The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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:c.631A>G
NM_000260.4(MYO7A):c.631A>G (p.Ser211Gly)
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 | PM2_Supporting | PP3 | PP4

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**

Evidence submitted by expert panel

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.
PM2_Supporting	✔	gnomAD - groupmax FAF 0.004% (62/1179900) European non-Finnish. PM2_Supporting
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.

Curation History

Showing 1 to 4 of 4 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000260.4(MYO7A):c.631A>G (p.Se...	Pathogenic	Usher Syndrome	2024-07-02	2.0	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	MYO7A
View	NM_000260.4(MYO7A):c.631A>G (p.Se...	Likely Pathogenic	Usher Syndrome	2020-05-12	1.2	-	MYO7A
View	NM_000260.4(MYO7A):c.631A>G (p.Se...	Likely Pathogenic	Usher Syndrome	2020-05-12	1.1	-	MYO7A
View	NM_000260.4(MYO7A):c.631A>G (p.Se...	Likely Pathogenic	Usher Syndrome	2020-05-12	1.0	-	MYO7A

Showing 1 to 4 of 4 rows

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