589G>T
CM000673.2:g.77181589G>T
NC_000011.9:g.76892635G>T
CM000673.1:g.76892635G>T
NC_000011.8:g.76570283G>T
NG_009086.1:g.58326G>T
NG_009086.2:g.58344G>T
ENST00000409709.9:c.2904G>T
ENST00000409893.6:c.969G>T
ENST00000670577.1:c.745G>T
ENST00000409619.6:c.2871G>T
ENST00000409709.7:c.2904G>T
ENST00000409893.5:c.2904G>T
ENST00000458169.2:c.447G>T
ENST00000458637.6:c.2904G>T
ENST00000481328.7:n.447G>T
ENST00000620575.4:c.2904G>T
NM_000260.3:c.2904G>T
NM_001127179.2:c.2904G>T
NM_001127180.1:c.2904G>T
NM_001127180.2:c.2904G>T
NM_001369365.1:c.2871G>T

Likely Pathogenic

Met criteria codes 4

PP1 PP4 PM2_Supporting PM3_Strong

Not Met criteria codes 3

PP3 PM5 BP4

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

Evidence submitted by expert panel

Hearing Loss VCEP

The c.2904G>T variant in MYO7A is a missense variant predicted to cause substitution of glutamic acid by aspartic acid at amino acid 968. The highest population minor allele frequency in gnomAD v2.1.1 is 0.0000064 (3/126898 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (<0.00007) for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.563, which is neither above nor below the thresholds predicting a damaging or benign impact on MYO7A function. At least one patient with this variant displayed Usher syndrome (PP4, PMID: 33089500). This variant has been detected in at least five individuals with Usher syndrome. Of those individuals, two were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and presumed to be in trans (c.631A>G (p.S211G) and c.3719G>A (p.D1240Q)) and three of those were confirmed in trans by family testing and all of whom had different variants on the other allele (c.224dup (p.D75fs), c.487G>C (p.G163R), c.1189G>A (p.A397T); 2.5 PM3 points, PMID: 25472526, 26969326, 33089500; ClinVar Variation ID: 43325, 43218, 553215) (PM3_Strong). The variant has been reported to segregate with Usher syndrome in three affected family members from one family (PP1; PMID:33089500). Another missense variant, c.2904G>C (p.E968D), in the same codon has been reported in a patient with Usher syndrome (PMID:27460420). However, this variant has not yet met the criteria to be classified as pathogenic or likely pathogenic by the ClinGen Hearing Loss VCEP (PM5 not met). 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: PM2_P, PP1, PP4, PM3_S (ClinGen Hearing Loss VCEP specifications version 2; 7/26/2022).

Met criteria codes

PP1	✔	The variant has been reported to segregate with Usher syndrome in three affected family members from one family (PP1; PMID:33089500).
PP4	✔	At least one patient with this variant displayed Usher syndrome (PP4, PMID: 33089500).
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v2.1.1 is 0.0000064 (3/126898 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (<0.00007) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PM3_Strong	✔	This variant has been detected in at least five individuals with Usher syndrome. Of those individuals, two were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and presumed to be in trans (c.631A>G (p.S211G) and c.3719G>A (p.D1240Q)) and three of those were confirmed in trans by family testing and all of whom had different variants on the other allele (c.224dup (p.D75fs), c.487G>C (p.G163R), c.1189G>A (p.A397T); 2.5 PM3 points, PMID: 25472526, 26969326, 33089500; ClinVar Variation ID: 43325, 43218, 553215) (PM3_Strong).

Not Met criteria codes

PP3	✖	The computational predictor REVEL gives a score of 0.563, which is neither above nor below the thresholds predicting a damaging or benign impact on MYO7A function.
PM5	✖	

Another missense variant, c.2904G>C (p.E968D), in the same codon has been reported in a patient with Usher syndrome (PMID:27460420). However, this variant has not yet met the criteria to be classified as pathogenic or likely pathogenic by the ClinGen Hearing Loss VCEP (PM5 not met).

BP4 ✖ The computational predictor REVEL gives a score of 0.563, which is neither above nor below the thresholds predicting a damaging or benign impact on MYO7A function.

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.2904G>T (p.G...	Likely Pathogenic	Usher Syndrome Type 1B	2022-08-03	1.1	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
View	NM_000260.4(MYO7A):c.2904G>T (p.G...	Likely Pathogenic	Usher Syndrome Type 1B	2022-08-03	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 2 of 2 rows

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