

Variant: NM_004360.4(CDH1):c.670C>T (p.Arg224Cys)

CA288074 [↗](#)

127932 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: d4d12c86-59cb-40a8-92ec-13925d97080a

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HGVS expressions

NM_004360.4:c.670C>T

NM_004360.4(CDH1):c.670C>T (p.Arg224Cys)

NC_000016.10:g.68808831C>T

CM000678.2:g.68808831C>T

NC_000016.9:g.68842734C>T

CM000678.1:g.68842734C>T

NC_000016.8:g.67400235C>T

NG_008021.1:g.76540C>T

ENST00000261769.10:c.670C>T

ENST00000261769.9:c.670C>T

ENST00000422392.6:c.670C>T

ENST00000561751.1:n.437C>T

ENST00000562836.5:n.741C>T

ENST00000564676.5:n.952C>T

ENST00000566510.5:c.531+264C>T

ENST00000566612.5:c.670C>T

ENST00000567320.1:n.180C>T

ENST00000611625.4:c.670C>T

ENST00000612417.4:c.670C>T

ENST00000621016.4:c.670C>T

NM_004360.3:c.670C>T

NM_001317184.1:c.670C>T

NM_001317185.1:c.-946C>T

NM_001317186.1:c.-1150C>T

NM_004360.5:c.670C>T

NM_001317184.2:c.670C>T

NM_001317185.2:c.-946C>T

NM_001317186.2:c.-1150C>T

NM_004360.5(CDH1):c.670C>T (p.Arg224Cys)

Likely Benign

Met criteria codes 1

BS2

Not Met criteria codes 25

BA1 **BP2** **BP3** **BP1** **BP4** **BP5**
BP7 **BS4** **BS3** **BS1** **PP1** **PP4**

Expert Panel

CDH1 VCEP [↗](#)

Criteria Specification Information

PP2

PP3

PS2

PS4

PS1

PS3

PM6

PM2

PM3

PM1

PM4

PM5

PVS1

Evidence Links

1

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.670C>T (p.Arg224Cys) variant has been observed in >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; internal laboratory contributors). In summary, the clinical significance of this variant is classified as likely benign based on BS2 alone. ACMG/AMP criteria applied, as specified by the CDH1 Variant Curation Expert Panel (Variant Interpretation Guidelines Version 3.1): BS2.

Met criteria codes

BS2

i

✓

Observed in 392 individuals w/o dx of HDGC

Not Met criteria codes

BA1	i	✗	Allele frequency of 1.7e-4 in ExAC and gnomAD.
BP2	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
BP4	i	✗	Multiple computational tools predict no or low impact.
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
BS4	i	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3	i	✗	Two functional studies suggest little or no impact on cell adhesion.

Found variant weakly activates E-cadherin induced cell adhesion. [PubMed:27582386](#)

BS1		✖	Allele frequency of 1.7e-4 in ExAC and gnomAD.
PP1		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4		✖	One proband with DGC reported in literature.
PP2		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3		✖	Multiple computational tools predict no or low impact.
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		✖	Two functional studies suggest little or no impact on cell adhesion.
Found variant weakly activates E-cadherin induced cell adhesion. PubMed:27582386			
PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2		✖	Allele frequency of 1.7e-4 in ExAC and gnomAD.
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
PM4		✖	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

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

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