

Variant: *NM_004360.5(CDH1):c.105G>C (p.Glu35Asp)*

Version: 1.0

CA16620230 [↗](#)

422466 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 39819349-145e-41c0-8276-9262ba171255

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HGVS expressions

NM_004360.5(CDH1):c.105G>C (p.Glu35Asp)

NM_004360.5:c.105G>C

NC_000016.10:g.68738353G>C

CM000678.2:g.68738353G>C

NC_000016.9:g.68772256G>C

CM000678.1:g.68772256G>C

NC_000016.8:g.67329757G>C

NG_008021.1:g.6062G>C

ENST00000261769.10:c.105G>C

ENST00000261769.9:c.105G>C

ENST00000422392.6:c.105G>C

ENST00000566510.5:c.105G>C

ENST00000566612.5:c.105G>C

ENST00000611625.4:c.105G>C

ENST00000612417.4:c.105G>C

ENST00000621016.4:c.105G>C

NM_004360.3:c.105G>C

NM_001317184.1:c.105G>C

NM_001317185.1:c.-1511G>C

NM_001317186.1:c.-1715G>C

NM_004360.4:c.105G>C

NM_001317184.2:c.105G>C

NM_001317185.2:c.-1511G>C

NM_001317186.2:c.-1715G>C

Uncertain Significance

Met criteria codes **2**

PM2_Supporting

BS2_Supporting

Not Met criteria codes **24**

PS1

PS2

PS3

PS4

BA1

PP1

PP2

PP3

PP4

PM1

PM3

PM5

PM4

PM6

BS1

BS4

BS3

BP5

BP7

BP4

BP3

BP1

BP2

PVS1

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information **!**

[↗](#) Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.105G>C (NM_004360.5) variant in CDH1 is a missense variant predicted to predicted to cause substitution of Glu by Asp at amino acid 35 (p.Glu35Asp). This variant has been observed in more than 3 heterozygous individuals without GC, DGC, SRC tumours or LBC and whose families do not suggest HDGC (BS2_Supporting; Ambry, GeneDx, Invitae). This variant is absent from gnomAD 2.1.1 (PM2_Supporting). In summary, this variant meets the criteria to be classified as uncertain significance for DGLBCS based on the ACMG/AMP criteria applied, as specified by the ClinGen CDH1 VCEP (CDH1 VCEP specifications version 3.1): PM2_Supporting, BS2_Supporting.

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD 2.1.1 (PM2_Supporting).
BS2_Supporting			This variant has been observed in six individuals without GC, DGC, SRC tumours or LBC and whose families do not suggest HDGC (BS2_Supporting; Ambry, GeneDx, Invitae). Note that this includes one individual with IDC with lobular features and one unaffected individual with a family history of gastric cancer.

Not Met criteria codes

PS1			No other pathogenic missense variants have been reported.
PS2			To our knowledge, this variant has not been reported as de novo.
PS3			Functional studies have not been reported for this variant.
PS4			This variant has been observed in five individuals without DGC, LBC, SRC tumours and whose families do not suggest HDGC (Ambry, GeneDx, Invitae). Note that this includes one individual with IDC with lobular features (Invitae).
BA1			This variant is absent from gnomAD.
PP1			Not available.
PP2			PP2 does not apply to CDH1.
PP3			Multiple computational tools do not suggest that this variant impacts splicing.
PP4			PP4 does not apply to CDH1.

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.
PM6		✖	To our knowledge, this variant has not been reported as de novo.
BS1		✖	This variant is absent from gnomAD.
BS4		✖	Not available.
BS3		✖	Functional studies have not been reported for this variant.
BP5		✖	To our knowledge, this variant has not been reported in a case with an alternate molecular basis for disease.
BP7		✖	BP7 does not apply to this variant.
BP4		✖	Multiple computational tools do not suggest that this variant impacts splicing.
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 known pathogenic variant.
PVS1		✖	PVS1 does not apply to this variant.

Curation History 

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