

Variant: NM_004360.5(CDH1):c.1578G>A (p.Trp526Ter)

Version: 2.1

CA10588624 [↗](#)

265511 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: dffb17c8-bb5d-434c-aefb-9a9dcaef0dc8

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HGVS expressions

NM_004360.5(CDH1):c.1578G>A (p.Trp526Ter)

NM_004360.5:c.1578G>A

NC_000016.10:g.68819292G>A

CM000678.2:g.68819292G>A

NC_000016.9:g.68853195G>A

CM000678.1:g.68853195G>A

NC_000016.8:g.67410696G>A

NG_008021.1:g.87001G>A

ENST00000261769.10:c.1578G>A

ENST00000261769.9:c.1578G>A

ENST00000422392.6:c.1395G>A

ENST00000562836.5:n.1649G>A

ENST00000566510.5:c.*244G>A

ENST00000566612.5:c.1566-2709G>A

ENST00000611625.4:c.1641G>A

ENST00000612417.4:c.1578G>A

ENST00000621016.4:c.1578G>A

NM_004360.3:c.1578G>A

NM_001317184.1:c.1395G>A

NM_001317185.1:c.30G>A

NM_001317186.1:c.-254-2709G>A

NM_004360.4:c.1578G>A

NM_001317184.2:c.1395G>A

NM_001317185.2:c.30G>A

NM_001317186.2:c.-254-2709G>A

Pathogenic

Met criteria codes 3

PM2_Supporting

PM5_Supporting

PVS1

Not Met criteria codes 23

BS2

BS1

BS4

BS3

BP5

BP7

BP4

BP3

BP1

BP2

PS1

PS2

PS3

PS4

BA1

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.1578G>A p.(Trp526Ter) 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>). 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, PM5_Supporting.

Met criteria codes

PM2_Supporting			Absent in population databases.
PM5_Supporting			Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PVS1			Exon 11 of 16, predicted NMD.

Not Met criteria codes

BS2			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
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		✖	Same amino acid change in the c.1577G>A p.(Trp526Ter) variant was reported in a proband meeting the HDGC phenotype criteria, which is an established pathogenic variant (PS1; PMID: 30466290). However, PS1 is not applicable for CDH1.
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		✖	SCV000322481.6 - proband does not meet HGDC criteria. PMID: 30466290 - c.1577G>A p.(Trp526*) in 34 yo with stage IV diffuse gastric ADC (signet ring cell).
BA1		✖	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
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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