

Variant: NM_000038.6(APC):c.1333C>T (p.Gln445Ter)

Version: 1.0

CA16024224 [↗](#)

438865 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: fafcfe81-f248-4981-ac44-126759178465

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HGVS expressions

NM_000038.6(APC):c.1333C>T (p.Gln445Ter)

NM_000038.6:c.1333C>T

NC_000005.10:g.112821916C>T

CM000667.2:g.112821916C>T

NC_000005.9:g.112157613C>T

CM000667.1:g.112157613C>T

NC_000005.8:g.112185512C>T

NG_008481.4:g.134396C>T

ENST00000502371.3:c.1333C>T

ENST00000504915.3:c.1333C>T

ENST00000505084.2:n.1389C>T

ENST00000505350.2:c.*1339C>T

ENST00000507379.6:c.1279C>T

ENST00000509732.6:c.1333C>T

ENST00000512211.7:c.1333C>T

ENST00000257430.9:c.1333C>T

ENST00000257430.8:c.1333C>T

ENST00000502371.2:c.21C>T

ENST00000507379.5:c.1279C>T

ENST00000508376.6:c.1333C>T

ENST00000508624.5:c.*655C>T

ENST00000512211.6:c.1333C>T

NM_000038.5:c.1333C>T

NM_001127510.2:c.1333C>T

NM_001127511.2:c.1279C>T

NM_001354895.1:c.1333C>T

NM_001354896.1:c.1333C>T

NM_001354897.1:c.1363C>T

NM_001354898.1:c.1258C>T

NM_001354899.1:c.1249C>T

NM_001354900.1:c.1156C>T

NM_001354901.1:c.1156C>T

NM_001354902.1:c.1060C>T

NM_001354903.1:c.1030C>T

NM_001354904.1:c.955C>T

NM_001354905.1:c.853C>T

NM_001354906.1:c.484C>T

NM_001127510.3:c.1333C>T
NM_001127511.3:c.1279C>T
NM_001354895.2:c.1333C>T
NM_001354896.2:c.1333C>T
NM_001354897.2:c.1363C>T
NM_001354898.2:c.1258C>T
NM_001354899.2:c.1249C>T
NM_001354900.2:c.1156C>T
NM_001354901.2:c.1156C>T
NM_001354902.2:c.1060C>T
NM_001354903.2:c.1030C>T
NM_001354904.2:c.955C>T
NM_001354905.2:c.853C>T
NM_001354906.2:c.484C>T

Pathogenic

Met criteria codes 3

PM2_Supporting

PVS1

PS4_Moderate

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.1333C>T (p.Gln445Ter) variant in APC is a nonsense variant located between codon 49 and 2645 and is predicted to cause a premature stop codon in exon 11 in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been reported in 2 probands meeting phenotypic criteria, resulting in a total phenotype score of 2.0 points (PS4_Moderate, [PMID: 19793053, Ambry Genetics]). The variant is reported in one additional proband with a colorectal cancer/polyposis associated phenotype not meeting phenotypic criteria (PMID: 35418818). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for autosomal-dominant inherited FAP based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP: PVS1, PS4_Moderate, PM2_Supporting (VCEP specifications version 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



The NM_000038.6(APC):c.1333C>T (p.Gln445Ter) variant in APC is a nonsense variant located between codon 49 and 2645 and is predicted to cause a premature stop codon in exon 11 in a gene in which loss-of-function is an established disease mechanism (PVS1).

PS4_Moderate



This variant has been reported in 2 probands meeting phenotypic criteria, resulting in a total phenotype score of 2.0 points (PS4_Moderate, [PMID: 19793053, Ambry Genetics]). The variant is reported in one additional proband with a colorectal cancer/polyposis associated phenotype not meeting phenotypic criteria (PMID: 35418818).

Curation History

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