

Variant: *NM_022124.6(CDH23):c.9569C>T (p.Ala3190Val)*

Version: 1.1

CA137643 [↗](#)

46076 (ClinVar) [↗](#)

Gene: CDH23 ([HGNC:64072](#))

Condition: Usher syndrome ([MONDO:0019501](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 7f246a3f-3877-4e1c-b536-a8da21fcd3b6

Approved on: 2023/11/15

Published on: 2024/4/1

HGVS expressions

NM_022124.6:c.9569C>T

NM_022124.6(CDH23):c.9569C>T (p.Ala3190Val)

NC_000010.11:g.71812826C>T

CM000672.2:g.71812826C>T

NC_000010.10:g.73572583C>T

CM000672.1:g.73572583C>T

NC_000010.9:g.73242589C>T

NG_008835.1:g.420880C>T

ENST00000224721.12:c.9569C>T

ENST00000642965.1:c.3502C>T

ENST00000647092.1:c.3166C>T

ENST00000224721.10:c.9584C>T

ENST00000398788.4:c.2849C>T

ENST00000475158.1:n.3105C>T

ENST00000619887.4:c.2849C>T

ENST00000622827.4:c.9569C>T

NM_001171933.1:c.2849C>T

NM_001171934.1:c.2849C>T

NM_001171935.1:c.260C>T

NM_001171936.1:c.260C>T

NM_022124.5:c.9569C>T

Uncertain Significance

Met criteria codes **2**

PP3 BS2

Not Met criteria codes **4**

PP4 PM2 PM3 BS1

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

Hearing Loss VCEP

The c.9569C>T variant (NM_022124.6(CDH23):c.9569C>T (p.Ala3190Val)) in CDH23 is a missense variant predicted to cause substitution of alanine by valine at amino acid 3190 (p.Ala3190Val). The highest minor allele frequency in gnomAD v4.0.0 is 694/1179698 alleles (0.0005517), in the European (non-Finnish) population (no population codes met). This variant has been observed in a homozygous state in one parent reported to have no features of Usher syndrome (BS2; Invitae internal data; ClinVar SCV001110059.2). The computational predictor REVEL gives a score of 0.836, which is above the Hearing Loss VCEP threshold of 0.7, evidence that correlates with impact to CDH23 function (PP3). The variant was found in a compound heterozygous state with a deletion of exon 29, a variant which was not able to be confirmed by aCGH (PMID: 25404053). The variant was also found in an unknown phase with p.Arg3206Cys (c.9616C>T), a variant of uncertain significance, in an affected patient with nonsyndromic hearing loss (PMID: 27068579; PM3 not met). In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss Expert Panel: BS2, PP3 (Version 2; 11/15/2023).

Met criteria codes

PP3			The computational predictor REVEL gives a score of 0.836, which is above the Hearing Loss VCEP threshold of 0.7, evidence that correlates with impact to CDH23 function (PP3). Nucleotide is very well-conserved among 100 vertebrates in UCSC database. Variant is not predicted to impact splicing according to splice AI scores.
BS2			This variant has been observed in a homozygous state in one parent reported to have no features of Usher Syndrome (BS2; Invitae internal data; ClinVar SCV001110059.2).

Not Met criteria codes

PP4			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 v4.0.0 is is 694/1179698 (0.0005883) in the European (non-Finnish) population (no population codes met).
PM3			The variant was found in a compound heterozygous state with a deletion of exon 29, a variant which was not confirmed. The variant was also found in an unknown phase with p.Arg3206Cys (c.9616C>T), a variant of uncertain significance, in an affected patient with nonsyndromic hearing loss (PM3 not met).
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline



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