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_004360.3:c.2265T>A

CA396469962

599653 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0007648)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2efeb055-c565-494f-8e8d-5ae0dccaa3e7
Approved on: 2018-11-22
Published on: 2018-12-07

HGVS expressions

NM_004360.3:c.2265T>A
NC_000016.10:g.68828274T>A
CM000678.2:g.68828274T>A
NC_000016.9:g.68862177T>A
CM000678.1:g.68862177T>A
NC_000016.8:g.67419678T>A
NG_008021.1:g.95983T>A
ENST00000261769.10:c.2265T>A
ENST00000261769.9:c.2265T>A
ENST00000422392.6:c.2082T>A
ENST00000562118.1:n.483T>A
ENST00000562836.5:n.2336T>A
ENST00000566510.5:c.*931T>A
ENST00000566612.5:c.*505T>A
ENST00000611625.4:c.2328T>A
ENST00000612417.4:c.1853+1720T>A
ENST00000621016.4:c.1866-5929T>A
NM_001317184.1:c.2082T>A
NM_001317185.1:c.717T>A
NM_001317186.1:c.300T>A
NM_004360.4:c.2265T>A
NM_004360.5:c.2265T>A
NM_001317184.2:c.2082T>A
NM_001317185.2:c.717T>A
NM_001317186.2:c.300T>A
NM_004360.5(CDH1):c.2265T>A (p.Tyr755Ter)

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PS4_Supporting PM5_Supporting

Not Met criteria codes 22

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

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 1 **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

CDH1 VCEP

The c.2265T>A (p.Tyr755*) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_Supporting). The variant is absent in the gnomAD cohort (PM2_Supporting; http://gnomad.broadinstitute.org). Additionally, this variant has been reported in at least one family meeting HDGC clinical criteria (PS4_Supporting; PMID: 26182300). 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 14 of 16.
PS4_Supporting	✔	Observed in unaffected proband (38yo). Mother - DGC at 33 (not known if carrier). MGM GC at 38 (not known if carrier). Excel sheet seems same as PMID: 26182300. eTable2 - Observed in the index case from a family meeting IGCLC 2010 clinical criteria for HDGC. Index case is unaffected, unknown ethnicity. 2 affected family members (1 confirmed DGC, 1 GC, at 33 and 38). Not clear if family members are carriers. PubMed:26182300
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.

Not Met criteria codes

BA1	✖	Absent from gnomAD
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	✖	Observed in unaffected proband (38yo). Mother - DGC at 33 (not known if carrier). MGM GC at 38 (not known if carrier). Excel sheet seems same as PMID: 26182300.

eTable2 - Observed in the index case from a family meeting IGCLC 2010 clinical criteria for HDGC. Index case is unaffected, unknown ethnicity. 2 affected family members (1 confirmed DGC, 1 GC, at 33 and 38). Not clear if family members are carriers. PubMed:26182300

PM6	✖	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
PM4	✖	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
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
PS1	✖	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
BP2	✖	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

Curation History

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