Variant: NM_016239.4(MYO15A):c.1111C>A (p.Pro371Thr)

Version: 1.0

CA8423023

423766 (ClinVar)

Gene: MYO15A (HGNC:51168)
Condition: nonsyndromic genetic deafness (MONDO:0019497)
Inheritance Mode: Autosomal recessive inheritance
UUID: c10734bd-038d-455b-87da-5aa88d185437
Approved on: 2021-05-13
Published on: 2022-05-13

HGVS expressions

NM_016239.4:c.1111C>A
NM_016239.4(MYO15A):c.1111C>A (p.Pro371Thr)
NC_000017.11:g.18119911C>A
CM000679.2:g.18119911C>A
NC_000017.10:g.18023225C>A
CM000679.1:g.18023225C>A
NC_000017.9:g.17963950C>A
NG_011634.1:g.16206C>A
NG_011634.2:g.16206C>A
ENST00000647165.2:c.1111C>A
ENST00000205890.9:c.1111C>A
ENST00000583079.1:n.744C>A
ENST00000615845.4:c.1111C>A
NM_016239.3:c.1111C>A

Likely Benign

Met criteria codes 2
BP4 BS1_Supporting

Not Met criteria codes 2
PM3 BS2

Evidence Links 0

Expert Panel
Hearing Loss VCEP

Criteria Specification Information
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hearing Loss VCEP

The c.1111C>A (p.Pro371Thr) variant in MYO15A was present in 0.208% (lower bound of the 95% CI of 295/128,454) of non-Finnish European alleles in gnomAD v2.1, which is a higher frequency than would be expected for an autosomal recessive pathogenic variant based on the thresholds defined by the ClinGen Hearing Loss Expert Panel (BS1_Supporting). Conservation analyses suggest that this variant may not impact the protein (BP4). In summary, the p.Pro371Thr variant in MYO15A variant meets criteria to be considered likely benign. ACMG/AMP criteria applied, as specified by the Hearing Loss Expert Panel: BS1_Supporting, BP4.

Met criteria codes

BP4	✔	REVEL 0.147. Not predicted to impact splicing. Thr is present in 1 animal (alligator) in the UCSC database. 10 other animals had different changes.
BS1_Supporting	✔	Present in 0.2297% (295/128,454) of non-Finnish European alleles in gnomAD v2 (lower bound of 95% CI = 0.2081%). Present in 0.2602% (177/68,012) of non-Finnish European alleles in gnomAD v3.

Not Met criteria codes

PM3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	✖	This variant was seen in the homozygous state in 1 reportedly healthy adult, however the reason for genetic testing was not a diagnosis of hearing loss, so there was no information on their hearing (GeneDx internal data, ClinVar SCV000573503.3). This variant has also been observed in the heterozygous state in individuals with hearing loss without a second variant in MYO15A (PMID: 29309402, GeneDx internal data ClinVar SCV000573503.3, CeGaT Praxis fuer Humangenetik Tuebingen internal data ClinVar SCV001246433.4).

Curation History

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