

Variant: NM_004360.4(CDH1):c.1085delT (p.Val362Glyfs)

CA658658486 [↗](#)

483264 (ClinVar) [↗](#)

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

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0007648](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: c5d03db0-c5d6-426b-9059-585ca0cccb44

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HGVS expressions

NM_004360.4(CDH1):c.1085delT (p.Val362Glyfs)

NM_004360.4:c.1085delT

NC_000016.10:g.68812211del

CM000678.2:g.68812211del

NC_000016.9:g.68846114del

CM000678.1:g.68846114del

NC_000016.8:g.67403615del

NG_008021.1:g.79920del

ENST00000261769.10:c.1085del

ENST00000261769.9:c.1085del

ENST00000422392.6:c.1085del

ENST00000561751.1:n.707del

ENST00000562836.5:n.1156del

ENST00000565810.1:n.129del

ENST00000566510.5:c.929del

ENST00000566612.5:c.1085del

ENST00000611625.4:c.1085del

ENST00000612417.4:c.1085del

ENST00000621016.4:c.1085del

NM_004360.3:c.1085del

NM_001317184.1:c.1085del

NM_001317185.1:c.-531del

NM_001317186.1:c.-735del

NM_004360.4:c.1085del

NM_004360.5:c.1085del

NM_001317184.2:c.1085del

NM_001317185.2:c.-531del

NM_001317186.2:c.-735del

NM_004360.5(CDH1):c.1085del (p.Val362fs)

Pathogenic

Met criteria codes 4

PM2_Supporting

PVS1

PM5_Supporting

PS4_Supporting

Not Met criteria codes 22

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

PS2

BP1

PP1

BA1

PS3

BP4

PM6

BS3

PS1

BP3

PM3

BS1

BP5

PP2

PM1

BS4

BP7

PP3

PM4

BP2

PP4

Evidence Links 0

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.1085delT (p.Val362Glyfs*31) 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>). This variant has been reported in at least one family meeting HDGC clinical criteria (PS4_Supporting; SCV000669065.1). Therefore, 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_Supporting, PM5_Supporting.

Met criteria codes

PM2_Supporting	i	✓	Absent in gnomAD.
PVS1	i	✓	Frameshift causing CDH1 truncation. Truncating mutations downstream of this mutation. CDH1 has significant pNull score in ExAC.
PM5_Supporting	i	✓	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PS4_Supporting	i	✓	gastric cancer observed in proband and sister

Not Met criteria codes

PS2	i	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	i	✗	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
BP5	i	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7	i	✗	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
BP1			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			Variant causes truncation/protein length change.
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
PP1			Although gastric cancer observed in sister, no segregation data for variant is available.
PM6			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
PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			Variant causes truncation/protein length change.
BA1			Absent in gnomAD.
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			Absent in gnomAD.
BS4			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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