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.5804T>C (p.Leu1935Pro)

Version: 1.3

CA278691

43298 (ClinVar)

Gene: MYO7A (HGNC:4647)
Condition: Usher syndrome (MONDO:0019501)
Inheritance Mode: Autosomal recessive inheritance
UUID: 1f484128-351e-49bd-a7a1-877c462ffac6
Approved on: 2024/9/24
Published on: 2024/9/27

HGVS expressions

NM_000260.4:c.5804T>C
NM_000260.4(MYO7A):c.5804T>C (p.Leu1935Pro)
NC_000011.10:g.77207350T>C
CM000673.2:g.77207350T>C
NC_000011.9:g.76918395T>C
CM000673.1:g.76918395T>C
NC_000011.8:g.76596043T>C
NG_009086.1:g.84086T>C
NG_009086.2:g.84105T>C
ENST00000409709.9:c.5804T>C
ENST00000670577.1:c.3631T>C
ENST00000409619.6:c.5657T>C
ENST00000409709.7:c.5804T>C
ENST00000458169.2:c.3230T>C
ENST00000458637.6:c.5690T>C
ENST00000481328.7:n.3340T>C
ENST00000605744.1:n.718T>C
NM_000260.3:c.5804T>C
NM_001127180.1:c.5690T>C
NM_001127180.2:c.5690T>C
NM_001369365.1:c.5657T>C

Likely Pathogenic

Met criteria codes 4

PP3 PP4 PM2_Supporting PM3_Strong

Not Met criteria codes 3

BA1 BS1 BP4

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.5804T>C variant in MYO7A is a missense variant predicted to cause substitution of leucine by proline at amino acid 1935 (p.Leu1935Pro). The highest population minor allele frequency in gnomAD v4.1 is 0.00002204 (26/1179460 alleles) in the European (non-Finnish) 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 0.961, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3). This variant has been detected in 2 individuals with autosomal recessive Usher syndrome. Both were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and both of those were confirmed in trans by family testing (2 PM3 points, SCV001239772.1, SCV000059855.6, Blueprint Genetics, Laboratory for Molecular Medicine) (PM3_Strong). At least one patient with this variant displayed sensorineural hearing loss with retinitis pigmentosa, which is highly specific for autosomal recessive Usher syndrome (PP4, SCV000059855.6, Laboratory for Molecular Medicine). 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 VCEP: PM3_Strong, PM2_Supporting, PP3, PP4. (ClinGen Hearing Loss VCEP specifications version 2; 9/24/2024)

Met criteria codes

PP3	✔	The computational predictor REVEL gives a score of 0.961, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3).
PP4	✔	At least one patient with this variant displayed hearing loss and retinitis pigmentosa, which is highly specific for Usher syndrome (PP4, PMIDs, Laboratory for Molecular Medicine, Blueprint Genetics, SCV000059855.6, SCV001239772.1).
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1 is 0.00002204 (26/1179460 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (≤0.00007) for PM2_Supporting, meeting this criterion (PM2_Supporting).
PM3_Strong	✔	This variant has been detected in 2 individuals with Usher syndrome. Of those individuals, both were compound heterozygous for the variant and a pathogenic or likely pathogenic variant and both of those were confirmed in trans by family testing (2 PM3 points, PMIDs, Laboratory for Molecular Medicine, Blueprint Genetics, SCV000059855.6, SCV001239772.1)(PM3_Strong).

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_000260.4(MYO7A):c.5804T>C (p.L...	Likely Pathogenic	Usher Syndrome	2024-09-27	1.3	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.5804T>C (p.L...	Likely Pathogenic	Usher Syndrome	2024-09-27	1.2	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.5804T>C (p.L...	Likely Pathogenic	Usher Syndrome	2024-09-24	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.5804T>C (p.L...	Likely Pathogenic	Usher Syndrome	2020-06-29	1.0	-	MYO7A

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