The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_206933.4:c.3547_3548del

Version: 2.1

CA262101

48503 (ClinVar)

Gene: USH2A
Condition: Usher syndrome (MONDO:0019501)
Inheritance Mode: Autosomal recessive inheritance
UUID: afc59df6-82ed-458e-aa96-f7857c925895
Approved on: 2022/11/22
Published on: 2023/2/6

HGVS expressions

NM_206933.4:c.3547_3548del
NC_000001.11:g.216199894_216199895del
CM000663.2:g.216199894_216199895del
NC_000001.10:g.216373236_216373237del
CM000663.1:g.216373236_216373237del
NC_000001.9:g.214439859_214439860del
NG_009497.1:g.228506_228507del
NG_009497.2:g.228558_228559del
ENST00000307340.8:c.3547_3548del
ENST00000674083.1:c.3547_3548del
ENST00000307340.7:c.3547_3548del
ENST00000366942.3:c.3547_3548del
NM_007123.5:c.3547_3548del
NM_206933.2:c.3547_3548del
NM_206933.3:c.3547_3548del
NM_007123.6:c.3547_3548del

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 24

PM6 PM1 PM3 PM5 PM4 BA1 BS2 BS1 BS4 BS3 BP5 BP7 BP4 BP3 BP1 BP2 PS1 PS2 PS3 PS4 PP1 PP2 PP3 PP4

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 p.Ile1183fs variant in USH2A introduces a premature stop codon in biologically-relevant-exon 17/72 that is predicted to lead to a truncated or absent protein in a gene in which loss-of-function is an established disease mechanism (PVS1; PMIDs: 9624053, 25211151, 20497194). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00088% (1/113352 alleles) in the European (non-Finnish) population, which is lower than the ClinGen Hearing Loss VCEP threshold (<0.007%) for PM2_Supporting, meeting this criterion (PM2_Supporting). One proband with autosomal recessive retinitis pigmentosa was identified to be carrying the p.Ile1183fs variant with no variant reported in trans (PMID: 35266249). This variant was re-reviewed on 11/22/2022 and because no additional evidence is available, professional judgment was used to retain this variant as likely pathogenic for autosomal recessive Usher Syndrome based on the ACMG/AMP criteria applied as specified by the ClinGen Hearing Loss VCEP: PVS1, PM2_P (ClinGen Hearing Loss VCEP specifications version 2; 11/22/2022).

Met criteria codes

PVS1	✔	This variant introduces a premature stop codon in biologically-relevant-exon 17/72 that is predicted to lead to a truncated or absent protein in a gene in which loss-of-function is an established disease mechanism
PM2_Supporting	✔	Highest MAF is 0.00088% (1/113352) in gnomAD v.2.1.1

Not Met criteria codes

PM6	✖	Variant has not been reported in patient or clinically-evaluated control populations.
PM1	✖	PM1 not applicable for USH2A
PM3	✖	One proband with autosomal recessive retinitis pigmentosa was identified to be carrying the p.Ile1183fs variant with no variant reported in trans (PMID: 35266249)
PM5	✖	Not applicable for frameshift variants
PM4	✖	Not applicable for frameshift variants
BA1	✖	Highest MAF is 0.00088% (1/113352) in gnomAD v.2.1.1
BS2	✖	Variant has not been reported in patient or clinically-evaluated control populations.
BS1	✖	Highest MAF is 0.00088% (1/113352) in gnomAD v.2.1.1
BS4	✖	Variant has not been reported in patient or clinically-evaluated control populations.
BS3	✖	Variant has not been evaluated experimentally.
BP5	✖	Relevant to dominant hearing loss disorders only.
BP7	✖	Not applicable for frameshift variants

BP4		✖	Not applicable for frameshift variants
BP3		✖	Not applicable for frameshift variants
BP1		✖	Not applicable for frameshift variants
BP2		✖	Variant has not been reported in patient or clinically-evaluated control populations.
PS1		✖	Not applicable for frameshift variants
PS2		✖	Variant has not been reported in patient or clinically-evaluated control populations.
PS3		✖	Variant has not been evaluated experimentally.
PS4		✖	Variant has not been reported in patient or clinically-evaluated control populations.
PP1		✖	Variant has not been reported in patient or clinically-evaluated control populations.
PP2		✖	Not applicable for frameshift variants
PP3		✖	Not applicable for frameshift variants
PP4		✖	Variant has not been reported in patient populations.

Curation History

Showing 1 to 3 of 3 rows

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