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Variant: NM_000038.6(APC):c.422G>C (p.Arg141Thr)

Version: 1.0

CA16022246

1056286 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: dc4d6a80-eb3a-4ce3-a2a5-bea49c46ee55
Approved on: 2025/5/19
Published on: 2025/5/19

HGVS expressions

NM_000038.6:c.422G>C
NM_000038.6(APC):c.422G>C (p.Arg141Thr)
NC_000005.10:g.112767390G>C
CM000667.2:g.112767390G>C
NC_000005.9:g.112103087G>C
CM000667.1:g.112103087G>C
NC_000005.8:g.112130986G>C
NG_008481.4:g.79870G>C
ENST00000502371.3:c.422G>C
ENST00000504915.3:c.422G>C
ENST00000505084.2:n.478G>C
ENST00000505350.2:c.*428G>C
ENST00000507379.6:c.452G>C
ENST00000509732.6:c.422G>C
ENST00000512211.7:c.422G>C
ENST00000257430.9:c.422G>C
ENST00000257430.8:c.422G>C
ENST00000507379.5:c.452G>C
ENST00000508376.6:c.422G>C
ENST00000508624.5:c.422G>C
ENST00000512211.6:c.422G>C
NM_000038.5:c.422G>C
NM_001127510.2:c.422G>C
NM_001127511.2:c.452G>C
NM_001354895.1:c.422G>C
NM_001354896.1:c.422G>C
NM_001354897.1:c.452G>C
NM_001354898.1:c.347G>C
NM_001354899.1:c.422G>C
NM_001354900.1:c.245G>C
NM_001354901.1:c.245G>C
NM_001354902.1:c.452G>C
NM_001354903.1:c.422G>C
NM_001354904.1:c.347G>C
NM_001354905.1:c.245G>C
NM_001354906.1:c.-614G>C
NM_001127510.3:c.422G>C

NM_001127511.3:c.452G>C
NM_001354895.2:c.422G>C
NM_001354896.2:c.422G>C
NM_001354897.2:c.452G>C
NM_001354898.2:c.347G>C
NM_001354899.2:c.422G>C
NM_001354900.2:c.245G>C
NM_001354901.2:c.245G>C
NM_001354902.2:c.452G>C
NM_001354903.2:c.422G>C
NM_001354904.2:c.347G>C
NM_001354905.2:c.245G>C
NM_001354906.2:c.-614G>C

Uncertain Significance

Met criteria codes 2

PM2_Supporting PVS1_Strong

Not Met criteria codes 2

BS2 PS4

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

Criteria Specification Information

Criteria Specification: *ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for APC Version 2.1.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

The NM_000038.6(APC):c.422G>C (p.Arg141Thr) variant in APC is a G to non-G change at the last nucleotide of exon 4. It is predicted to cause skipping of exon 4, resulting in a frameshift in a gene in which loss-of-function is an established disease mechanism (PVS1_Strong). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant has been reported in 1 proband meeting phenotypic criteria, resulting in a phenotype score of 0.5 points (Invitae, internal data) (PS4 not applicable). Moreover, the variant has been observed in heterozygous state in two individuals without a colorectal cancer/polyposis associated phenotype, worth 1 healthy individual point in total (BS2_Supporting not met; [Ambry Genetics, internal data]). In summary, this variant is a variant of uncertain significance (VUS) for autosomal-dominant inherited FAP based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP: criteria PVS1_Strong and PM2_Supporting applied (VCEP specifications v2.0.3; date of approval 7/24/2023).

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1_Strong	✔	The NM_000038.6(APC):c.422G>C (p.Arg141Thr) variant in APC is a G to non-G change at the last nucleotide of exon 4. It is predicted to cause skipping of exon 4, resulting in a frameshift in a gene in which loss-of-function is an established disease mechanism (PVS1_Strong).

Not Met criteria codes

BS2	✖	Moreover, the variant has been observed in heterozygous state in two individuals without a colorectal cancer/polyposis associated phenotype, worth 1 healthy individual point in total (BS2_Supporting not met; [Ambry Genetics, internal data]).
PS4	✖	This variant has been reported in 1 proband meeting phenotypic criteria, resulting in a phenotype score of 0.5 points (Invitae, internal data) (PS4 not applicable).

Curation History

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