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Variant: NM_005422.2(TECTA):c.4085G>A (p.Trp1362Ter)

Version: 1.0

CA6327349

498538 (ClinVar)

Gene: TECTA
Condition: nonsyndromic genetic deafness (MONDO:0019497)
UUID: 3cef6ced-0d25-4c76-9b45-dc177c59acc4
Approved on: 2020/1/21
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HGVS expressions

NM_005422.2:c.4085G>A
NM_005422.2(TECTA):c.4085G>A (p.Trp1362Ter)
NC_000011.10:g.121146096G>A
CM000673.2:g.121146096G>A
NC_000011.9:g.121016805G>A
CM000673.1:g.121016805G>A
NC_000011.8:g.120522015G>A
NG_011633.1:g.48431G>A
ENST00000392793.6:c.4085G>A
ENST00000642222.1:c.4085G>A
ENST00000645008.1:c.1392G>A
ENST00000646278.1:n.21G>A
ENST00000264037.2:c.4085G>A
ENST00000392793.5:c.4085G>A
ENST00000478058.1:n.650G>A
NM_001378761.1:c.5042G>A
NM_005422.4:c.4085G>A

Pathogenic

Met criteria codes 3

PM3_Supporting PM2_Supporting PVS1

Not Met criteria codes 1

BP5

Evidence Links 1

Expert Panel

Hearing Loss VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hearing Loss VCEP

The c.4085G>A (p.Trp1362Ter) nonsense variant in TECTA is predicted to cause a premature stop codon in biologically-relevant exon 11 of 23 total exons, leading to a truncated or absent protein in a gene in which loss of function is an established mechanism of autosomal recessive nonsyndromic hearing loss (PVS1; PMID: 30192042). This variant is present in 0.01121% (14/124864) of non-Finnish European

chromosomes in gnomAD v2 (PM2_Supporting). It has been observed in at least two probands presenting with nonsyndromic hearing loss (PMID: 31163360; LMM internal data SCV000711208.2). One individual harbored another nonsense variant in TECTA, which was suspected to be pathogenic (PM3_Supporting). In summary, this variant meets criteria to be classified as pathogenic for autosomal recessive nonsyndromic hearing loss. ACMG/AMP Criteria applied as specified by the Hearing Loss Expert Panel: PVS1, PM2_Supporting, PM3_Supporting.

Met criteria codes

PM3_Supporting ✔

Seen in 1 individual who harbored another nonsense variant, p.Tyr1942Ter, in TECTA, classified as pathogenic in ClinVar by EGL (PMID: 31163360). Also seen by LMM in 1 individual who also carried a VUS in TECTA, however no points were applied since the phase was unknown.

PubMed:31163360

PM2_Supporting ✔

Present in 0.01121% (14/124864) of non-Finnish European chromosomes in gnomAD v2 and 0.02013% (13/64582) v3.

PVS1 ✔

Nonsense mutation in exon 11/23 of TECTA in Alamut, predicted to undergo NMD. Present in biologically-relevant transcript as indicated by GTEx exon expression data. LOF variants in TECTA are dispersed relatively evenly throughout the gene in gnomAD.

Not Met criteria codes

BP5 ✖

Seen in 1 family at LMM with alternate mechanisms for disease, but not applied because all individuals were only heterozygous for this variant.

Curation History

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