

Variant: *NM_004360.4(CDH1):c.2451G>A (p.Ala817=)*

Version: 2.0

CA186706 [↗](#)

183842 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 20f73f9f-5a02-4ed6-855f-69e4e63e0e22

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HGVS expressions

NM_004360.4(CDH1):c.2451G>A (p.Ala817=)

NM_004360.4:c.2451G>A

NC_000016.10:g.68833301G>A

CM000678.2:g.68833301G>A

NC_000016.9:g.68867204G>A

CM000678.1:g.68867204G>A

NC_000016.8:g.67424705G>A

NG_008021.1:g.101010G>A

ENST00000261769.10:c.2451G>A

ENST00000261769.9:c.2451G>A

ENST00000422392.6:c.2268G>A

ENST00000562118.1:n.669G>A

ENST00000562836.5:n.2522G>A

ENST00000566510.5:c.*1117G>A

ENST00000566612.5:c.*691G>A

ENST00000611625.4:c.2514G>A

ENST00000612417.4:c.1854-890G>A

ENST00000621016.4:c.1866-902G>A

NM_004360.3:c.2451G>A

NM_001317184.1:c.2268G>A

NM_001317185.1:c.903G>A

NM_001317186.1:c.486G>A

NM_004360.5:c.2451G>A

NM_001317184.2:c.2268G>A

NM_001317185.2:c.903G>A

NM_001317186.2:c.486G>A

Likely Benign

Met criteria codes **2**

BS2 BP7

Not Met criteria codes **24**

BA1 BS1 BS4 BS3 BP5 BP4
BP3 BP1 BP2 PVS1 PS1
PS2 PS3 PS4 PP1 PP2 PP3

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

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

Evidence submitted by expert panel

CDH1 VCEP

The c.2451G>A variant is predicted silent and 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). The nucleotide is not conserved (BP7). Therefore, this variant meets criteria to be classified as likely benign. ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BS2, BP7.

Met criteria codes

BS2			>50 probands (and families) that do not meet clinical criteria for HDGC (SCV000253421.4). 45 families that do not meet clinical criteria for HDGC (SCV000213120.4). 22 propands that do not meet clinical criteria for HDGC (SCV000512531.4).
BP7			The nucleotide is not conserved. There are four primates (Rhesus, macaque, baboon, bushbaby) with the variant as the reference nucleotide.

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			Allele frequency is <0.1%. The gnomAD PopMax AF for East Asians is 0.007%. In total there are 17/282,864 total alleles in gnomAD v2.1.1, 0 homozygotes.
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			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			MaxEntScan and NNSplice predict no splice impact. HSF predicts activation of an exonic cryptic acceptor site.
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
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
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

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

Curation History 	
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