

Variant: *NM_001317186.2:c.561del*

Version: 2.0

CA1139532475 [↗](#)

981224 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: b361f4f7-29de-4a4a-99e2-94bafec6f4f

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HGVS expressions

NM_001317186.2:c.561del

NC_000016.10:g.68833376del

CM000678.2:g.68833376del

NC_000016.9:g.68867279del

CM000678.1:g.68867279del

NC_000016.8:g.67424780del

NG_008021.1:g.101085del

ENST00000261769.10:c.2526del

ENST00000261769.9:c.2526del

ENST00000422392.6:c.2343del

ENST00000562118.1:n.744del

ENST00000562836.5:n.2597del

ENST00000566510.5:c.*1192del

ENST00000566612.5:c.*766del

ENST00000611625.4:c.2589del

ENST00000612417.4:c.1854-815del

ENST00000621016.4:c.1866-827del

NM_004360.3:c.2526del

NM_001317184.1:c.2343del

NM_001317185.1:c.978del

NM_001317186.1:c.561del

NM_004360.4:c.2526del

NM_004360.5:c.2526del

NM_001317184.2:c.2343del

NM_001317185.2:c.978del

Uncertain Significance

Met criteria codes **3**

PVS1_Moderate

PM2_Supporting

PS4_Supporting

Not Met criteria codes **23**

PS1

PS2

PS3

BP5

BP7

BP4

BP3

BP1

BP2

PP1

PP2

PP3

PP4

PM6

PM1

PM3

PM5

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.2526del (p.Ala843LeufsTer3) variant results in a premature stop codon that leads to a truncated protein. It is located within the nonsense mediated decay resistant zone, and downstream of codon 836 where the most 3' pathogenic variant in CDH1 terminates (PVS1_Moderate, PMID: 29798843). This variant is absent in the gnomAD cohort (PM2_Supporting; <http://gnomad.broadinstitute.org>). One family meets the HDGC criteria (PS4_Supporting; Internal lab contributor). In summary, the clinical significance of this variant is uncertain based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): PVS1_Moderate, PM2_Supporting, PS4_Supporting. This VUS variant is trending to the pathogenic side. The CDH1 VCEP will re-evaluate it, if more evidence emerge in the future.

Met criteria codes

PVS1_Moderate			PTC created in exon 16/16 at position 846 in the NMD-resistant zone, downstream of p.Glu836Ter (p.Ala843LeufsTer3)
PM2_Supporting			Absent in gnomAD v2.1 & v3 in a region of sufficient coverage
PS4_Supporting			One family meets the HDGC criteria.

Not Met criteria codes

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
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
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
PM6		✖	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
PM5		✖	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
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

Curation History 		
		
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