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Variant: NM_004360.4(CDH1):c.1792C>T (p.Arg598Ter)

CA281000

12241 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0007648)
Inheritance Mode: Autosomal dominant inheritance
UUID: 8d966550-3108-4786-8d4d-092988c239d6
Approved on: 2018-11-21
Published on: 2018-12-07

HGVS expressions

NM_004360.4(CDH1):c.1792C>T (p.Arg598Ter)
NM_004360.4:c.1792C>T
NC_000016.10:g.68822081C>T
CM000678.2:g.68822081C>T
NC_000016.9:g.68855984C>T
CM000678.1:g.68855984C>T
NC_000016.8:g.67413485C>T
NG_008021.1:g.89790C>T
ENST00000261769.10:c.1792C>T
ENST00000261769.9:c.1792C>T
ENST00000422392.6:c.1609C>T
ENST00000562836.5:n.1863C>T
ENST00000566510.5:c.*458C>T
ENST00000566612.5:c.*32C>T
ENST00000611625.4:c.1855C>T
ENST00000612417.4:c.1792C>T
ENST00000621016.4:c.1792C>T
NM_004360.3:c.1792C>T
NM_001317184.1:c.1609C>T
NM_001317185.1:c.244C>T
NM_001317186.1:c.-174C>T
NM_004360.5:c.1792C>T
NM_001317184.2:c.1609C>T
NM_001317185.2:c.244C>T
NM_001317186.2:c.-174C>T
NM_004360.5(CDH1):c.1792C>T (p.Arg598Ter)

Pathogenic

Met criteria codes 6

PP1_Strong PS4 PS2 PVS1 PM2_Supporting PM5_Supporting

Not Met criteria codes 20

PP4 PP2 PP3 PM4 PM3 PM1 BA1 PM6 BS3 BS4 BS1 BS2 PS1 PS3 BP7 BP5 BP3 BP2 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 4 **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

CDH1 VCEP

The c.1792C>T (p.Arg598*) 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). This variant was found to co-segregate with disease in multiple affected family members, with >7 meioses observed across at least two families (PP1_Strong; PMID: 21696387, 16061854, 11419427 and SCV000275702.5). This variant has also been reported in at least four families meeting HDGC clinical criteria (PS4_Strong; PMID: 9751616, 21696387, 16061854, 11419427). There is one known de novo observation of this variant with parental confirmation in a patient with diffuse gastric cancer and/or lobular breast cancer (PS2; PMID: 21696387). 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, PP1_Strong, PS4, PS2, PM5_Supporting.

Met criteria codes

PP1_Strong	Four families (3 in literature one provided in excel sheet - SCV000275702.5) with multiple family members with the variant and with diffuse gastric cancer. Variant in 5 family members with 4 having gastric cancers and 1 having diffuse gastric cancer PubMed:16061854 Variant found in proband and her mother both with diffuse gastric cancer PubMed:21696387
PS4	Multiple families with history of gastric cancer and multiple family members with the variant Variant identified in three sisters (two are identical twins) with gastric cancer with a dominant family history of gastric cancer. PubMed:11419427 Variant in 5 family members with 4 having gastric cancers and 1 having diffuse gastric cancer PubMed:16061854 Variant identified in identical twin sisters with gastric cancer dx in their 20's with a dominant family history of gastric cancer. PubMed:9751616 Variant found in proband and her mother both with diffuse gastric cancer PubMed:21696387
PS2	Variant confirmed de novo in patient with gastric cancer. Daughter also had the variant and presented with gastric cancer. Maternity and Paternity confirmed.
PVS1	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2_Supporting	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5_Supporting	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.

Not Met criteria codes

PP4		✖	Multiple families with history of gastric cancer and multiple family members with the variant
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3	ℹ	✖	Splicing models show disruption of an exonic ese site.
PM4	ℹ	✖	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
BA1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6	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
BS4	ℹ	✖	Variant in 5 family members with 4 having gastric cancers and 1 having diffuse gastric cancer PubMed:16061854 Variant found in proband and her mother both with diffuse gastric cancer PubMed:21696387
BS1	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
PS3	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
BP5	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
BP2	ⓘ	✖	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	ⓘ	✖	Splicing models show disruption of an exonic ese site.

Curation History

Showing 1 to 2 of 2 rows

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