

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

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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

PM3_Strong

PP1

PP4

PM2_Supporting

Not Met criteria codes 3

BP4

PP3

PM5

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**

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

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).
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).

Not Met criteria codes

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.
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).

Curation History [↗](#)

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