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_206933.2(USH2A):c.5039A>G (p.Lys1680Arg)

Version: 1.2

CA179559

166499 (ClinVar)

Gene: USH2A (HGNC:7399)
Condition: Usher syndrome (MONDO:0019501)
Inheritance Mode: Autosomal recessive inheritance
UUID: 201650f0-4a5b-446d-98e4-65dbae845631
Approved on: 2025-05-21
Published on: 2025-06-30

HGVS expressions

NM_206933.2:c.5039A>G
NM_206933.2(USH2A):c.5039A>G (p.Lys1680Arg)
NC_000001.11:g.216084826T>C
CM000663.2:g.216084826T>C
NC_000001.10:g.216258168T>C
CM000663.1:g.216258168T>C
NC_000001.9:g.214324791T>C
NG_009497.1:g.343571A>G
NG_009497.2:g.343623A>G
ENST00000307340.8:c.5039A>G
ENST00000674083.1:c.5039A>G
ENST00000307340.7:c.5039A>G
ENST00000463147.1:n.283A>G
ENST00000481786.1:n.281A>G
NR_125992.1:n.266-1896T>C
NR_125993.1:n.137-1896T>C
NM_206933.3:c.5039A>G
NM_206933.4:c.5039A>G

Uncertain Significance

Met criteria codes 2

PP4 PM3_Supporting

Not Met criteria codes 24

BP5 BP7 BP4 BP3 BP1 BP2 PVS1 PS1 PS2 PS3 PS4 PP1 PP2 PP3 PM6 PM2 PM1 PM5 PM4 BA1 BS1 BS4 BS3 BS2

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.5039A>G (p.Lys1680Arg) variant in USH2A is a missense variant that replaces lysine with arginine at codon 1680. (Add gnomad information) The REVEL score for this variant is 0.252, which does not meet the threshold for PP3. This variant has been observed in the homozygous state in one individual with a clinical diagnosis of Usher syndrome (PMID: 36909829), meeting PM3_Supporting. The phenotype observed is highly specific for Usher syndrome, meeting PP4. In summary, this variant meets criteria to be classified as uncertain significance for autosomal recessive Usher syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Hearing Loss VCEP: PM3_Supporting, PP4. (ClinGen Hearing Loss VCEP specifications version 2; 5/21/2025)

Met criteria codes

PP4	✔	The variant has been reported in one homozygous proband, who was diagnosed with Usher syndrome.
PM3_Supporting	✔	The variant has been reported in one homozygous proband, who was diagnosed with Usher syndrome.

Not Met criteria codes

BP5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4	✖	The REVEL computational prediction analysis tool produced a score of 0.252, which also meets no codes.
BP3	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	✖	

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	ℹ	✖	The REVEL computational prediction analysis tool produced a score of 0.252, which also meets no codes.
PM6	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2		✖	The MAF is 0.00057 (20/35312 alleles, 0 homozygotes) for the Latino population, which meets no codes.
PM1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	The variant is present in 0.05% Latino alleles in gnomAD.
BS1	ℹ	✖	The variant is present in 0.05% Latino alleles in gnomAD.
BS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

Showing 1 to 3 of 3 rows