

Variant: *NM_022124.6(CDH23):c.6085C>T (p.Arg2029Trp)*

Version: 1.0

CA5545996 [↗](#)

446446 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal recessive inheritance

UUID: e333b58d-b3ca-4e2b-b958-09402de4c847

Approved on: 2023/6/26

Published on: 2023/6/30

HGVS expressions

NM_022124.6:c.6085C>T

NM_022124.6(CDH23):c.6085C>T (p.Arg2029Trp)

NC_000010.11:g.71791167C>T

CM000672.2:g.71791167C>T

NC_000010.10:g.73550924C>T

CM000672.1:g.73550924C>T

NC_000010.9:g.73220930C>T

NG_008835.1:g.399221C>T

ENST00000224721.12:c.6085C>T

ENST00000224721.10:c.6100C>T

ENST00000622827.4:c.6085C>T

NM_022124.5:c.6085C>T

Pathogenic

Met criteria codes **3**

PM3_Very Strong

PP1

PP3

Not Met criteria codes **1**

PM2

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 c.6085C>T variant in CDH23 is a missense variant predicted to cause substitution of arginine by tryptophan at amino acid 2029 (p.Arg2029Trp). The highest population minor allele frequency in gnomAD v2.1.1 is 0.02% (3/17816 alleles) in the East Asian population. (PM2_Supporting, BS1, and BA1 are not met). The computational predictor REVEL gives a score of 0.7, evidence that correlates with impact to CDH23 function (PP3). This variant has been detected in many individuals with hearing loss or deafness, without any reported vision

loss or evidence of retinopathy. Of those individuals, over 10 were homozygous or compound heterozygous for the variant and a pathogenic or likely pathogenic and many of those were confirmed in trans (6.75 PM3_Very Strong points, PMID: 35020051, 25963016, 22899989, 17850630). The variant has been reported to segregate with hearing loss in 1 affected family member from 1 family (PP1_Supporting; PMID: 22899989, 17850630). In summary, this variant meets the criteria to be classified as Pathogenic for autosomal recessive hearing loss based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PM3_VeryStrong, PP3, PP1. (VCEP specifications version 2; 06.26.2023).

Met criteria codes

PM3_Very Strong			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1			Miyagawa 2012 PMID:22899989. 1 segregation in affected sib variants never seen on same haplotype per gnomAD co-occurrence tool, variants confirmed in trans in PMID: 17850630, likely same family based on author overlap.
PP3			REVEL 0.701

Not Met criteria codes

PM2		0.01% (3/17816) East asian alleles gnomad v2.1.1
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Curation History



 

 

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