

Variant: NM_004360.4(CDH1):c.2430delT (p.Phe810Leufs)

CA197715 [↗](#)

187464 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 9eee2198-3726-4f14-81e7-c8c62c01506a

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HGVS expressions

NM_004360.4(CDH1):c.2430delT (p.Phe810Leufs)

NM_004360.4:c.2430delT

NC_000016.10:g.68829788del

CM000678.2:g.68829788del

NC_000016.9:g.68863691del

CM000678.1:g.68863691del

NC_000016.8:g.67421192del

NG_008021.1:g.97497del

ENST00000261769.10:c.2430del

ENST00000261769.9:c.2430del

ENST00000422392.6:c.2247del

ENST00000562118.1:n.648del

ENST00000562836.5:n.2501del

ENST00000566510.5:c.*1096del

ENST00000566612.5:c.*670del

ENST00000611625.4:c.2493del

ENST00000612417.4:c.1853+3234del

ENST00000621016.4:c.1866-4415del

NM_004360.3:c.2430del

NM_001317184.1:c.2247del

NM_001317185.1:c.882del

NM_001317186.1:c.465del

NM_004360.4:c.2430del

NM_004360.5:c.2430del

NM_001317184.2:c.2247del

NM_001317185.2:c.882del

NM_001317186.2:c.465del

NM_004360.5(CDH1):c.2430del (p.Phe810fs)

Pathogenic

Met criteria codes 3

PVS1_Strong

PS4

PM2_Supporting

Not Met criteria codes 23

PS3

PS1

PS2

BP7

BP5

BP3

BP1

BP4

BP2

PP2

PP3

PP4

PP1

PM6

PM1

PM4

PM5

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen CDH1 Expert Panel
Specifications to the ACMG/AMP Variant Interpretation

Evidence submitted by expert panel

CDH1 VCEP

The c.2430delT (p.Phe810Leufs*6) variant is predicted to result in a premature stop codon that leads to a truncated protein. However, it is located within the nonsense mediated decay resistance region upstream of c.2506G>T (p.Glu836*) (PVS1_Strong). This variant is absent in the gnomAD cohort (PM2_Supporting; <http://gnomad.broadinstitute.org>). This variant has been reported in at least 4 families meeting HDGC clinical criteria (PS4; PMID 26182300, SCV000261293.4, SCV000218032.4). 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_Strong, PM2_Supporting, PS4.

Met criteria codes

PVS1_Strong			Frameshift variant and LOF is a known mechanism of disease in CDH1.
PS4			Variant reported in family with 3 cases of DGC, meeting IGCLC criteria. Unclear if all relatives had variant. Clinvar entry: This variant has been reported in at least three families affected with diffuse gastric cancer and gastric cancer (PMID: 26182300). Total 4 families.
			Variant reported in one family where the proband had DGC at age 45. There were 3 cases total in the family, one of which was DGC (unclear if this is the proband). Family meets IGCLC criteria. PubMed:26182300 
PM2_Supporting			Not in ExAC or GnomAD

Not Met criteria codes

PS3			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
BP7			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

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
BP4		✖	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		✖	Variant reported in one family where the proband had DGC at age 45. There were 3 cases total in the family, one of which was DGC (unclear if this is the proband). Family meets IGCLC criteria. PubMed:26182300 
PP1		✖	Variant present in unaffected proband. Brother had gastric cancer at age 33 (not clear if he carries variant) and father with variant had gastric cancer at age 56.
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
PM4		✖	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
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1		✖	Not in ExAC or GnomAD
BS3		✖	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
BS1			Not in ExAC or GnomAD
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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