

Variant: NM_000038.6(APC):c.70C>T (p.Arg24Ter)

Version: 1.0

CA012843 [↗](#)

184702 (ClinVar) [↗](#)

Gene: APC ([HGNC:324](#))
Condition: familial adenomatous polyposis 1 ([MONDO:0021056](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 2648e21f-e671-42e2-b3ec-67e364423e2c
Approved on: 2025/5/15
Published on: 2025/5/19

HGVS expressions

NM_000038.6:c.70C>T
NM_000038.6(APC):c.70C>T (p.Arg24Ter)
NC_000005.10:g.112754960C>T
CM000667.2:g.112754960C>T
NC_000005.9:g.112090657C>T
CM000667.1:g.112090657C>T
NC_000005.8:g.112118556C>T
NG_008481.4:g.67440C>T
ENST00000502371.3:c.70C>T
ENST00000504915.3:c.70C>T
ENST00000505084.2:n.126C>T
ENST00000505350.2:c.*76C>T
ENST00000507379.6:c.166-11366C>T
ENST00000509732.6:c.70C>T
ENST00000512211.7:c.70C>T
ENST00000257430.9:c.70C>T
ENST00000257430.8:c.70C>T
ENST00000505350.1:c.*76C>T
ENST00000507379.5:c.166-11366C>T
ENST00000508376.6:c.70C>T
ENST00000508624.5:c.70C>T
ENST00000509732.5:c.70C>T
ENST00000512211.6:c.70C>T
NM_000038.5:c.70C>T
NM_001127510.2:c.70C>T
NM_001127511.2:c.166-11366C>T
NM_001354895.1:c.70C>T
NM_001354896.1:c.70C>T
NM_001354897.1:c.166-11366C>T
NM_001354898.1:c.61-11366C>T
NM_001354899.1:c.70C>T
NM_001354900.1:c.-42-11366C>T
NM_001354901.1:c.-42-11366C>T
NM_001354902.1:c.166-11366C>T
NM_001354903.1:c.70C>T
NM_001354904.1:c.61-11366C>T
NM_001354905.1:c.-42-11366C>T

NM_001354906.1:c.-966C>T
NM_001127510.3:c.70C>T
NM_001127511.3:c.166-11366C>T
NM_001354895.2:c.70C>T
NM_001354896.2:c.70C>T
NM_001354897.2:c.166-11366C>T
NM_001354898.2:c.61-11366C>T
NM_001354899.2:c.70C>T
NM_001354900.2:c.-42-11366C>T
NM_001354901.2:c.-42-11366C>T
NM_001354902.2:c.166-11366C>T
NM_001354903.2:c.70C>T
NM_001354904.2:c.61-11366C>T
NM_001354905.2:c.-42-11366C>T
NM_001354906.2:c.-966C>T

Uncertain Significance

Met criteria codes 2

BS2 PS4_Supporting

Not Met criteria codes 4

PM2 BA1 BS1 PVS1

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polypsis VCEP

Criteria Specification Information

[Criteria Specification:](#) ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis 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/Polypsis VCEP

The NM_000038.6(APC):c.70C>T (p.Arg24Ter) in APC is a nonsense variant located 5' of codon 49, thus PVS1 is not applicable based on the ACMG/AMP criteria specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis VCEP (HCCP VCEP). The total minor allele frequency in gnomAD v2.1.1 (non-cancer) is 0.00002 (6/268,098 alleles), however, no value is given for the "filtering allele frequency" (FAF) (PM2_Supporting and BS1 not met). This variant has been observed in heterozygous state in 67 individuals, which are reported either with a very mild polyposis phenotype (only 3 carriers fulfilled 0.5 phenotype points each; PS4_Supporting) or without a colorectal cancer/polypsis associated phenotype (at least 10 healthy unrelated adult individuals worth ≥ 10 healthy individual points in total; BS2) (PMID: 28135145 and 18433509, internal data Ambry Genetics, GeneDX and Labcorp Genetics (formerly Invitae)). Due to conflicting evidence, this variant is classified as a variant of uncertain significance for autosomal-dominant inherited FAP based on the ACMG/AMP criteria applied, as specified by the HCCP VCEP: criterion PS4_Supporting and BS2 applied (VCEP specifications version v2.1.0; date of approval 11/24/2023).

Met criteria codes

BS2



This variant has been observed in heterozygous state in 67 individuals, which are reported either with a very mild polyposis phenotype (only 3 carriers fulfilled 0.5 phenotype points each; PS4_Supporting) or without a colorectal cancer/polypsis associated phenotype (at least 10 healthy unrelated adult individuals worth ≥ 10 healthy individual

points in total; BS2) (PMID: 28135145 and 18433509, internal data Ambry Genetics, GeneDX and Labcorp Genetics (formerly Invitae)).

PS4_Supporting

i

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This variant has been observed in heterozygous state in 67 individuals, which are reported either with a very mild polyposis phenotype (only 3 carriers fulfilled 0.5 phenotype points each; PS4_Supporting) or without a colorectal cancer/polyposis associated phenotype (at least 10 healthy unrelated adult individuals worth $\geq$ 10 healthy individual points in total; BS2) (PMID: 28135145 and 18433509, internal data Ambry Genetics, GeneDX and Labcorp Genetics (formerly Invitae)).

Not Met criteria codes

PM2		✗	The total minor allele frequency in gnomAD v2.1.1 (non-cancer) is 0.00002 (6/268,098 alleles), however, no value is given for the “filtering allele frequency” (FAF) (PM2_Supporting not met).
BA1	i	✗	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1	i	✗	The total minor allele frequency in gnomAD v2.1.1 (non-cancer) is 0.00002 (6/268,098 alleles), however, no value is given for the “filtering allele frequency” (FAF) (BS1 not met).
PVS1	i	✗	The NM_000038.6(APC):c.70C>T (p.Arg24Ter) in APC is a nonsense variant located 5’ of codon 49, thus PVS1 is not applicable based on the ACMG/AMP criteria specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP (HCCP VCEP).

Curation History [↗](#)

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