

Variant: NM_004360.4(CDH1):c.88C>A (p.Pro30Thr)

CA151524 [↗](#)

127933 (ClinVar) [↗](#)

Gene: CDH1 ([HGNC:999](#))

Condition: CDH1-related diffuse gastric and lobular breast cancer ([MONDO:0007648](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: d1e6757d-87b2-428c-a699-e2ac2893485c

Approved on: 2018-11-21

Published on: 2018-12-07

HGVS expressions

NM_004360.4:c.88C>A

NM_004360.4(CDH1):c.88C>A (p.Pro30Thr)

NC_000016.10:g.68738336C>A

CM000678.2:g.68738336C>A

NC_000016.9:g.68772239C>A

CM000678.1:g.68772239C>A

NC_000016.8:g.67329740C>A

NG_008021.1:g.6045C>A

ENST00000261769.10:c.88C>A

ENST00000261769.9:c.88C>A

ENST00000422392.6:c.88C>A

ENST00000566510.5:c.88C>A

ENST00000566612.5:c.88C>A

ENST00000611625.4:c.88C>A

ENST00000612417.4:c.88C>A

ENST00000621016.4:c.88C>A

NM_004360.3:c.88C>A

NM_001317184.1:c.88C>A

NM_001317185.1:c.-1528C>A

NM_001317186.1:c.-1732C>A

NM_004360.5:c.88C>A

NM_001317184.2:c.88C>A

NM_001317185.2:c.-1528C>A

NM_001317186.2:c.-1732C>A

NM_004360.5(CDH1):c.88C>A (p.Pro30Thr)

Benign

Met criteria codes 2

BS2 BA1

Not Met criteria codes 24

PM6 PM2 PM4 PM3 PM1
PM5 BS4 BS3 BS1 PVS1
PS2 PS4 PS1 PS3 BP5 BP7
BP3 BP2 BP1 BP4 PP4 PP1
PP2 PP3

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**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

CDH1 VCEP

The c.88C>A (p.Pro30Thr) variant has an allele frequency of 0.00249 (0.25%, 178/71372 alleles) in the European (non-Finnish) subpopulation of the gnomAD cohort (BA1). In addition to meeting stand along criteria for a benign classification, this variant has also been seen in >900 individuals without a diagnosis of diffuse gastric cancer, signet ring tumor or lobular breast cancer and whose family histories do not suggest HDGC (BS2; internal laboratory contributors). In summary, this variant meets criteria to be classified as benign. 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			Vast majority of patients with this variant had neither lobular breast cancer nor gastric cancer. 929 non-HDGC individuals with allele number of 178,576.
BA1			0.25% frequency with 178 alleles in European subpopulation meets stand alone criteria for CDH1.

Not Met criteria codes

PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			0.25% frequency with 178 alleles in European subpopulation meets stand alone criteria for CDH1.
PM4			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
PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			Mutation resulted in abnormal localization and reduced aggregation in CHO cells. Invasion and expression not significantly different to wild type (Vogelaar et al.) Does not meet CDH1 criteria.

BS1			0.25% frequency with 178 alleles in European subpopulation meets stand alone criteria for CDH1.
PVS1			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
PS4			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			Mutation resulted in abnormal localization and reduced aggregation in CHO cells. Invasion and expression not significantly different to wild type (Vogelaar et al.) Does not meet CDH1 criteria.
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
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			In silico predictors are only valid for splicing according to CDH1 criteria.
PP4			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

In silico predictors are only valid for splicing according to CDH1 criteria.

Curation History [↗](#)

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