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.2549_2550delCC (p.Ser850Phefs)

Version: 2.0

CA166884

141951 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: d170d032-2b2a-4b4c-930b-07c0d30139ca
Approved on: 2023/8/4
Published on: 2023/8/4

HGVS expressions

NM_004360.4(CDH1):c.2549_2550delCC (p.Ser850Phefs)
NM_004360.4:c.2549_2550del
NC_000016.10:g.68833399_68833400del
CM000678.2:g.68833399_68833400del
NC_000016.9:g.68867302_68867303del
CM000678.1:g.68867302_68867303del
NC_000016.8:g.67424803_67424804del
NG_008021.1:g.101108_101109del
ENST00000261769.10:c.2549_2550del
ENST00000261769.9:c.2549_2550del
ENST00000422392.6:c.2366_2367del
ENST00000562118.1:n.767_768del
ENST00000562836.5:n.2620_2621del
ENST00000566510.5:c.*1215_*1216del
ENST00000566612.5:c.*789_*790del
ENST00000611625.4:c.2612_2613del
ENST00000612417.4:c.1854-792_1854-791del
ENST00000621016.4:c.1866-804_1866-803del
NM_004360.3:c.2549_2550del
NM_001317184.1:c.2366_2367del
NM_001317185.1:c.1001_1002del
NM_001317186.1:c.584_585del
NM_004360.5:c.2549_2550del
NM_001317184.2:c.2366_2367del
NM_001317185.2:c.1001_1002del
NM_001317186.2:c.584_585del

Uncertain Significance

Met criteria codes 2

PM2_Supporting PVS1_Moderate

Not Met criteria codes 24

PM6 PM1 PM3 PM5 PM4 BA1 BS2 BS1 BS4 BS3 BP5 BP7 BP4 BP3 BP1 BP2 PS1

Expert Panel

CDH1 VCEP

Criteria Specification Information

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

PS2 PS3 PS4 PP1 PP2 PP3 PP4

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.2549_2550delCC (p.Ser850PhefsTer10) variant results in a premature stop codon that leads to a truncated protein. It is located within the nonsense mediated decay resistant zone, and downstream of codon 836 where the most 3' pathogenic variant in CDH1 terminates (PVS1_Moderate, PMID: 29798843). This variant is absent in the gnomAD cohort (PM2_Supporting; http://gnomad.broadinstitute.org). In summary, the clinical significance of this variant is uncertain based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel (CDH1 VCEP specifications version 3.1): PVS1_Moderate, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	Absent in gnomAD
PVS1_Moderate	✔	A 2 bp deletion in the last exon predicted to result in a premature termination codon in the NMD-resistant zone, downstream of codon 836

Not Met criteria codes

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
PM5	✖	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
BA1	✖	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

BS1		✖	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
BP5		✖	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
BP4		✖	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
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
PS4		✖	No reported cases that meet HDGC clinical criteria. Family does not meet HDGC clinical criteria. Proband with bilateral/contralateral DCIS and IDC/ILC <50, and adenomatous polyps. Same case that has been submitted to ClinVar (SCV000185568.5). PubMed:29798843
PP1		✖	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	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_004360.4(CDH1):c.2549_2550delC...	Uncertain Significance	CDH1-Related Diffuse Gastric And Lobular Breast Cancer	2023-08-04	2.0	ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1	CDH1
View	NM_004360.4(CDH1):c.2549_2550delC...	Uncertain Significance	Hereditary Diffuse Gastric Cancer	2019-09-17	1.0	-	CDH1

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