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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
Approved on: 2024/9/24
Published on: 2024/9/27

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 PM3 PP3

Not Met criteria codes 5
PM2 BA1 BS1 BP4 PP4

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.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).
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).
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).

Not Met criteria codes

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

PP4	ℹ	✖	No ophthalmologic testing performed on Shahzad family and Naz family was specifically noted to not have RP

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.1183C>T (p.Ar...	Likely Pathogenic	Nonsyndromic Genetic Deafness	2024-09-27	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.1183C>T (p.Ar...	Likely Pathogenic	Nonsyndromic Genetic Deafness	2020-10-20	1.0	-	MYO7A

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