

Variant: *NM_000260.4(MYO7A):c.1183C>T (p.Arg395Cys)*

Version: 1.1

CA6197402 [↗](#)

555138 (ClinVar) [↗](#)

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

Condition: nonsyndromic genetic deafness ([MONDO:0019497](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 55512a59-1ed0-41e4-80d2-be897c90cfe6

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HGVS expressions

NM_000260.4(MYO7A):c.1183C>T (p.Arg395Cys)

NM_000260.4:c.1183C>T

NC_000011.10:g.77160265C>T

CM000673.2:g.77160265C>T

NC_000011.9:g.76871311C>T

CM000673.1:g.76871311C>T

NC_000011.8:g.76548959C>T

NG_009086.1:g.37002C>T

NG_009086.2:g.37020C>T

ENST00000409709.9:c.1183C>T

ENST00000409619.6:c.1150C>T

ENST00000409709.7:c.1183C>T

ENST00000409893.5:c.1183C>T

ENST00000458637.6:c.1183C>T

ENST00000620575.4:c.1183C>T

NM_000260.3:c.1183C>T

NM_001127179.2:c.1183C>T

NM_001127180.1:c.1183C>T

NM_001127180.2:c.1183C>T

NM_001369365.1:c.1150C>T

Likely Pathogenic

Met criteria codes **3**

PP1_Strong

PP3

PM3

Not Met criteria codes **5**

BP4

PP4

PM2

BA1

BS1

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.1183C>T variant in MYO7A is a missense variant predicted to cause substitution of arginine by cysteine at amino acid 395. The highest population minor allele frequency in gnomAD v4.1 is 0.00008472 (2/23608 alleles) in the South Asian population. (PM2_Supporting, BS1, and BA1 are not met). The computational predictor REVEL gives a score of 0.773, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3). This variant has been detected in 6 individuals with nonsyndromic genetic hearing loss. Out of 3 of those individuals, 1 was compound heterozygous for the variant and a pathogenic or likely pathogenic variant for Usher syndrome and none of those were confirmed in trans (c.401T>A (p.Ile134Asn), 0 PM3 points, SCV: SCV001232108.5, Invitae). The other 2 were compound heterozygous for the variant and a variant of uncertain significance for nonsyndromic genetic hearing loss, 1 of them was confirmed in trans by family testing (0.25 PM3 points, c.1496T>C (p.Ile499Thr); c.1496T>C(p.Ile499Thr), PMIDs: 34416374, 34979615). 3 individuals were homozygous for the variant (1 PM3 point, PMIDs: 23770805, 27573290, ClinVar SCV: SCV001232108.5, Invitae) (PM3). The variant has been reported to segregate with nonsyndromic genetic hearing loss in 8 affected family members from 3 families (PP1_Strong; PMIDs: 23770805, 27573290, 34979615). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal recessive nonsyndromic genetic hearing loss based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PP1_Strong, PM3, PP3. (ClinGen Hearing Loss VCEP specifications version 2; 7/23/2024)

Met criteria codes

PP1_Strong			The variant has been reported to segregate with nonsyndromic genetic hearing loss in 8 affected family members from 3 families (PP1_Strong; PMIDs: 23770805, 27573290, 34979615).
PP3			The computational predictor REVEL gives a score of 0.773, which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3).
PM3			This variant has been detected in 6 individuals with nonsyndromic genetic hearing loss. Out of 3 of those individuals, 1 was compound heterozygous for the variant and a pathogenic or likely pathogenic variant for Usher syndrome and none of those were confirmed in trans (c.401T>A (p.Ile134Asn), 0 PM3 points, SCV: SCV001232108.5, Invitae). The other 2 were compound heterozygous for the variant and a variant of uncertain significance for nonsyndromic genetic hearing loss, 1 of them was confirmed in trans by family testing (0.25 PM3 points, c.1496T>C (p.Ile499Thr); c.1496T>C(p.Ile499Thr), PMIDs: 34416374, 34979615). 3 individuals were homozygous for the variant (1 PM3 point, PMIDs: 23770805, 27573290, ClinVar SCV: SCV001232108.5, Invitae) (PM3).

Not Met criteria codes

BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4			No ophthalmologic testing performed on Shahzad family and Naz family was specifically noted to not have RP
PM2			The highest population minor allele frequency in gnomAD v4.1 is 0.00008472 (2/23608 alleles) in the South Asian population. (PM2_Supporting, BS1, and BA1 are not met).
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

Curation History

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