

Variant: *NM_000260.4(MYO7A):c.1817G>A (p.Arg606His)*

CA6197622 [↗](#)

517357 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: afa3b665-0c01-40e2-9432-4938ce1c8bff

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HGVS expressions

NM_000260.4(MYO7A):c.1817G>A (p.Arg606His)

NM_000260.4:c.1817G>A

NC_000011.10:g.77172767G>A

CM000673.2:g.77172767G>A

NC_000011.9:g.76883813G>A

CM000673.1:g.76883813G>A

NC_000011.8:g.76561461G>A

NG_009086.1:g.49504G>A

NG_009086.2:g.49522G>A

ENST00000409709.9:c.1817G>A

ENST00000669443.1:c.181G>A

ENST00000409619.6:c.1784G>A

ENST00000409709.7:c.1817G>A

ENST00000409893.5:c.1817G>A

ENST00000458637.6:c.1817G>A

ENST00000620575.4:c.1817G>A

NM_000260.3:c.1817G>A

NM_001127179.2:c.1817G>A

NM_001127180.1:c.1817G>A

NM_001127180.2:c.1817G>A

NM_001369365.1:c.1784G>A

Uncertain Significance

Met criteria codes **2**

PP3 PM3

Not Met criteria codes **24**

PS2 PS4 PS3 PS1 BA1 PP4
PP1 PP2 PM1 PM4 PM5
PM6 PM2 BS4 BS3 BS1
BS2 BP5 BP7 BP2 BP3 BP1
BP4 PVS1

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

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Hearing Loss VCEP

The c.1817 G>A (NM_000260.4(MYO7A):c.1817G>A (p.Arg606His)) variant in MYO7A is a missense variant predicted to cause substitution of Arginine by Histidine at amino acid 606. The highest major allele frequency in gnomAD v2.1.1 is 0.00035 (0.035 % or 8/23092 alleles) in the South Asian population (PM2_supporting, BS1, and BA1 not met). The computational predictor REVEL gives a score of 0.832, (which is above the threshold of 0.7), evidence that correlates with impact to MYO7A function (PP3). This variant has been detected in at least one individual with autosomal recessive nonsyndromic genetic hearing loss. This proband was compound heterozygous for the variant and a pathogenic variant, confirmed in trans by parental testing (PM3; 1.0 point; LMM Internal Data). The patient with this variant displayed moderate to severe sensorineural hearing loss, although no vision anomalies or difficulty seeing at night were noted (PP4 not met; LMM Internal Data). In summary, this variant meets the criteria to be classified as uncertain significance for autosomal recessive nonsyndromic genetic deafness, based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: (PP3, PM3; Version 2, 7.19.2023).

Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.832, (which is above the threshold of 0.7, evidence that correlates with impact to MYO7A function (PP3).
PM3			This variant has been detected in at least one individual with autosomal recessive nonsyndromic genetic hearing loss. This proband was compound heterozygous for the variant and a pathogenic variant, confirmed in trans by parental testing (PM3; 1.0 point; LMM Internal Data).

Not Met criteria codes

PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4			The patient had congenital progressive moderately severe to severe sensorineural hearing loss and delayed walking. The proband was 16 at time of testing, and had normal eye exam and could see reasonably at night (LMM internal data; PP4 not met).
PP1			

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline			
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2		✖	The highest major allele frequency in gnomAD v2.1.1 is 0.00035 (0.035 % or 8/23092 alleles) in the South Asian population (PM2_supporting, BS1, BA1 not met).
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	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
BS2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

