Variant: NM_004360.5(CDH1):c.808T>G (p.Ser270Ala)

Version: 2.0

CA294235

142011 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: f736f74f-a045-4573-aa21-41c5dfa9dd12
Approved on: 2023-08-17
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HGVS expressions

NM_004360.5:c.808T>G
NM_004360.5(CDH1):c.808T>G (p.Ser270Ala)
NC_000016.10:g.68810317T>G
CM000678.2:g.68810317T>G
NC_000016.9:g.68844220T>G
CM000678.1:g.68844220T>G
NC_000016.8:g.67401721T>G
NG_008021.1:g.78026T>G
ENST00000261769.10:c.808T>G
ENST00000261769.9:c.808T>G
ENST00000422392.6:c.808T>G
ENST00000561751.1:c.455-1367T>G
ENST00000562836.5:n.879T>G
ENST00000566510.5:c.652T>G
ENST00000566612.5:c.808T>G
ENST00000611625.4:c.808T>G
ENST00000612417.4:c.808T>G
ENST00000621016.4:c.808T>G
NM_004360.3:c.808T>G
NM_001317184.1:c.808T>G
NM_001317185.1:c.-808T>G
NM_001317186.1:c.-1012T>G
NM_004360.4:c.808T>G
NM_001317184.2:c.808T>G
NM_001317185.2:c.-808T>G
NM_001317186.2:c.-1012T>G

Benign

Met criteria codes 2

BS2 BA1

Not Met criteria codes 24

PP1 PP2 PP3 PP4 PM1 PM3 PM5 PM4 PM6 PM2 PVS1 BS1 BS4 BS3 BP5

Expert Panel

Criteria Specification Information

Criteria Specification: *ClinGen CDH1 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 3.1*
Criteria Specification Approval History

BP7 BP4 BP3 BP1 BP2 PS1 PS2 PS3 PS4

Criteria Specifications for this VCEP

Evidence Links 1

Evidence submitted by expert panel

CDH1 VCEP

The c.808T>G (p.Ser270Ala) variant has a maximum subpopulation frequency of 0.002269 (0.2269%, 57 of 25124 alleles) in the European (Finnish) subpopulation of the gnomAD v2.1.1 cohort (BA1). This variant has also has been observed in more than 10 individuals without a diagnosis of diffuse gastric cancer, signet ring tumor or lobular breast cancer and whose family histories do not suggest HDGC (BS2; SCV000185687.6, SCV000254832.8). In summary, this variant meets criteria to be classified as benign based the ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BA1, BS2.

Met criteria codes

BS2	✔	PMID: 11705864 - Detected in 5 of 923 controls. SCV000185687.6 (Ambry) - 23 families that do not meet HDGC clinical criteria. SCV000254832.8 (Invitae) - 43 families without CDH1 phenotypes described.
BA1	✔	gnomAD 2.1.1 = 57 of 25124 alleles (0.2269%) in in Finnish populations (>0.2%). gnomAD 3.1 = 26 of 10598 alleles (0.2453%) in Finnish populations (>0.2%).

Not Met criteria codes

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	✖	VarSEAK - No splicing effect. SpliceAI - Donor Gain: score 0.03 at 12 bp.
PP4	✖	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
PM5	✖	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
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2		✖	gnomAD 2.1.1 = 57 of 25124 alleles (0.2269%) in Finnish populations >0.2% and 9 of 7222 alleles (0.1246%) in others >0.1% and 59 of 129148 allelles (0.04568%) in Non-Finnish Europeans. gnomAD 3.1 = 26 of 10598 alleles (0.2453%) in Finnish populations and 25 of 68004 (0.03676%) in Non-Finnish Europeans.
PVS1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1		✖	gnomAD 2.1.1 = 57 of 25124 alleles (0.2269%) in Finnish populations >0.2% and 9 of 7222 alleles (0.1246%) in others >0.1% and 59 of 129148 allelles (0.04568%) in Non-Finnish Europeans. gnomAD 3.1 = 26 of 10598 alleles (0.2453%) in Finnish populations and 25 of 68004 (0.03676%) in Non-Finnish Europeans.
BS4		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3		✖	Exhibits strong adhesion, although a bit lower than WT, but cannot be activated by stimuli. PubMed:27582386
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		✖	VarSEAK - No splicing effect. SpliceAI - Donor Gain: score 0.03 at 12 bp.
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
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		✖	PMID: 27582386 - Exhibits strong adhesion, although a bit lower than WT, but cannot be activated by stimuli. Exhibits strong adhesion, although a bit lower than WT, but cannot be activated by stimuli. PubMed:27582386
PS4		✖	PMID: 11705864 - 2 diffuse gastric cancer cases, but no ages provided. PMID: 26898890 - 1 breast/ovarian cancer, no pathology provided. PMID: 30333958 - 2 breast/ovarian cancer, no pathology provided. Ambry - none of the 23 families provided meets criteria (additional data for 70 probands could be made available).

Curation History

Showing 1 to 2 of 2 rows