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.1208A>G (p.Tyr403Cys)

Version: 1.1

CA278736

178667 (ClinVar)

Gene: MYO7A (HGNC:4647)
Condition: Usher syndrome (MONDO:0019501)
Inheritance Mode: Autosomal recessive inheritance
UUID: 6c14c3d8-0f17-4a22-90e6-a7d1b5164306
Approved on: 2022/12/21
Published on: 2023/2/6

HGVS expressions

NM_000260.4:c.1208A>G
NM_000260.4(MYO7A):c.1208A>G (p.Tyr403Cys)
NC_000011.10:g.77160980A>G
CM000673.2:g.77160980A>G
NC_000011.9:g.76872026A>G
CM000673.1:g.76872026A>G
NC_000011.8:g.76549674A>G
NG_009086.1:g.37717A>G
NG_009086.2:g.37735A>G
ENST00000409709.9:c.1208A>G
ENST00000409619.6:c.1175A>G
ENST00000409709.7:c.1208A>G
ENST00000409893.5:c.1208A>G
ENST00000458637.6:c.1208A>G
ENST00000620575.4:c.1208A>G
NM_000260.3:c.1208A>G
NM_001127179.2:c.1208A>G
NM_001127180.1:c.1208A>G
NM_001127180.2:c.1208A>G
NM_001369365.1:c.1175A>G

Likely Pathogenic

Met criteria codes 5

PP1 PP3 PP4 PM3 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

Evidence submitted by expert panel

Hearing Loss VCEP

The NM_000260.4:c.1208A>G variant in the MYO7A gene is a missense variant predicted to cause substitution of tyrosine to cysteine at amino acid 403 (p.Tyr403Cys).The highest population minor allele frequency in gnomAD v2.1.1 is 0.006% (1/15398 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (<0.007%) for PM2_Supporting. The computational predictor REVEL gives a score of 0.941, evidence that correlates with impact to MYO7A function (PP3). This variant has been identified in 1 individual with clinical features consistent with Usher syndrome who harbored a pathogenic variant, c.6326C>T (p.Thr2109Ile), in trans. These variants segregated in a similarly affected sibling (SCV000205114.4) (PM3, PP1, PP4). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive Usher syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss Variant Curation Expert Panel: (PM3, PM2_Supporting, PP1, PP3, PP4). (VCEP specifications version 2.0.0; December 21, 2022)

Met criteria codes

PP1	✔	1 segregation in a family affected with profound hearing loss and retinitis pigmentosa who carried another variant (VCV000164724.1) in trans (SCV000199631.4, LMM internal evidence: 1 proband & 1 affected sibling: In trans with Thr2109Ile (Likely Path by VCEP) in a proband with congenital, profound SNHL and retinitis pigmentosa. These variants segregated in a sibling with similar features)
PP3	✔	REVEL: .941
PP4	✔	2 affected siblings with profound hearing loss and retinitis pigmentosa who carried another variant (VCV000164724.1) in trans (SCV000199631.4, LMM internal evidence: 1 proband & 1 affected sibling: In trans with Thr2109Ile (Likely Path by VCEP) in a proband with congenital, profound SNHL and retinitis pigmentosa. These variants segregated in a sibling with similar features.
PM3	✔	LMM internal evidence: 1 proband & 1 affected sibling: In trans with Thr2109Ile (Likely Path by VCEP) in a proband with congenital, profound SNHL and retinitis pigmentosa. These variants segregated in a sibling with similar features
PM2_Supporting	✔	[12.21.2022] 0.00006 in European non-Finnish in gnomAD v.2.1.1 [Previous] Present in .0064% (1/15398) of European non-Finnish alleles in gnomAD

Curation History

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000260.4(MYO7A):c.1208A>G (p.T...	Likely Pathogenic	Usher Syndrome	2023-02-06	1.1	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.1208A>G (p.T...	Likely Pathogenic	Usher Syndrome	2019-11-26	1.0	-	MYO7A

Showing 1 to 2 of 2 rows

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