

Variant: *NM_004360.3(CDH1):c.1009_1010delAG*
(*p.Ser337Phefs*)

Version: 1.1

CA186248 [↗](#)

183727 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 1df1468c-5fef-4c6c-956a-e4d26dc68f5e

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HGVS expressions

NM_004360.3(CDH1):c.1009_1010delAG (p.Ser337Phefs)

NC_000016.10:g.68812135_68812136del

CM000678.2:g.68812135_68812136del

NC_000016.9:g.68846038_68846039del

CM000678.1:g.68846038_68846039del

NC_000016.8:g.67403539_67403540del

NG_008021.1:g.79844_79845del

ENST00000261769.10:c.1009_1010del

ENST00000261769.9:c.1009_1010del

ENST00000422392.6:c.1009_1010del

ENST00000561751.1:c.631_632del

ENST00000562836.5:n.1080_1081del

ENST00000565810.1:n.53_54del

ENST00000566510.5:c.853_854del

ENST00000566612.5:c.1009_1010del

ENST00000611625.4:c.1009_1010del

ENST00000612417.4:c.1009_1010del

ENST00000621016.4:c.1009_1010del

NM_004360.3:c.1009_1010del

NM_001317184.1:c.1009_1010del

NM_001317185.1:c.-607_-606del

NM_001317186.1:c.-811_-810del

NM_004360.4:c.1009_1010del

NM_004360.5:c.1009_1010del

NM_001317184.2:c.1009_1010del

NM_001317185.2:c.-607_-606del

NM_001317186.2:c.-811_-810del

Pathogenic

Met criteria codes **4**

PS4_Moderate PM5_Supporting

PVS1 PM2_Supporting

Not Met criteria codes **22**

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

PS1

PP4

BS4

BP4

PS2

BA1

BS3

BP3

PS3

BS2

PM1

BP1

PP1

PM6

PM3

BP2

PP2

BS1

PM4

BP5

PP3

BP7

[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 Links

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Evidence submitted by expert panel

CDH1 VCEP

The c.1009_1010delAG (p.Ser337Phefs) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). The variant is absent in the gnomAD cohort (PM2_Supporting; <http://gnomad.broadinstitute.org/>). Two probands meet HDGC phenotype criteria (PS4_Moderate; SCV000212776.4). In summary, this variant meets criteria to be classified as Pathogenic based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): PVS1, PM2_Supporting, PS4_Moderate, PM5_Supporting.

Met criteria codes

PS4_Moderate		✓	SCV000212776.4: Two probands have signet ring gastric cancer at 40s and 50s.
PM5_Supporting		✓	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PVS1		✓	Variant predicted to undergo NMD with premature stop at position 348
PM2_Supporting		✓	Variant is absent in gnomAD cohort

Not Met criteria codes

PS1		✗	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein
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
PP1		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✗	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein
PP3		✗	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein

PP4		✖	Use PS4 in place of PP4
BA1		✖	Variant is absent in gnomAD cohort
BS2		✖	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
BS1		✖	Variant is absent in gnomAD cohort
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
PM1		✖	Do not use for this gene
PM3		✖	dominant disorder
PM4		✖	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein
BP4		✖	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein
BP3		✖	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein
BP1		✖	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein
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		✖	variant is predicted to result in a premature stop codon that leads to a truncated or absent protein

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