

Variant: *NM_000260.4(MYO7A):c.631A>G (p.Ser211Gly)*

Version: 2.0

CA278707 [↗](#)

43325 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: fe99b50b-ba3f-4ebf-9816-12fa2f37b939

Approved on: 2024/5/1

Published on: 2024/7/2

HGVS expressions

NM_000260.4(MYO7A):c.631A>G (p.Ser211Gly)

NM_000260.4:c.631A>G

NC_000011.10:g.77156900A>G

CM000673.2:g.77156900A>G

NC_000011.9:g.76867946A>G

CM000673.1:g.76867946A>G

NC_000011.8:g.76545594A>G

NG_009086.1:g.33637A>G

NG_009086.2:g.33655A>G

ENST00000409709.9:c.631A>G

ENST00000409619.6:c.598A>G

ENST00000409709.7:c.631A>G

ENST00000409893.5:c.631A>G

ENST00000458637.6:c.631A>G

ENST00000620575.4:c.631A>G

NM_000260.3:c.631A>G

NM_001127179.2:c.631A>G

NM_001127180.1:c.631A>G

NM_001127180.2:c.631A>G

NM_001369365.1:c.598A>G

Pathogenic

Met criteria codes **4**

PM3_Very Strong

PP3

PP4

PM2_Supporting

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.631A>G variant in MYO7A is a missense variant predicted to cause substitution of serine by glycine at amino acid 211 (p.Ser211Gly). The highest population minor allele frequency in gnomAD v4.1.0 is 0.005% (62/1179900 alleles) in the European non-Finnish population, which is lower than the ClinGen Hearing Loss threshold (<0.007%) for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.957, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3). This variant has been detected in at least 7 individuals with clinical features or a diagnosis of Usher syndrome. Of those individuals, 2 were homozygous, and 5 were compound heterozygous for the variant and a pathogenic or likely pathogenic variant (4.5 PM3 points, PMID:25472526 and 37466950, Laboratory for Molecular Medicine internal data, SCV000059882.6). At least one patient with this variant displayed congenital profound sensorineural hearing loss, retinitis pigmentosa, and vestibular dysfunction, which is highly specific for Usher syndrome type 1 (PP4). In summary, this variant meets the criteria to be classified as Pathogenic for autosomal recessive Usher syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PM2_Supporting, PP3, PM3_VeryStrong, PP4. ClinGen Hearing Loss VCEP specifications version 2.0.0; 04.17.24.

Met criteria codes

PM3_Very Strong			4.5 points total from Zhao 2015 (PMID: 25472526), Stephenson 2023 (PMID: 37466950) and internal evidence from LMM.
PP3			REVEL score 0.957. Alamut does not predict an impact to splicing. Entirely conserved in UCSC database.
PP4			Both LMM probands and the published proband had a combination of SNHL and RP.
PM2_Supporting			gnomAD - groupmax FAF 0.004% (62/1179900) European non-Finnish. PM2_Supporting

Curation History



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