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_004360.5(CDH1):c.1921C>T (p.Gln641Ter)

Version: 2.0

CA169506

142826 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: a13097ce-e827-4856-9d7e-7df256027eb9
Approved on: 2023/8/25
Published on: 2023/8/25

HGVS expressions

NM_004360.5(CDH1):c.1921C>T (p.Gln641Ter)
NM_004360.5:c.1921C>T
NC_000016.10:g.68822210C>T
CM000678.2:g.68822210C>T
NC_000016.9:g.68856113C>T
CM000678.1:g.68856113C>T
NC_000016.8:g.67413614C>T
NG_008021.1:g.89919C>T
ENST00000261769.10:c.1921C>T
ENST00000261769.9:c.1921C>T
ENST00000422392.6:c.1738C>T
ENST00000562836.5:n.1992C>T
ENST00000566510.5:c.*587C>T
ENST00000566612.5:c.*161C>T
ENST00000611625.4:c.1984C>T
ENST00000612417.4:c.1830+91C>T
ENST00000621016.4:c.1865+56C>T
NM_004360.3:c.1921C>T
NM_001317184.1:c.1738C>T
NM_001317185.1:c.373C>T
NM_001317186.1:c.-45C>T
NM_004360.4:c.1921C>T
NM_001317184.2:c.1738C>T
NM_001317185.2:c.373C>T
NM_001317186.2:c.-45C>T

Pathogenic

Met criteria codes 4

PM2_Supporting PVS1 PS4_Supporting PM5_Supporting

Not Met criteria codes 22

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

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 0

Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.1921C>T p.(Gln641Ter) variant is predicted to result in a premature stop codon that leads to a truncated or absent protein (PVS1, PM5_supporting). The variant is present in <1/100,000 alleles 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; SCV000187340.5). 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	✔	Present in 1 of 251462 alleles (0.001%).
PVS1	✔	predicted NMD, exon 12 of 16.
PS4_Supporting	✔	SCV000187340.5 - meet HDGC phenotype criteria (same proband as DOI: 10.1200/PO.16.00021)
PM5_Supporting	✔	Apply PM5_Supporting to nonsense/frameshift variants that are predicted/proved to undergo NMD.

Not Met criteria codes

BA1	✖	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	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4	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
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
PS2	ℹ	✖	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
BP5	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
BP4	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
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

Curation History

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