Variant: NM_022124.6(CDH23):c.2959G>A (p.Asp987Asn)

Version: 1.0

CA5544406

1036903 (ClinVar)

Gene: CDH23 (HGNC:64072)
Condition: nonsyndromic genetic deafness (MONDO:0019497)
Inheritance Mode: Autosomal recessive inheritance
UUID: 3416d7b1-0fe1-4322-9212-25dc08cd6bbe
Approved on: 2025-10-08
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HGVS expressions

NM_022124.6:c.2959G>A
NM_022124.6(CDH23):c.2959G>A (p.Asp987Asn)
NC_000010.11:g.71706902G>A
CM000672.2:g.71706902G>A
NC_000010.10:g.73466659G>A
CM000672.1:g.73466659G>A
NC_000010.9:g.73136665G>A
NG_008835.1:g.314956G>A
ENST00000224721.12:c.2959G>A
ENST00000398809.9:c.2959G>A
ENST00000442677.4:c.2959G>A
ENST00000466757.8:c.2390G>A
ENST00000224721.10:c.2974G>A
ENST00000299366.11:c.2959G>A
ENST00000398809.8:c.2959G>A
ENST00000442677.3:c.1734G>A
ENST00000466757.7:c.2390G>A
ENST00000616684.4:c.2959G>A
ENST00000622827.4:c.2959G>A
NM_001171930.1:c.2959G>A
NM_001171931.1:c.2959G>A
NM_022124.5:c.2959G>A
NM_001171930.2:c.2959G>A
NM_001171931.2:c.2959G>A

Uncertain Significance

Met criteria codes 2

PM3 PM2_Supporting

Not Met criteria codes 4

BS1 BP4 PP3 BA1

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 NM_022124.6(CDH23):c.2959G>A variant in the CDH23 gene is a missense variant predicted to cause the substitution of aspartic acid vy asparagine at amino acid 987. This variant has been reported in 1 proband with apparently isolated hearing loss. This individual is compound heterozygous for the variant and a pathogenic variant confirmed in trans by family testing (PMID : 26226137)(PM3). An additional patient with isolated HL at the age of 28 y.o have been reported, in association with another missense of unknown significance (phase unknown, PMID : 38855775). The allele frequency of this variant is 0.001% (3/58080) of Admixed American chromosomes by gnomAD v.4, which is lower than the thresholds defined by the ClinGen Hearing Loss Expert Panel for PM2_Supporting, meeting this criterion (PM2_Supporting). The computational predictor REVEL gives a score of 0.48, which is neither above nor below the thresholds predicting a damaging or benign impact on CDH23 function. In summary, this variant has been classified as a variant of uncertain significance for autosomal recessive hearing loss based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PM2_P, PM3 (ClinGen Hearing Loss VCEP specifications version 2; 10/8/2025).

Met criteria codes

PM3	✔	This variant has been reported in 1 proband with apparently isolated hearing loss. This individual is compound heterozygous for the variant and the c.3628C>T - (p.Gln1210Ter) pathogenic variant, confirmed in trans by family testing
PM2_Supporting	✔	The allele frequency of this variant is 0.001% (3/58080) of Admixed American chromosomes by gnomAD v.4, which is lower than the thresholds defined by the ClinGen Hearing Loss Expert Panel for PM2_Supporting, meeting this criterion (PM2_Supporting).

Not Met criteria codes

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
PP3	✖	The computational predictor REVEL gives a score of 0.48, which is neither above nor below the thresholds predicting a damaging or benign impact on CDH23 function.
BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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