Variant: NM_206933.4(USH2A):c.1966G>A (p.Asp656Asn)

Version: 1.1

CA143431

48481 (ClinVar)

Gene: USH2A (HGNC:7399)
Condition: Usher syndrome (MONDO:0019501)
Inheritance Mode: Autosomal recessive inheritance
UUID: a5c58407-b571-46b2-b787-30711d1fd9f3
Approved on: 2025-06-18
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HGVS expressions

NM_206933.4:c.1966G>A
NM_206933.4(USH2A):c.1966G>A (p.Asp656Asn)
NC_000001.11:g.216289285C>T
CM000663.2:g.216289285C>T
NC_000001.10:g.216462627C>T
CM000663.1:g.216462627C>T
NC_000001.9:g.214529250C>T
NG_009497.1:g.139112G>A
NG_009497.2:g.139164G>A
ENST00000307340.8:c.1966G>A
ENST00000674083.1:c.1966G>A
ENST00000307340.7:c.1966G>A
ENST00000366942.3:c.1966G>A
NM_007123.5:c.1966G>A
NM_206933.2:c.1966G>A
NM_206933.3:c.1966G>A
NM_007123.6:c.1966G>A

Likely Benign

Met criteria codes 2
BS1_Supporting BP4

Not Met criteria codes 4
PP3 BA1 PM2 PM3

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 allele frequency of the c.1966G>A (p.Asp656Asn) variant in USH2A is 0.09251% (1246/1613836 CI 95%) of European (Non Finnish) alleles in gnomAD v4, 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). The variant has been identified in 3 probands with hearing loss and 2 probands with Usher syndrome (SCV000065500.6; PMID: 16963483); however an alternate cause of hearing loss in other genes was identified in 3 probands (SCV000065500.6), and a second variant in USH2A was not identified in the other two probands (SCV000065500.6; PMID: 16963483). Finally, in the last proband, another likely benign variant was identified with phasing unknown (SCV000065500.6). Altogether, this evidence does not meet the criteria set to apply PM3_Supporting. Additionally, computational prediction analysis using the metapredictor tool REVEL suggests that the variant may not impact the protein (BP4). In summary, the c.1966G>A (p.Asp656Asn) variant meets criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the Hearing Loss Expert Panel: BS1_Supporting, BP4.

Met criteria codes

BS1_Supporting	ℹ	✔	This variant is present in 0.09251% (1246/1613836 CI 95%) non-Finnish European alleles in gnomAD v4
BP4	ℹ	✔	This variant has a REVEL score of 0.073

Not Met criteria codes

PP3	ℹ	✖	BP4
BA1	ℹ	✖	BS1_P
PM2		✖	BS1_P
PM3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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