

Variant: NM_000260.3(MYO7A):c.905G>A (p.Arg302His)

CA132454 [↗](#)

11852 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: dc239e28-ecae-44c9-998a-c69771a041f3

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HGVS expressions

NM_000260.3:c.905G>A

NM_000260.3(MYO7A):c.905G>A (p.Arg302His)

NC_000011.10:g.77158332G>A

CM000673.2:g.77158332G>A

NC_000011.9:g.76869378G>A

CM000673.1:g.76869378G>A

NC_000011.8:g.76547026G>A

NG_009086.1:g.35069G>A

NM_001127179.2:c.905G>A

NM_001127180.1:c.905G>A

NM_000260.4:c.905G>A

ENST00000409619.6:c.872G>A

ENST00000409709.7:c.905G>A

ENST00000409893.5:c.905G>A

ENST00000458637.6:c.905G>A

ENST00000620575.4:c.905G>A

Likely Benign

Met criteria codes **3**

BS3_Supporting **BS1** **BP2**

Not Met criteria codes **1**

BP5

Evidence Links **3**

Expert Panel

Hearing Loss VCEP [↗](#)

Criteria Specification Information **!**

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

Evidence submitted by expert panel

Hearing Loss VCEP

The filtering allele frequency of the c.905G>A (p.Arg302His) variant in the MYO7A gene is 0.4% for European chromosomes by gnomAD (587/126276 with 95% CI), which is a high enough frequency to be classified as likely benign based on the thresholds defined by the ClinGen Hearing Loss Expert Panel for autosomal recessive hearing loss variants (BS1). While this variant has been reported in several individuals with Usher syndrome, in 2 individuals it was identified in cis with another pathogenic MYO7A variant (BP2; PMID 8900236). This variant has also been reported in at least 2 additional individuals with Usher syndrome who had alternate genetic etiologies identified

(PMID: 25468891). In addition, in vitro functional evidence from one study suggests that the Arg302His variant had little effect on motor activity of MYO7A (BS3_Supporting PMID: 18700726). In summary, this variant meets criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the Hearing Loss Expert Panel : BS1, BP2, BS3_Supporting.

Met criteria codes

BS3_Supporting			Actin-translocating activity revealed the similar velocity of R302H mutant to that of the wild-type, consistent with the actin-activated ATPase activity that showed little difference from the wild-type. In all of the functional assays performed in this study, the R302H mutation showed little effect on the motor activity of myosin VIIa. Sf9 cells were infected with viruses expressing a construct of human MYO7A that harbored previously reported Ush variants. Construct contained the entire motor domain plus two IQ motifs of myosin VIIa. The Arg302His variant showed little effect on motor activity of MYO7A. Studied ATPase activity (similar to WT), rate of ADP release from actin myosin (all other mutants showed dissociation from actin in presence of ADP, actin translocating velocity was similar to WT). Furthermore, Arg302 is not conserved among members of the myosin superfamily, suggesting that Arg302 is not critical for the authentic function of myosin VIIa. Therefore, they concluded that the R302H mutation is not directly responsible for the USH1B phenotype. PubMed:18700726 
BS1			filtering allele frequency calculated from gnomAD = 0.4% (587/126276) of European chromosomes
BP2			Variant identified in cis with a pathogenic MYO7A variant in 2 individuals. The Arg302His variant was identified in four individuals with Usher syndrome from Holland, Sweden and Belgium. One individual was heterozygous for Arg302His, which was also in cis with Arg212His (classified as pathogenic or likely pathogenic by LMM and Counsyl in ClinVar). Oneindividual was homozygous, for both Arg302His and Arg212His. Two individuals were found to be heterozygous for only Arg302His. PubMed:8900236 

Not Met criteria codes

BP5			DO NOT USE BP5 FOR RECESSIVE. reported as likely neutral, 1 patient had two likely pathogenic variants in CDH23 (Arg1219X and Arg1746Gln), another patient had 2 likely pathogenic variants (V72V and 496+1G>T) in USH1C PubMed:25468891 
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Curation History



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