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_004360.4(CDH1):c.457A>T (p.Lys153Ter)

Version: 3.0

CA396457656

569046 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: a5c65338-7170-417c-941a-c6aec2c6df65
Approved on: 2023/8/4
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HGVS expressions

NM_004360.4(CDH1):c.457A>T (p.Lys153Ter)
NM_004360.4:c.457A>T
NC_000016.10:g.68808493A>T
CM000678.2:g.68808493A>T
NC_000016.9:g.68842396A>T
CM000678.1:g.68842396A>T
NC_000016.8:g.67399897A>T
NG_008021.1:g.76202A>T
ENST00000261769.10:c.457A>T
ENST00000261769.9:c.457A>T
ENST00000422392.6:c.457A>T
ENST00000561751.1:c.224A>T
ENST00000562836.5:n.528A>T
ENST00000564676.5:n.739A>T
ENST00000564745.1:n.452A>T
ENST00000566510.5:c.457A>T
ENST00000566612.5:c.457A>T
ENST00000611625.4:c.457A>T
ENST00000612417.4:c.457A>T
ENST00000621016.4:c.457A>T
NM_004360.3:c.457A>T
NM_001317184.1:c.457A>T
NM_001317185.1:c.-1159A>T
NM_001317186.1:c.-1363A>T
NM_004360.5:c.457A>T
NM_001317184.2:c.457A>T
NM_001317185.2:c.-1159A>T
NM_001317186.2:c.-1363A>T

Pathogenic

Met criteria codes 3

PM5_Supporting PVS1 PM2_Supporting

Not Met criteria codes 23

Expert Panel

CDH1 VCEP

Criteria Specification Information

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

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence Links 0

Evidence submitted by expert panel

CDH1 VCEP

The c.457A>T (p.Lys153Ter) variant is predicted to result in a premature stop codon that leads to nonsense mediate decay (PVS1 and PM5_supporting). The variant is absent in the gnomAD cohort (PM2_supporting; http://gnomad.broadinstitute.org). Therefore, this variant meets criteria to be classified as pathogenic based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (CDH1 VCEP specifications version 3.1): PVS1, PM2_supporting, PM5_supporting.

Met criteria codes

PM5_Supporting	✔	This variant is predicted to results in a premature stop codon in exon 4.
PVS1	✔	This variant is predicted to results in a premature stop codon in exon 4.
PM2_Supporting	✔	This allele is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.

Not Met criteria codes

PS1	✖	PS1 does not apply to CDH1.
PS2	✖	To our knowledge, de novo occurrence of this variant has not been reported.
PS3	✖	PS3 applies only to splicing variants.
PS4	✖	SCV000817235.1 - this family does not meet IGCLC criteria for HDGC.
PP1	✖	To our knowledge, segregation of this variant has not been reported.
PP2	✖	PP2 does not apply to CDH1.
PP3	✖	PP3 does not apply to nonsense variants.
PP4	✖	PP4 does not apply to CDH1.

BA1	ℹ	✖	This allele is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.
BS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	ℹ	✖	To our knowledge, de novo occurrence of this variant has not been reported.
BS1	ℹ	✖	This allele is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.
BS4	ℹ	✖	To our knowledge, segregation of this variant has not been reported.
BS3	ℹ	✖	BS3 applies only to splicing variants.
PM1		✖	PM1 does not apply to CDH1.
PM3		✖	To our knowledge, this variant has not been reported in cis or trans with a pathogenic variant.
PM4	ℹ	✖	PM4 does not apply to nonsense variants
BP4	ℹ	✖	BP4 does not apply to nonsense variants.
BP3		✖	BP3 does not apply to CDH1.
BP1		✖	BP1 does not apply to CDH1.
BP2	ℹ	✖	To our knowledge, this variant has not been reported in cis or trans with a pathogenic variant.
BP5	ℹ	✖	To our knowledge, this variant has not been reported in a case with an alternate molecular basis for disease.
BP7	ℹ	✖	BP7 does not apply to nonsense variants.

Curation History

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