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Variant: NM_004086.3(COCH):c.259G>T (p.Gly87Trp)

Version: 1.0

CA389344541

1297642 (ClinVar)

Gene: COCH (HGNC:1690)
Condition: nonsyndromic genetic deafness (MONDO:0019497)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1600fb4a-a1af-4849-852c-f40e7bafeca6
Approved on: Wed, 16 Sep 2026 00:00:00 +0000
Published on: Mon, 28 Sep 2026 00:00:00 +0000

HGVS expressions

NM_004086.3(COCH):c.259G>T (p.Gly87Trp)
NM_004086.3:c.259G>T
NC_000014.9:g.30878830G>T
CM000676.2:g.30878830G>T
NC_000014.8:g.31348036G>T
CM000676.1:g.31348036G>T
NC_000014.7:g.30417787G>T
NG_008211.2:g.9296G>T
ENST00000216361.9:c.454G>T
ENST00000396618.9:c.259G>T
ENST00000555117.2:c.259G>T
ENST00000643575.1:c.259G>T
ENST00000643697.1:n.504G>T
ENST00000644874.2:c.259G>T
ENST00000216361.8:c.259G>T
ENST00000396618.7:c.259G>T
ENST00000460581.6:c.-78G>T
ENST00000475087.5:c.259G>T
ENST00000553772.5:c.239+1102G>T
ENST00000553833.5:n.413G>T
ENST00000555881.5:c.83-1622G>T
ENST00000556908.5:c.211G>T
ENST00000557065.1:c.156-593G>T
NM_001135058.1:c.259G>T
NM_004086.2:c.259G>T
NR_038356.1:n.1618-2278C>A
NM_001347720.1:c.454G>T
NM_001135058.2:c.259G>T
NM_001347720.2:c.454G>T

Likely Pathogenic

Met criteria codes 4

PP1_Strong PP3 PP4 PM2_Supporting

Not Met criteria codes 2

Expert Panel

Hearing Loss VCEP

Criteria Specification Information

BS3 PS4

Evidence Links 0

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 2.0*

PDF

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hearing Loss VCEP

The variant NM_004086.3:c.259G>T in COCH is a missense variant predicted to cause substitution of Glycine to Tryptophan at amino acid 87 (p.Gly87Trp). The highest population minor allele frequency in gnomAD v4.1.1 is 0.00008474% (1/1180026 -European [non-Finnish], PM2_Supporting met). The in silico predictor REVEL yields a score of 0.911, which is above the threshold of 0.7 (PP3 met). This variant was identified in a Dutch family (PMID:16835921), in which it segregated with progressive, late-onset HL and concomitant vestibular dysfunction in 16 affected family members (PP1_Strong met). Given the highly specific phenotype of progressive hearing loss with vestibular dysfunction, the HL-VCEP decided to apply PP4 evidence criteria. Functional studies showed no alteration in protein secretion or aggregate formation; however, protein cleavage was not evaluated. Therefore, BS3_Supporting was not applied. In summary, based on the current evidence (PP1_Strong, PP4, PP3 & PM2_Supporting), the variant NM_004086.3(COCH):c.259G>T (p.Gly87Trp) is classified as Likely-Pathogenic for autosomal dominant non-syndromic SNHL based on the ACMG/AMP criteria applied, as specified by the ClinGen HL-VCEP (ClinGen Hearing Loss VCEP specifications version 2; 09/16/2026).

Met criteria codes

PP1_Strong	✔	This variant was identified in a Dutch family (PMID:16835921), in which it segregated with progressive, late-onset HL and concomitant vestibular dysfunction in 16 affected family members.
PP3	✔	The in silico predictor REVEL yields a score of 0.911, which is above the threshold of 0.7
PP4	✔	Given the highly specific phenotype of progressive hearing loss with vestibular dysfunction, the HL-VCEP decided to apply PP4 evidence criteria.
PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.1.1 is 0.00008474% (1/1180026 -European [non-Finnish]).

Not Met criteria codes

BS3	✖	Functional studies showed no alteration in protein secretion or aggregate formation; however, protein cleavage was not evaluated. Therefore, BS3_P was not applied.
PS4	✖	This variant was identified in only one Dutch family (PMID:16835921).

Curation History

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