Variant: NM_004360.5(CDH1):c.360dup (p.His121fs)

Version: 1.0

CA10583408

239903 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: e116f274-4c06-47a0-a9a0-fef88440fff9
Approved on: 2023-08-25
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HGVS expressions

NM_004360.5:c.360dup
NM_004360.5(CDH1):c.360dup (p.His121fs)
NC_000016.10:g.68801866dup
CM000678.2:g.68801866dup
NC_000016.9:g.68835769dup
CM000678.1:g.68835769dup
NC_000016.8:g.67393270dup
NG_008021.1:g.69575dup
ENST00000261769.10:c.360dup
ENST00000261769.9:c.360dup
ENST00000422392.6:c.360dup
ENST00000561751.1:c.127dup
ENST00000562836.5:n.431dup
ENST00000564676.5:n.642dup
ENST00000564745.1:n.355dup
ENST00000566510.5:c.360dup
ENST00000566612.5:c.360dup
ENST00000611625.4:c.360dup
ENST00000612417.4:c.360dup
ENST00000621016.4:c.360dup
NM_004360.3:c.360dup
NM_001317184.1:c.360dup
NM_001317185.1:c.-1256dup
NM_001317186.1:c.-1460dup
NM_004360.4:c.360dup
NM_001317184.2:c.360dup
NM_001317185.2:c.-1256dup
NM_001317186.2:c.-1460dup

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PM5_Supporting PS4_Supporting

Not Met criteria codes 22

Expert Panel

Criteria Specification Information

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

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

Evidence Links 0

Guidelines Version 3.1

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.360dupG (p.His121Alafs*47) 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). This variant has been reported in at least one family meeting HDGC clinical criteria (PS4_Supporting, SCV000288479.2). 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	✔	This variant is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.
PVS1	✔	This variant occurs in exon 3 and is predicted to result in a premature stop codon that leads to a truncated or absent protein.
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.
PS4_Supporting	✔	This variant was identified in a proband meeting the HDGC criteria (SCV000288479.2).

Not Met criteria codes

BA1	✖	This variant is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.
PS1	✖	PS1 does not apply to this variant.
PS2	✖	To our knowledge, this variant has not been reported as de novo.
PS3	✖	PS3 does not apply to frameshift variants.
PP1	✖	To our knowledge, segregation of this variant has not been reported.
PP2	✖	PP2 does not apply to CDH1.
PP3	✖	PP3 does not apply to frameshift variants.

PP4		✖	PP4 does not apply to CDH1.
PM1		✖	PM1 does not apply to CDH1.
PM3		✖	PM3 does not apply to CDH1.
PM4	ℹ	✖	PM4 does not apply to frameshift variants.
PM6	ℹ	✖	To our knowledge, this variant has not been reported as de novo.
BS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	This variant is absent from populations in gnomAD, ExAC, 1000 Genomes and ESP.
BS4	ℹ	✖	To our knowledge, segregation of this variant has not been reported.
BS3	ℹ	✖	BS3 does not apply to frameshift variants.
BP4	ℹ	✖	BP4 does not apply to frameshift variants.
BP3		✖	BP3 does not apply to CDH1.
BP1		✖	BP1 does not apply to CDH1.
BP2	ℹ	✖	To our knowledge, this variant has not been reported in cis or trans with a pathogenic variant.
BP5	ℹ	✖	To our knowledge, this variant has not been reported in a case with an alternate molecular basis for disease.
BP7	ℹ	✖	BP7 does not apply to frameshift variants.

Curation History

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