

Variant: *NM_000260.3(MYO7A):c.1007G>A (p.Arg336His)*

Version: 1.1

CA132194 [↗](#)

43134 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 63bd6cea-9e2a-4ad6-a8c4-5a0d13f28c7e

Approved on: 2024/11/20

Published on: 2025/3/18

HGVS expressions

NM_000260.3:c.1007G>A

NM_000260.3(MYO7A):c.1007G>A (p.Arg336His)

NC_000011.10:g.77159450G>A

CM000673.2:g.77159450G>A

NC_000011.9:g.76870496G>A

CM000673.1:g.76870496G>A

NC_000011.8:g.76548144G>A

NG_009086.1:g.36187G>A

NG_009086.2:g.36205G>A

ENST00000409709.9:c.1007G>A

ENST00000409619.6:c.974G>A

ENST00000409709.7:c.1007G>A

ENST00000409893.5:c.1007G>A

ENST00000458637.6:c.1007G>A

ENST00000620575.4:c.1007G>A

NM_001127179.2:c.1007G>A

NM_001127180.1:c.1007G>A

NM_000260.4:c.1007G>A

NM_001127180.2:c.1007G>A

NM_001369365.1:c.974G>A

Likely Benign

Met criteria codes **2**

BP2

BS1_Supporting

Not Met criteria codes **1**

PP3

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 c.1007G>A (p.Arg336His) variant in MYO7A is a missense variant predicted to cause a substitution of arginine by histidine at amino acid 336. The highest population minor allele frequency in gnomAD v4.1.0 is 0.00286 (2854/996858) in the non-Finnish European population, including 4 homozygous individuals, at least two of whom were beyond the average age of onset for MYO7A-related Usher syndrome. This frequency is higher than would be expected for an autosomal recessive condition based on the thresholds defined by the ClinGen Hearing Loss Expert Panel (BS1_Supporting). This variant has been reported in individuals with nonsyndromic, mild-moderate hearing loss in whom a second variant was not detected (PMID: 23804846) as well as an individual with Usher syndrome but lacking a second variant (PMID: 16470552). A patient with Usher syndrome was homozygous for both p.Arg336His and a likely pathogenic/pathogenic variant (BP2; PMID: 33363762, ClinVar IDs: 551533). The REVEL computational prediction tool produced a score of 0.734, which is above the threshold necessary to apply PP3. However, after discussion the expert panel decided not to apply PP3 based upon case level and frequency data. In summary, this variant meets criteria to be classified as likely benign for both Usher syndrome and nonsyndromic hearing loss. ACMG/AMP criteria applied, as specified by the Hearing Loss Expert Panel: BS1_Supporting, BP2. (ClinGen Hearing Loss VCEP specifications version 2; 11.20.2024).

Met criteria codes

BP2			A patient with Usher syndrome was homozygous for both p.Arg336His and a likely pathogenic/pathogenic variant (BP2; PMID: 33363762, ClinVar IDs: 551533).
BS1_Supporting			The highest population minor allele frequency in gnomAD v4.1.0 is 0.00286 (2854/996858) in the non-Finnish European population, including 4 homozygous individuals, at least two of whom were beyond the average age of onset for MYO7A-related Usher syndrome. This frequency is higher than would be expected for an autosomal recessive condition based on the thresholds defined by the ClinGen Hearing Loss Expert Panel.

Not Met criteria codes

PP3			REVEL score is 0.734, which is >0.7 threshold. After expert discussion, not applied because it is conflicting with case level and frequency data.
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Curation History [↗](#)



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