

Variant: *NM\_000260.4(MYO7A):c.6326C>T (p.Thr2109Ile)*

Version: 1.1

CA278724 [↗](#)

164724 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal recessive inheritance

**UUID:** a0970228-dea0-44d1-aa6d-d35746a8cff7

**Approved on:** 2023/1/18

**Published on:** 2023/2/6

### HGVS expressions

**NM\_000260.4(MYO7A):c.6326C>T (p.Thr2109Ile)**

**NM\_000260.4:c.6326C>T**

NC\_000011.10:g.77211909C>T

CM000673.2:g.77211909C>T

NC\_000011.9:g.76922954C>T

CM000673.1:g.76922954C>T

NC\_000011.8:g.76600602C>T

NG\_009086.1:g.88645C>T

NG\_009086.2:g.88664C>T

ENST00000409709.9:c.6326C>T

ENST00000670577.1:c.4127C>T

ENST00000409619.6:c.6179C>T

ENST00000409709.7:c.6326C>T

ENST00000458169.2:c.3752C>T

ENST00000458637.6:c.6212C>T

ENST00000481328.7:n.3862C>T

ENST00000526863.2:n.26-636C>T

ENST00000605744.1:n.1793C>T

NM\_000260.3:c.6326C>T

NM\_001127180.1:c.6212C>T

NM\_001127180.2:c.6212C>T

NM\_001369365.1:c.6179C>T

**Likely Pathogenic**

**Met criteria codes** **5**

PP1\_Moderate

PM3\_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 variant NM\_000260.4:c.6326C>T in MYO7A is a missense variant predicted to cause substitution of threonine by isoleucine at amino acid 2109 (p.Thr2109Ile). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00006 (8/128408 alleles, 0 homozygotes) for the European (Non-Finnish) population, which meets PM2\_supporting criteria. The REVEL computational prediction analysis tool produced a score of 0.821, meeting PP3 criteria. This variant has been reported in two unrelated probands, both with Usher syndrome (PP4; SCV000199631.4). In addition, both probands had an additional MYO7A pathogenic or likely pathogenic variant in trans, meeting PM3\_Strong criteria. Finally, the variant was shown to segregate with two affected family members (PP1\_Moderate). In summary, the variant meets criteria to be classified as likely pathogenic for AR Usher syndrome. ACMG/AMP criteria met, as specified by the ClinGen Hearing Loss VCEP: PM2\_supporting, PP3, PP4, PM3\_Strong, PP1\_Moderate (ClinGen Hearing Loss VCEP specifications version 2; 1/18/2023).

Met criteria codes

|                |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                |
|----------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PP1_Moderate   |    |    | Variant and likely path/path variant (VCV000043313.2 ) segregated in two affected family members (SCV000199631.4).                                                                                                                                                                                                                                                             |
| PM3_Strong     |    |    | Two probands with clinical features of Usher syndrome carried the variant (VCV000043313.2) in trans with likely path/path variants (SCV000199631.4). (2 PM3 pts.) Proband with congenital progressive profound sensorineural hearing loss and retinitis pigmentosa also carried a variant of uncertain significance (VCV000178667.1) in trans (SCV000199631.4). (.25 PM3 pts.) |
| PP3            |  |  | REVEL: .821                                                                                                                                                                                                                                                                                                                                                                    |
| PP4            |  |  | Proband with congenital progressive profound sensorineural hearing loss and retinitis pigmentosa (SCV000199631.4).                                                                                                                                                                                                                                                             |
| PM2_Supporting |  |  | The MAF in GnomAD is 0.00006 (8/128408 alleles), which is below the threshold of 0.00007 set by the HL VCEP to met PM2_Supporting criteria.                                                                                                                                                                                                                                    |

Curation History 



 

 

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