

Variant: NM_004360.5(CDH1):c.1531C>T (p.Gln511Ter)

Version: 2.0

CA396463469 [↗](#)

428621 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 8c4ec2f8-cea4-44f6-ab24-a65cde5ecde7

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HGVS expressions

NM_004360.5:c.1531C>T

NM_004360.5(CDH1):c.1531C>T (p.Gln511Ter)

NC_000016.10:g.68815725C>T

CM000678.2:g.68815725C>T

NC_000016.9:g.68849628C>T

CM000678.1:g.68849628C>T

NC_000016.8:g.67407129C>T

NG_008021.1:g.83434C>T

ENST00000261769.10:c.1531C>T

ENST00000261769.9:c.1531C>T

ENST00000422392.6:c.1348C>T

ENST00000562836.5:n.1602C>T

ENST00000566510.5:c.*197C>T

ENST00000566612.5:c.1531C>T

ENST00000611625.4:c.1594C>T

ENST00000612417.4:c.1531C>T

ENST00000621016.4:c.1531C>T

NM_004360.3:c.1531C>T

NM_001317184.1:c.1348C>T

NM_001317185.1:c.-18C>T

NM_001317186.1:c.-289C>T

NM_004360.4:c.1531C>T

NM_001317184.2:c.1348C>T

NM_001317185.2:c.-18C>T

NM_001317186.2:c.-289C>T

Pathogenic

Met criteria codes **4**

PS4_Moderate

PVS1

PM5_Supporting

PM2_Supporting

Not Met criteria codes **22**

BA1

BS1

BS4

BS3

BS2

BP5

BP7

BP4

BP3

BP1

BP2

PS1

PS2

PS3

PP1

PP2

PP3

PP4

PM1

PM3

PM4

PM6

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**

Evidence submitted by expert panel

CDH1 VCEP

The c.1531C>T p.(Gln511*) 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 two families meeting HDGC clinical criteria (PS4_moderate; PMID: 31600923 and SCV000580698.3). 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			Two probands meet HDGC phenotype criteria (PMID: 31600923; SCV000580698.3).
PVS1			Predicted NMD, exon 10 of 16.
PM5_Supporting			Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PM2_Supporting			Absent in population databases.

Not Met criteria codes

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			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
BS2			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
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
PP1		✖	Proband and sibling affected with DGC, while mother, maternal grandmother, mother's sister and mother's sister's son have chronic gastritis and intestinal metaplasia (PMID: 31600923).
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

Curation History [↗](#)

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