

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(MYO7A):c.5804T>C (p.Leu1935Pro)

NM_000260.4:c.5804T>C

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

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				
Showing 1 to 4 of 4 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.