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.187C>T (p.Arg63Ter)

156496 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0007648)
Inheritance Mode: Autosomal dominant inheritance
UUID: be4384f2-4317-4809-956c-12533c2847e1
Approved on: 2018-11-21
Published on: 2018-12-07

HGVS expressions

NM_004360.4:c.187C>T
NM_004360.4(CDH1):c.187C>T (p.Arg63Ter)
NM_004360.5(CDH1):c.187C>T (p.Arg63Ter)

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PS4_Supporting PM5_Supporting

Not Met criteria codes 22

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

Evidence Links 1

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**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

CDH1 VCEP

The c.187C>T (p.Arg63*) 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 one family meeting HDGC clinical criteria (PS4_Supporting; PMID: 9751616). 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_Supporting, PM5_Supporting.

Met criteria codes

PM2_Supporting	✔	Absent from gnomAD

PVS1	✔	Truncating variant in Exon 3 of 16.
PS4_Supporting	✔	Observed in an individual with bilateral LBC at 39yo. Father DGC at 47 (not known if carrier), brother DGC at 39yo (not known if carrier), sister DGC at 44yo (not known if carrier), Paternal Aunt breast in 60s. From excel document. Used PMID: 9751616 only for PS4_Supporting code. Variant identified in father and son with gastric cancer. PubMed:9751616
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.

Not Met criteria codes

BA1	✖	Absent from gnomAD
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
PP1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4	✖	Observed in an individual with bilateral LBC at 39yo. Father DGC at 47 (not known if carrier), brother DGC at 39yo (not known if carrier), sister DGC at 44yo (not known if carrier), Paternal Aunt breast in 60s. Excel document.
PM6	✖	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
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
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

BS1		✖	Absent from gnomAD
BS2		✖	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
PS3		✖	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

Curation History

Showing 1 to 2 of 2 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_004360.4(CDH1):c.187C>T (p.Arg6...	Pathogenic	CDH1-Related Diffuse Gastric And Lobular Breast Cancer	2023-08-29	2.0	ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1	CDH1
View	NM_004360.4(CDH1):c.187C>T (p.Arg6...	Pathogenic	Hereditary Diffuse Gastric Cancer	2020-06-03	1.0	-	CDH1

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