

Variant: *NM_000260.4(MYO7A):c.3491G>A (p.Arg1164Gln)*

Version: 1.1

CA6198071 [↗](#)

229012 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: 7eb4b5cf-80fd-4791-b09c-9e683db74a34

Approved on: 2024/3/28

Published on: 2024/3/28

HGVS expressions

NM_000260.4(MYO7A):c.3491G>A (p.Arg1164Gln)

NM_000260.4:c.3491G>A

NC_000011.10:g.77184703G>A

CM000673.2:g.77184703G>A

NC_000011.9:g.76895748G>A

CM000673.1:g.76895748G>A

NC_000011.8:g.76573396G>A

NG_009086.1:g.61439G>A

NG_009086.2:g.61458G>A

ENST00000409709.9:c.3491G>A

ENST00000409893.6:c.1556G>A

ENST00000670577.1:c.1332G>A

ENST00000409619.6:c.3458G>A

ENST00000409709.7:c.3491G>A

ENST00000409893.5:c.3491G>A

ENST00000458169.2:c.1034G>A

ENST00000458637.6:c.3491G>A

ENST00000467137.1:n.18G>A

ENST00000481328.7:n.1034G>A

ENST00000620575.4:c.3500G>A

NM_000260.3:c.3491G>A

NM_001127179.2:c.3491G>A

NM_001127180.1:c.3491G>A

NM_001127180.2:c.3491G>A

NM_001369365.1:c.3458G>A

Uncertain Significance

Met criteria codes **2**

PP3

PM2_Supporting

Not Met criteria codes **2**

PP4

PM3

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

Evidence submitted by expert panel

Hearing Loss VCEP

The c.3491G>A variant in MYO7A is a missense variant predicted to cause substitution of arginine by glutamine at amino acid 1164 (p.Arg1164Gln). The highest population filtering allele frequency with a confidence interval of 0.95 in gnomAD v4 is 0.00001446 (4/89272 alleles) in the South Asian 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 0.935, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3). In summary, this variant meets the criteria to be classified as uncertain significance for autosomal recessive Usher syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PM2_P, PP3. (ClinGen Hearing Loss VCEP specifications version 2, 01.17.2024)

Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.935, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3).
PM2_Supporting			The highest population filtering allele frequency with a confidence interval of 0.95 in gnomAD v4 is 0.00001446 (4/89272 alleles) in the South Asian 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

PP4			Not met due to possible alternate cause of RP in proband from LMM.
PM3			LMM reported this variant in 1 individual with hearing loss and RP (SCV000272160.2). The variant was in trans with a second missense variant that was pathogenic/likely pathogenic in ClinVar. NGS indicated that the two MYO7A variants are present in trans configuration. In addition, this individual is reported to have LCHAD, which may explain the RP (Tyni 1998).

Curation History [↗](#)



▼

▼

Showing 1 to 2 of 2 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.