The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Approved on: 2018-11-21
Published on: 2018-12-07

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

PS4 PVS1_Strong PM2_Supporting

Not Met criteria codes 23

PS3 PS1 PS2 PP2 PP3 PP4 PP1 PM1 PM4 PM5 PM3 PM6 BA1 BS3 BS4 BS1

Expert Panel

CDH1 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation*

BS2 BP7 BP5 BP3 BP1 BP4 BP2

Evidence Links 1

Guidelines Version 3.1

Criteria Specification Approval History

Criteria Specifications for this VCEP

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

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
PVS1_Strong	✔	Frameshift variant and LOF is a known mechanism of disease in CDH1.
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
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	ℹ	✖	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.
PM1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4	ℹ	✖	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
PM6	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1	ℹ	✖	Not in ExAC or GnomAD
BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	Not in ExAC or GnomAD
BS2	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
BP5	ℹ	✖	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

Curation History

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.