

Variant: *NM_000038.6(APC):c.715G>C (p.Ala239Pro)*

Version: 1.0

CA047113 [↗](#)

220329 (ClinVar) [↗](#)

Gene: APC ([HGNC:324](#))

Condition: familial adenomatous polyposis 1 ([MONDO:0021056](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: cfd3f93d-673f-4e46-ba4f-6e1c877b3c0b

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HGVS expressions

NM_000038.6(APC):c.715G>C (p.Ala239Pro)

NM_000038.6:c.715G>C

NC_000005.10:g.112792515G>C

CM000667.2:g.112792515G>C

NC_000005.9:g.112128212G>C

CM000667.1:g.112128212G>C

NC_000005.8:g.112156111G>C

NG_008481.4:g.104995G>C

ENST00000502371.3:c.715G>C

ENST00000504915.3:c.715G>C

ENST00000505084.2:n.771G>C

ENST00000505350.2:c.*721G>C

ENST00000507379.6:c.676-8764G>C

ENST00000509732.6:c.715G>C

ENST00000512211.7:c.715G>C

ENST00000257430.9:c.715G>C

ENST00000257430.8:c.715G>C

ENST00000507379.5:c.676-8764G>C

ENST00000508376.6:c.715G>C

ENST00000508624.5:c.715G>C

ENST00000512211.6:c.715G>C

NM_000038.5:c.715G>C

NM_001127510.2:c.715G>C

NM_001127511.2:c.676-8764G>C

NM_001354895.1:c.715G>C

NM_001354896.1:c.715G>C

NM_001354897.1:c.745G>C

NM_001354898.1:c.640G>C

NM_001354899.1:c.646-8764G>C

NM_001354900.1:c.538G>C

NM_001354901.1:c.538G>C

NM_001354902.1:c.745G>C

NM_001354903.1:c.715G>C

NM_001354904.1:c.640G>C

NM_001354905.1:c.538G>C

NM_001354906.1:c.-321G>C

NM_001127510.3:c.715G>C

NM_001127511.3:c.676-8764G>C
NM_001354895.2:c.715G>C
NM_001354896.2:c.715G>C
NM_001354897.2:c.745G>C
NM_001354898.2:c.640G>C
NM_001354899.2:c.646-8764G>C
NM_001354900.2:c.538G>C
NM_001354901.2:c.538G>C
NM_001354902.2:c.745G>C
NM_001354903.2:c.715G>C
NM_001354904.2:c.640G>C
NM_001354905.2:c.538G>C
NM_001354906.2:c.-321G>C

Benign

Met criteria codes 3

BP1 BS2 BS1

Not Met criteria codes 1

BP4

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

The c.715G>C variant in APC is a missense variant predicted to cause substitution of alanine by proline at amino acid 239 (p.Ala239Pro). This variant has been observed in ≥ 35 heterozygous individuals with no features or family history of FAP, worth ≥ 10 healthy individual points (BS2; Ambry, Invitae internal data). The highest allele frequency of this variant in gnomAD v2.1.1 (non-cancer) is 0.0002269 in East Asian population, which is higher than the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation Expert Panel (HCCP VCEP) threshold (≥ 0.00001) for BS1 (BS1). Finally, APC is defined by the HCCP VCEP as a gene for which primarily truncating variants are known to cause disease (BP1). In summary, this variant meets the criteria to be classified as Benign for FAP based on the ACMG/AMP criteria applied, as specified by the HCCP VCEP: BS1, BS2, BP1. (VCEP specifications version 1; date of approval 12/12/2022).

Met criteria codes

BP1			APC, in which the variant was identified, is defined by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP as a gene for which primarily truncating variants are known to cause disease (BP1).
BS2			This variant has been observed in ≥ 35 heterozygous individuals with no features or family history of FAP meeting ≥ 10 healthy individual points (BS2; Ambry, Invitae).
BS1			The highest population minor allele frequency of the variant c.715G>C in gnomAD v2.1.1 (non-cancer) is 0.0002269 (4/17632 alleles) in East Asian population, which is higher than the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation Expert Panel threshold (≥ 0.00001) for BS1.

Not Met criteria codes

BP4



The results from ≥ 2 in silico splicing predictors (SpliceAI, varSEAK) support that this variant does not affect splicing (BP4 not applicable for missense variant).

Curation History [↗](#)

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