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Variant: NM_004360.4(CDH1):c.1023T>G (p.Tyr341Ter)

Version: 2.0

CA281453

156374 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: 36f417ce-8eb5-453a-99cc-96c68913737f
Approved on: 2023/8/29
Published on: 2023/8/29

HGVS expressions

NM_004360.4(CDH1):c.1023T>G (p.Tyr341Ter)
NM_004360.4:c.1023T>G
NC_000016.10:g.68812149T>G
CM000678.2:g.68812149T>G
NC_000016.9:g.68846052T>G
CM000678.1:g.68846052T>G
NC_000016.8:g.67403553T>G
NG_008021.1:g.79858T>G
ENST00000261769.10:c.1023T>G
ENST00000261769.9:c.1023T>G
ENST00000422392.6:c.1023T>G
ENST00000561751.1:c.645T>G
ENST00000562836.5:n.1094T>G
ENST00000565810.1:n.67T>G
ENST00000566510.5:c.867T>G
ENST00000566612.5:c.1023T>G
ENST00000611625.4:c.1023T>G
ENST00000612417.4:c.1023T>G
ENST00000621016.4:c.1023T>G
NM_004360.3:c.1023T>G
NM_001317184.1:c.1023T>G
NM_001317185.1:c.-593T>G
NM_001317186.1:c.-797T>G
NM_004360.5:c.1023T>G
NM_001317184.2:c.1023T>G
NM_001317185.2:c.-593T>G
NM_001317186.2:c.-797T>G

Pathogenic

Met criteria codes 4

PVS1 PM5_Supporting PS4_Supporting PM2_Supporting

Not Met criteria codes 22

BA1 BP5 BP7 BP4 BP3 BP1 BP2 BS1 BS4 BS3 BS2 PP1

Expert Panel

CDH1 VCEP

Criteria Specification Information

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

PP2 PP3 PP4 PM6 PM1
PM3 PM4 PS1 PS2 PS3

Evidence Links 5

Guidelines Version 3.1

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.1023T>G (p.Tyr341*) 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: 27192129). 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

PVS1	✔	Introduction of a PTC at codon 341 in exon 8 of 16. Predicted to undergo NMD
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PS4_Supporting	✔	One Northern Brazilian family that fulfils the clinical criteria for HDGC (PMID: 27192129) Review article in German PubMed:20824432 Review article that references the presence of the variant in two other studies (Guliford et al & El-Husny et al) PubMed:29511593 References the proband from Guilford et al 2010 PubMed:22225527 One Northern Brazilian family that fulfils the clinical criteria for HDGC of the International Gastric Cancer Linkage Consortium. Case1 and case 3 are siblings and both carriers (1 meiosis). PubMed:27192129 Review article. Only information about the variant is that it is unpublished results from University of Otago. PubMed:20373070
PM2_Supporting	✔	Absent in gnomAD

Not Met criteria codes

BA1	✖	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
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
BS2	✖	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
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		✖	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

Curation History

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