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_004360.5(CDH1):c.1531C>T (p.Gln511Ter)

Version: 2.0

CA396463469

428621 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8c4ec2f8-cea4-44f6-ab24-a65cde5ecde7
Approved on: 2023/8/25
Published on: 2023/8/25

HGVS expressions

NM_004360.5(CDH1):c.1531C>T (p.Gln511Ter)
NM_004360.5:c.1531C>T
NC_000016.10:g.68815725C>T
CM000678.2:g.68815725C>T
NC_000016.9:g.68849628C>T
CM000678.1:g.68849628C>T
NC_000016.8:g.67407129C>T
NG_008021.1:g.83434C>T
ENST00000261769.10:c.1531C>T
ENST00000261769.9:c.1531C>T
ENST00000422392.6:c.1348C>T
ENST00000562836.5:n.1602C>T
ENST00000566510.5:c.*197C>T
ENST00000566612.5:c.1531C>T
ENST00000611625.4:c.1594C>T
ENST00000612417.4:c.1531C>T
ENST00000621016.4:c.1531C>T
NM_004360.3:c.1531C>T
NM_001317184.1:c.1348C>T
NM_001317185.1:c.-18C>T
NM_001317186.1:c.-289C>T
NM_004360.4:c.1531C>T
NM_001317184.2:c.1348C>T
NM_001317185.2:c.-18C>T
NM_001317186.2:c.-289C>T

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PS4_Moderate PM5_Supporting

Not Met criteria codes 22

BA1 PP1 PP2 PP3 PP4 PM6 PM1 PM3 PM4 BS1 BS4 BS3 BS2 PS1 PS2 PS3 BP5 BP7 BP4 BP3 BP1 BP2

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 Links 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.1531C>T p.(Gln511*) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_supporting). This variant is absent in the gnomAD cohort (PM2_supporting; http://gnomad.broadinstitute.org). The variant has been reported in at least two families meeting HDGC clinical criteria (PS4_moderate; PMID: 31600923 and SCV000580698.3). 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, PS4_moderate, PM5_supporting.

Met criteria codes

PM2_Supporting	✔	Absent in population databases.
PVS1	✔	Predicted NMD, exon 10 of 16.
PS4_Moderate	✔	Two probands meet HDGC phenotype criteria (PMID: 31600923; SCV000580698.3).
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	✖	Proband and sibling affected with DGC, while mother, maternal grandmother, mother's sister and mother's sister's son have chronic gastritis and intestinal metaplasia (PMID: 31600923).
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
PM4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	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
BS3	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2	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
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
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
BP4	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

BP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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