

Variant: *NM_004360.5(CDH1):c.112A>C (p.Thr38Pro)*

Version: 1.0

CA396452065 [↗](#)

489846 (ClinVar) [↗](#)

Gene: CDH1 ([HGNC:999](#))

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0100488](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: eba86107-ad2f-4d6f-8e01-bb7a2412ea45

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HGVS expressions

NM_004360.5(CDH1):c.112A>C (p.Thr38Pro)

NM_004360.5:c.112A>C

NC_000016.10:g.68738360A>C

CM000678.2:g.68738360A>C

NC_000016.9:g.68772263A>C

CM000678.1:g.68772263A>C

NC_000016.8:g.67329764A>C

NG_008021.1:g.6069A>C

ENST00000261769.10:c.112A>C

ENST00000261769.9:c.112A>C

ENST00000422392.6:c.112A>C

ENST00000566510.5:c.112A>C

ENST00000566612.5:c.112A>C

ENST00000611625.4:c.112A>C

ENST00000612417.4:c.112A>C

ENST00000621016.4:c.112A>C

NM_004360.3:c.112A>C

NM_001317184.1:c.112A>C

NM_001317185.1:c.-1504A>C

NM_001317186.1:c.-1708A>C

NM_004360.4:c.112A>C

NM_001317184.2:c.112A>C

NM_001317185.2:c.-1504A>C

NM_001317186.2:c.-1708A>C

Uncertain Significance

Met criteria codes **2**

BS2_Supporting

PM2_Supporting

Not Met criteria codes **24**

PM6

PM1

PM3

PM5

PM4

BS1

BS4

BS3

PVS1

PS1

PS2

PS3

PS4

BP5

BP7

BP4

BP3

BP1

BP2

BA1

PP1

PP2

PP3

PP4

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.112A>C (NM_004360.5) variant in CDH1 is a missense variant predicted to cause substitution in exon 2 (p.Thr38Pro). This variant was observed in seven individuals with no DGC, LBC or SRC tumours and whose families do not suggest HDGC (BS2_Supporting; Invitae). Note that this includes two individuals with a family history of stomach cancer NOS. This variant is absent from gnomAD 2.1.1 (PM2_Spporting). In summary, this variant is classified as uncertain significance for DGLBCS based on the ACMG/AMP criteria applied, as specified by the ClinGen CDH1 VCEP: PM2_Supporting, BS2_supporting. (CDH1 VCEP specifications version 3.1; 04/24/2023)

Met criteria codes

BS2_Supporting			This variant was observed in seven individuals with no DGC, LBC or SRC tumours and whose families do not suggest HDGC (BS2_Supporting; Invitae and Ambry). Note that this includes two individuals with personal histories of endometrial cancer and colorectal cancer and family history of gastric cancer NOS.
PM2_Supporting			This variant is absent from gnomAD 2.1.1 (PM2_Supporting).

Not Met criteria codes

PM6			To our knowledge, this variant has not been reported as de novo.
PM1			PM1 does not apply to CDH1.
PM3			PM3 does not apply to CDH1.
PM5			PM5 does not apply to CDH1.
PM4			PM4 does not apply to this variant.
BS1			This variant is absent from gnomAD. Note the G allele is present in one in 156,712 alleles (0.000006381).
BS4			Segregation unknown.
BS3			Functional studies not available for this variant.
PVS1			PVS1 does not apply to this variant.
PS1			There are no pathogenic missense variants at this position.

PS2			To our knowledge, this variant has not been reported as de novo.
PS3			Functional studies not available for this variant.
PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			This variant has not been found in a case with an alternate molecular basis for disease.
BP7			BP7 does not apply to this variant.
BP4			This variant is not predicted to alter splicing (not applied).
BP3			BP3 does not apply to CDH1.
BP1			BP1 does not apply to CDH1.
BP2			To our knowledge, this variant has not been reported in cis or trans with a pathogenic variant.
BA1			This variant is absent from gnomAD. Note the G allele is present in one in 156,712 alleles (0.000006381).
PP1			Segregation unknown.
PP2			PP2 does not apply to CDH1.
PP3			This variant is not predicted to alter splicing.
PP4			PP4 does not apply to CDH1.

Curation History 		
 Showing 1 to 1 of 1 rows		

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