

Variant: NM_004360.4(CDH1):c.1225T>C (p.Trp409Arg)

CA157989 [↗](#)

133855 (ClinVar) [↗](#)

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

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0007648](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 26997937-9088-4611-9ef8-bd80077ed64c

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HGVS expressions

NM_004360.4:c.1225T>C

NM_004360.4(CDH1):c.1225T>C (p.Trp409Arg)

NC_000016.10:g.68813400T>C

CM000678.2:g.68813400T>C

NC_000016.9:g.68847303T>C

CM000678.1:g.68847303T>C

NC_000016.8:g.67404804T>C

NG_008021.1:g.81109T>C

ENST00000261769.10:c.1225T>C

ENST00000261769.9:c.1225T>C

ENST00000422392.6:c.1137+1137T>C

ENST00000562836.5:n.1296T>C

ENST00000565810.1:n.269T>C

ENST00000566510.5:c.1069T>C

ENST00000566612.5:c.1225T>C

ENST00000611625.4:c.1225T>C

ENST00000612417.4:c.1225T>C

ENST00000621016.4:c.1225T>C

NM_004360.3:c.1225T>C

NM_001317184.1:c.1137+1137T>C

NM_001317185.1:c.-391T>C

NM_001317186.1:c.-595T>C

NM_004360.5:c.1225T>C

NM_001317184.2:c.1137+1137T>C

NM_001317185.2:c.-391T>C

NM_001317186.2:c.-595T>C

NM_004360.5(CDH1):c.1225T>C (p.Trp409Arg)

Likely Benign

Met criteria codes 1

BS2

Not Met criteria codes 25

PS2 PS4 PS1 PS3 BA1 PP4
PP1 PP2 PP3 PM3 PM1
PM4 PM5 PM6 PM2 BS4

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen CDH1 Expert Panel
Specifications to the ACMG/AMP Variant Interpretation
Guidelines Version 3.1

BS3

BS1

BP5

BP7

BP2

BP3

BP1

BP4

PVS1

[Criteria Specification Approval History](#)
[Criteria Specifications for this VCEP](#)

Evidence Links 0

Evidence submitted by expert panel			
<i>CDH1 VCEP</i>			
The c.1225T>C (p. Trp409Arg) 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, the clinical significance of this variant is classified as likely benign based on BS2 alone. ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BS2.			
Met criteria codes			
BS2			Observed in 40 individuals w/o dx HDGC
Not Met criteria codes			
PS2			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
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			PMID: 15235021: increased invasion in collagen gel and impaired cell-cell adhesion in cells transfected with this variant compared to wild type. PMID: 27582386: no effect on cell adhesion in cell culture
BA1			ExAC - 0.003% 4 allele count (European non-Finnish) gnomAD - 0.002% 5 allele count (European non-Finnish).
PP4			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		
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1		✖	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
PM5		✖	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 allele count (European non-Finnish) gnomAD - 0.002% 5 allele count (European non-Finnish).
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	PMID: 15235021: increased invasion in collagen gel and impaired cell-cell adhesion in cells transfected with this variant compared to wild type. PMID: 27582386: no effect on cell adhesion in cell culture
BS1		✖	ExAC - 0.003% 4 allele count (European non-Finnish) gnomAD - 0.002% 5 allele count (European non-Finnish).
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
BP2		✖	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
BP4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline





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