

Variant: NM_004360.5(CDH1):c.1409C>T (p.Thr470Ile)

Version: 2.0

CA151518 [↗](#)

127913 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 1149db17-78d8-4b2c-bbd4-e5f6b193a1eb

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HGVS expressions

NM_004360.5:c.1409C>T

NM_004360.5(CDH1):c.1409C>T (p.Thr470Ile)

NC_000016.10:g.68815603C>T

CM000678.2:g.68815603C>T

NC_000016.9:g.68849506C>T

CM000678.1:g.68849506C>T

NC_000016.8:g.67407007C>T

NG_008021.1:g.83312C>T

ENST00000261769.10:c.1409C>T

ENST00000261769.9:c.1409C>T

ENST00000422392.6:c.1226C>T

ENST00000562836.5:n.1480C>T

ENST00000566510.5:c.*75C>T

ENST00000566612.5:c.1409C>T

ENST00000611625.4:c.1472C>T

ENST00000612417.4:c.1409C>T

ENST00000621016.4:c.1409C>T

NM_004360.3:c.1409C>T

NM_001317184.1:c.1226C>T

NM_001317185.1:c.-140C>T

NM_001317186.1:c.-411C>T

NM_004360.4:c.1409C>T

NM_001317184.2:c.1226C>T

NM_001317185.2:c.-140C>T

NM_001317186.2:c.-411C>T

Benign

Met criteria codes **2**

BS2 BP2_Strong

Not Met criteria codes **24**

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

Expert Panel

Criteria Specification Information

[↗](#) **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.1409C>T (p.Thr470Ile) variant was observed in trans with a known pathogenic CDH1 variant with phase confirmed (BP2_Strong; PMID: 9537325). This variant was also observed in the homozygous state in at least 6 individuals without a personal and/or family history of diffuse gastric cancer, signet ring cell tumor or lobular breast cancer (BP2_Strong; internal laboratory contributors). Additionally, this variant has been observed in >10 individuals without a diagnosis of diffuse gastric cancer, signet ring tumor or lobular breast cancer and whose family histories do not suggest HDGC (BS2; internal laboratory contributors). In summary, this variant meets criteria to be classified as benign. ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BP2_Strong, BS2.

Met criteria codes

BS2			388 non-HDGC individuals.
BP2_Strong			PMID:9537325 - Observed in an early onset diffuse gastric cancer family. A pathogenic (c.2382-2386insC) CDH1 variant was also identified and reported to segregate with disease in the family. This variant p.Thr470Ile, is reported NOT to segregate with disease in the family, this suggests that the two variants are in trans. Also, seen in 6 homozygotes. PMID:9537325 - Observed in an early onset diffuse gastric cancer family. A pathogenic (c.2382-2386insC) CDH1 variant was identified and reported to segregate with disease in the family. This variant p.Thr470Ile, is reported NOT to segregate with disease in the family, this suggests that the two variants are in trans. PubMed:9537325

Not Met criteria codes

BS1			ExAC - 0.003% - 4 total allele count. (East Asian 0.03%). GnomAD 0.004% - 10 total allele count. (East Asian 0.04%).
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
BP5			Observed in 4 patients with pathogenic variants in other cancer assoc. genes.; concern for overlapping phenotypes
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

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			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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
BA1			ExAC - 0.003% - 4 total allele count. (East Asian 0.03%). GnomAD 0.004% - 10 total allele count. (East Asian 0.04%).
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM3			PMID:9537325 - Observed in an early onset diffuse gastric cancer family. A pathogenic (c.2382-2386insC) CDH1 variant was identified and reported to segregate with disease in the family. This variant p.Thr470Ile, is reported NOT to segregate with disease in the family, this suggests that the two variants are in trans. PubMed:9537325 
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
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

PM2



ExAC - 0.003% - 4 total allele count. (East Asian 0.03%). GnomAD 0.004% - 10 total allele count. (East Asian 0.04%).

Curation History [↗](#)

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