Variant: NM_004360.5(CDH1):c.214G>A (p.Asp72Asn)

Version: 1.0

CA294297

136064 (ClinVar)

Gene: CDH1 (HGNC:999)
Condition: CDH1-related diffuse gastric and lobular breast cancer (MONDO:0100488)
Inheritance Mode: Autosomal dominant inheritance
UUID: 302f2528-fb93-4046-8918-31d40168855a
Approved on: 2023-08-03
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HGVS expressions

NM_004360.5:c.214G>A
NM_004360.5(CDH1):c.214G>A (p.Asp72Asn)
NC_000016.10:g.68801720G>A
CM000678.2:g.68801720G>A
NC_000016.9:g.68835623G>A
CM000678.1:g.68835623G>A
NC_000016.8:g.67393124G>A
NG_008021.1:g.69429G>A
ENST00000261769.10:c.214G>A
ENST00000261769.9:c.214G>A
ENST00000422392.6:c.214G>A
ENST00000562836.5:n.285G>A
ENST00000564676.5:n.496G>A
ENST00000564745.1:n.209G>A
ENST00000566510.5:c.214G>A
ENST00000566612.5:c.214G>A
ENST00000611625.4:c.214G>A
ENST00000612417.4:c.214G>A
ENST00000621016.4:c.214G>A
NM_004360.3:c.214G>A
NM_001317184.1:c.214G>A
NM_001317185.1:c.-1402G>A
NM_001317186.1:c.-1606G>A
NM_004360.4:c.214G>A
NM_001317184.2:c.214G>A
NM_001317185.2:c.-1402G>A
NM_001317186.2:c.-1606G>A

Likely Benign

Met criteria codes 1

BS2

Not Met criteria codes 25

BA1 BP5 BP7 BP4 BP3 BP1
BP2 BS1 BS4 BS3 PP1 PP2
PP3 PP4 PS1 PS2 PS3 PS4

Expert Panel

Criteria Specification Information

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

PM1 PM3 PM5 PM4 PM6
PM2 PVS1

Evidence Links 0

Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

CDH1 VCEP

The c.214G>A (p.Asp72Asn) missense variant has a maximum subpopulation frequency of 0.048% in the gnomAD v2.1.1 cohort (http://gnomad.broadinstitute.org). This variant has been observed in over 300 probands not meeting HDGC phenotype criteria (BS2; SCV000210893.13, SCV000186096.8, SCV000166549.12). In summary, this variant meets criteria to be classified as Likely Benign based on the ACMG/AMP criteria applied as specified by the CDH1 Variant Curation Expert Panel: BS2. (CDH1 VCEP specifications version 3.1; 06/26/2023)

Met criteria codes

BS2	ℹ	✓	>300 probands/families not meeting HDGC criteria

Not Met criteria codes

BA1	ℹ	✗	Max subpopulation frequency 0.04797% in gnomAD v2.1.1
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	✗	Do not use protein-based computational prediction models for missense variants.
BP3		✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP1		✗	Not applicable for CDH1.
BP2	ℹ	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	ℹ	✗	Max subpopulation frequency 0.04797% in gnomAD v2.1.1
BS4	ℹ	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

BS3	ℹ	✖	This rule can only be used to demonstrate lack of splicing and can only be applied to Synonymous, Intronic or Non-coding variants.
PP1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP2		✖	Not applicable for CDH1.
PP3	ℹ	✖	Do not use protein-based computational prediction models for missense variants.
PP4		✖	Not applicable for CDH1.
PS1		✖	Not applicable for CDH1.
PS2	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	ℹ	✖	This rule can only be applied to demonstrate splicing defects.
PS4	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM1		✖	Not applicable for CDH1.
PM3		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM5		✖	PM5_supporting is applicable to nonsense and frameshift variants that are predicted/proved to undergo NMD or located upstream of the last known pathogenic truncating variant. Site-specific recommendations for the application of PM5_Supporting for canonical splicing variants.
PM4	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
PM2		✖	Max subpopulation frequency 0.04797% in gnomAD v2.1.1
PVS1	ℹ	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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