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_004360.5(CDH1):c.499G>A (p.Glu167Lys)

Version: 2.0

CA350337

219431 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: eb5cec7b-ca99-48f1-b112-76e09312355a
Approved on: 2023/8/10
Published on: 2023/8/10

HGVS expressions

NM_004360.5(CDH1):c.499G>A (p.Glu167Lys)
NM_004360.5:c.499G>A
NC_000016.10:g.68808535G>A
CM000678.2:g.68808535G>A
NC_000016.9:g.68842438G>A
CM000678.1:g.68842438G>A
NC_000016.8:g.67399939G>A
NG_008021.1:g.76244G>A
ENST00000261769.10:c.499G>A
ENST00000261769.9:c.499G>A
ENST00000422392.6:c.499G>A
ENST00000561751.1:c.266G>A
ENST00000562836.5:n.570G>A
ENST00000564676.5:n.781G>A
ENST00000564745.1:n.494G>A
ENST00000566510.5:c.499G>A
ENST00000566612.5:c.499G>A
ENST00000567320.1:n.9G>A
ENST00000611625.4:c.499G>A
ENST00000612417.4:c.499G>A
ENST00000621016.4:c.499G>A
NM_004360.3:c.499G>A
NM_001317184.1:c.499G>A
NM_001317185.1:c.-1117G>A
NM_001317186.1:c.-1321G>A
NM_004360.4:c.499G>A
NM_001317184.2:c.499G>A
NM_001317185.2:c.-1117G>A
NM_001317186.2:c.-1321G>A

Likely Benign

Met criteria codes 1

BS2

Not Met criteria codes 25

Expert Panel

CDH1 VCEP

Criteria Specification Information

BP5 BP7 BP4 BP3 BP1 BP2
PS1 PS2 PS3 PS4 PP1 PP2
PP3 PP4 PM6 PM2 PM1
PM3 PM5 PM4 PVS1 BA1
BS1 BS4 BS3

Evidence Links 0

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 submitted by expert panel

CDH1 VCEP

The c.499G>A (p.Glu167Lys) variant has also been observed in >10 (28) individuals without a diagnosis of diffuse gastric cancer, signet ring tumor or lobular breast cancer and whose family histories do not suggest HDGC (BS2; SCV000329225.7; SCV000259296.7). In summary, this variant meets criteria to be classified as likely benign based the ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BS2.

Met criteria codes

BS2	✔		Variant seen in 28 individuals w/o DCG, SRC tumors, or LBC & whose families do not suggest HDGC (SCV000329225.7, SCV000259296.7).

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	✖		No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
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		✖	Variant seen in 28 individuals w/o DCG, SRC tumors, or LBC & whose families do not suggest HDGC (SCV000329225.7, SCV000259296.7). But only one individual was reported to meet HDGC criteria which is less than 30% (3.4%).
PP1		✖	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		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2		✖	Variant presents 4 times out of 282610 alleles in gnomAD cohort (>One out of 100,000 alleles).
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4		✖	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
BA1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	✖	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

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_004360.5(CDH1):c.499G>A (p.Glu...)	Likely Benign	CDH1-Related Diffuse Gastric And Lobular Breast Cancer	2023-08-10	2.0	ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1	CDH1
View	NM_004360.5(CDH1):c.499G>A (p.Glu...)	Likely Benign	Hereditary Diffuse Gastric Cancer	2021-05-04	1.0	-	CDH1

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