

Variant: *NM_022124.6(CDH23):c.902G>A (p.Arg301Gln)*

Version: 1.2

CA239352 [↗](#)

4929 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: d6cbe7a7-85b2-4f00-9283-cb95a511be9c

Approved on: 2020/11/2

Published on: 2020/11/2

HGVS expressions

NM_022124.6(CDH23):c.902G>A (p.Arg301Gln)

NM_022124.6:c.902G>A

NC_000010.11:g.71615573G>A

CM000672.2:g.71615573G>A

NC_000010.10:g.73375330G>A

CM000672.1:g.73375330G>A

NC_000010.9:g.73045336G>A

NG_008835.1:g.223627G>A

ENST00000224721.12:c.902G>A

ENST00000398809.9:c.902G>A

ENST00000442677.4:c.902G>A

ENST00000466757.8:c.273G>A

ENST00000643732.1:n.678G>A

ENST00000646131.1:c.566G>A

ENST00000224721.10:c.917G>A

ENST00000299366.11:c.902G>A

ENST00000398809.8:c.902G>A

ENST00000398842.7:c.653G>A

ENST00000461841.7:c.902G>A

ENST00000466757.7:c.273G>A

ENST00000616684.4:c.902G>A

ENST00000622827.4:c.902G>A

NM_001171930.1:c.902G>A

NM_001171931.1:c.902G>A

NM_001171932.1:c.902G>A

NM_022124.5:c.902G>A

NM_052836.3:c.902G>A

NM_001171930.2:c.902G>A

NM_001171931.2:c.902G>A

NM_052836.4:c.902G>A

NM_001171932.2:c.902G>A

Met criteria codes **2**

Uncertain Significance

PM2

PM3

Expert Panel

Hearing Loss VCEP [↗](#)

Not Met criteria codes 2

PP1

PP3

Evidence Links 2

Criteria Specification Information !

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Hearing Loss VCEP

The allele frequency of the c.902G>A (p.Arg301Gln) variant in the CDH23 gene is 0.0046% (3/64572) of European (non-Finnish) chromosomes by gnomAD v3, which is a low enough frequency to apply PM2 based on the thresholds defined by the ClinGen Hearing Loss Expert Panel for autosomal recessive hearing loss. This variant was detected in 4 individuals with sensorineural hearing loss with the P240L variant in CDH23. For 2 of these probands the pathogenic P240L variant in CDH23 was present in trans; however, because all the families were of East Asian descent and this variant was always observed with the P240L variant, PM3 was kept at the moderate level (PM3, PMIDs: 17850630, 22443853, 22899989). Computational prediction tools and conservation analyses do not provide strong support for or against an impact to the protein (PP3 not met). In summary, the clinical significance of this variant is uncertain. ACMG/AMP criteria applied, as specified by the Hearing Loss Expert Panel: PM2, PM3.

Met criteria codes

PM2



This variant is present in 0.00413% (1/24192) of African alleles in gnomAD v2.1.1 and in 0.00465% (3/64572) of African alleles in gnomAD v3.

PM3



This variant was present in 5 different individuals from 4 families all with the P240L variant in CDH23 present in trans. All individuals had sensorineural hearing loss. Because this variant was always found with the P240L variant the HL-EP decided to keep the code at the moderate level.

PubMed:22899989 [↗](#)

PubMed:17850630 [↗](#)

Not Met criteria codes

PP1



The variant segregated with the nonsyndromic hearing loss phenotype in 1 family with affected dizygotic twins. PP1 not applied because unclear if the twin is monozygotic or dizygotic.

PP3



The REVEL score is 0.563 although the variant is conserved across all vertebrates in the UCSC database and may create a possible 3' cryptic splice site as predicted by MaxEntScan.

Curation History [↗](#)

