

Variant: *NM_004360.4(CDH1):c.70G>T (p.Glu24Ter)*

Version: 2.0

CA280997 [↗](#)

12240 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 7b7c5f44-b3d4-4d24-8272-50aaad05a175

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HGVS expressions

NM_004360.4:c.70G>T

NM_004360.4(CDH1):c.70G>T (p.Glu24Ter)

NC_000016.10:g.68738318G>T

CM000678.2:g.68738318G>T

NC_000016.9:g.68772221G>T

CM000678.1:g.68772221G>T

NC_000016.8:g.67329722G>T

NG_008021.1:g.6027G>T

ENST00000261769.10:c.70G>T

ENST00000261769.9:c.70G>T

ENST00000422392.6:c.70G>T

ENST00000566510.5:c.70G>T

ENST00000566612.5:c.70G>T

ENST00000611625.4:c.70G>T

ENST00000612417.4:c.70G>T

ENST00000621016.4:c.70G>T

NM_004360.3:c.70G>T

NM_001317184.1:c.70G>T

NM_001317185.1:c.-1546G>T

NM_001317186.1:c.-1750G>T

NM_004360.5:c.70G>T

NM_001317184.2:c.70G>T

NM_001317185.2:c.-1546G>T

NM_001317186.2:c.-1750G>T

Pathogenic

Met criteria codes 5

PS4_Supporting PM5_Supporting

PP1 PVS1 PM2_Supporting

Not Met criteria codes 21

PS1 PS2 PS3 BP5 BP7 BP4
BP3 BP1 BP2 PP2 PP3 PP4
PM1 PM3 PM4 PM6 BA1
BS1 BS4 BS3 BS2

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

[↗](#) **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 submitted by expert panel

CDH1 VCEP

The c.70G>T p.(Glu24Ter) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). This variant is absent in the gnomAD cohort (PM2_Supporting; <http://gnomad.broadinstitute.org>). The variant has been reported in at least one family meeting HDGC clinical criteria (PS4_Supporting; PMID: 10477433, 11104024). The variant was also found to co-segregate with disease in multiple affected family members, with 3 meioses observed (PP1; PMID: 10477433, 11104024). 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, PP1, PS4_Supporting, PM5_Supporting.

Met criteria codes

PS4_Supporting			Found in one family with DGC (at least 3 members (siblings) affected in family 4201) [PMID: 10477433, 11104024]. Follow up publication to PMID: 10477433. This paper reports on the family with c.70G>T, which is affected with diffuse gastric carcinoma. Three who tested positive and were affected (with diffuse gastric carcinoma) are now deceased. PubMed:11104024  Variant found in unaffected proband, and is also detected in her 3 affected children with gastric cancer in microdissected normal tissue from gastric biopsies. PubMed:10477433 
PM5_Supporting			Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PP1			Found in one family with DGC (at least 3 members (siblings) affected) [PMID: 10477433, 11104024]. 3-4 meioses in at least one family. Follow up publication to PMID: 10477433. This paper reports on the family with c.70G>T, which is affected with diffuse gastric carcinoma. Three siblings who tested positive and were affected (with diffuse gastric carcinoma) are now deceased. Pedigree not given, unable to tell which other family members are positive for the variant. PubMed:11104024  Family 4201 (pedigree provided) - Variant found in unaffected proband, and is also detected in her 3 affected children with gastric cancer in microdissected normal tissue from gastric biopsies. Husband of proband not tested for the variant. PubMed:10477433 
PVS1			Predicted NMD and upstream of the most 3' pathogenic variant c.2506G>T.
PM2_Supporting			Not observed in population databases.

Not Met criteria codes

PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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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
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
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
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
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

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			Follow up publication to PMID: 10477433. This paper reports on the family with c.70G>T, which is affected with diffuse gastric carcinoma. Three siblings who tested positive and were affected (with diffuse gastric carcinoma) are now deceased. Pedigree not given, unable to tell which other family members are positive for the variant. PubMed:11104024  Family 4201 (pedigree provided) - Variant found in unaffected proband, and is also detected in her 3 affected children with gastric cancer in microdissected normal tissue from gastric biopsies. Husband of proband not tested for the variant. PubMed:10477433 
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			Absent in population database

Curation History 		
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