

Variant: *NM_004360.5(CDH1):c.1223C>T (p.Ala408Val)*

Version: 2.0

CA288022 [↗](#)

127908 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: de121013-db34-4461-8027-65ef657a9e2a

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HGVS expressions

NM_004360.5(CDH1):c.1223C>T (p.Ala408Val)

NM_004360.5:c.1223C>T

NC_000016.10:g.68813398C>T

CM000678.2:g.68813398C>T

NC_000016.9:g.68847301C>T

CM000678.1:g.68847301C>T

NC_000016.8:g.67404802C>T

NG_008021.1:g.81107C>T

ENST00000261769.10:c.1223C>T

ENST00000261769.9:c.1223C>T

ENST00000422392.6:c.1137+1135C>T

ENST00000562836.5:n.1294C>T

ENST00000565810.1:n.267C>T

ENST00000566510.5:c.1067C>T

ENST00000566612.5:c.1223C>T

ENST00000611625.4:c.1223C>T

ENST00000612417.4:c.1223C>T

ENST00000621016.4:c.1223C>T

NM_004360.3:c.1223C>T

NM_001317184.1:c.1137+1135C>T

NM_001317185.1:c.-393C>T

NM_001317186.1:c.-597C>T

NM_004360.4:c.1223C>T

NM_001317184.2:c.1137+1135C>T

NM_001317185.2:c.-393C>T

NM_001317186.2:c.-597C>T

Benign

Met criteria codes 2

BS2 BS1

Not Met criteria codes 24

BA1 BP4 BP3 BP1 BP2 BP5
BP7 BS4 BS3 PP1 PP2 PP3
PP4 PS1 PS2 PS3 PS4 PM6

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

CDH1 VCEP

The c.1223C>T (p.Ala408Val) missense variant has a frequency of 0.114% (>0.1%) in South Asians (35 of 30616 alleles) in the gnomAD v2.1.1 cohort (BS1). This variant has been observed in ≥10 (122) individuals without DGC, SRC tumours or LBC and whose families do not suggest HDGC (BS2; SCV000260430.7, SCV000186167.6). In summary, the clinical significance of this variant is classified as of benign based the ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BS1, BS2.

Met criteria codes

BS2			Observed in 122 individuals without HDGC phenotypes (SCV000260430.7, SCV000186167.6).
BS1			gnomAD 2.1.1 = 35 of 30616 alleles (0.114%) in South Asians. MAF > 0.1%. gnomAD 3.1 = 3 of 4822 alleles (0.06221%) in South Asians.

Not Met criteria codes

BA1			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
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

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
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
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			PS4 cannot be applied to variants that meet BS1 or BA1.
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			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
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

Curation History 		
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