

Variant: *NM_000038.6(APC):c.847C>T (p.Arg283Ter)*

Version: 1.0

CA015543 [↗](#)

184999 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 34ea9707-51d8-44df-818d-f69b075295c5

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HGVS expressions

NM_000038.6(APC):c.847C>T (p.Arg283Ter)

NM_000038.6:c.847C>T

NC_000005.10:g.112815507C>T

CM000667.2:g.112815507C>T

NC_000005.9:g.112151204C>T

CM000667.1:g.112151204C>T

NC_000005.8:g.112179103C>T

NG_008481.4:g.127987C>T

ENST00000502371.3:c.847C>T

ENST00000504915.3:c.847C>T

ENST00000505084.2:n.903C>T

ENST00000505350.2:c.*853C>T

ENST00000507379.6:c.793C>T

ENST00000509732.6:c.847C>T

ENST00000512211.7:c.847C>T

ENST00000257430.9:c.847C>T

ENST00000257430.8:c.847C>T

ENST00000507379.5:c.793C>T

ENST00000508376.6:c.847C>T

ENST00000508624.5:c.*169C>T

ENST00000512211.6:c.847C>T

NM_000038.5:c.847C>T

NM_001127510.2:c.847C>T

NM_001127511.2:c.793C>T

NM_001354895.1:c.847C>T

NM_001354896.1:c.847C>T

NM_001354897.1:c.877C>T

NM_001354898.1:c.772C>T

NM_001354899.1:c.763C>T

NM_001354900.1:c.670C>T

NM_001354901.1:c.670C>T

NM_001354902.1:c.877C>T

NM_001354903.1:c.847C>T

NM_001354904.1:c.772C>T

NM_001354905.1:c.670C>T

NM_001354906.1:c.-3C>T

NM_001127510.3:c.847C>T

NM_001127511.3:c.793C>T
NM_001354895.2:c.847C>T
NM_001354896.2:c.847C>T
NM_001354897.2:c.877C>T
NM_001354898.2:c.772C>T
NM_001354899.2:c.763C>T
NM_001354900.2:c.670C>T
NM_001354901.2:c.670C>T
NM_001354902.2:c.877C>T
NM_001354903.2:c.847C>T
NM_001354904.2:c.772C>T
NM_001354905.2:c.670C>T
NM_001354906.2:c.-3C>T

Pathogenic

Met criteria codes 4

PP1_Strong PVS1 PS4
PM2_Supporting

Not Met criteria codes 11

PM6 PM1 PM3 BS1 BS4
BS3 BS2 PS2 BP5 BP2 BA1

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.847C>T (p.Arg283*) variant in APC is a nonsense variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 9 in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been reported in 15 probands meeting 8 phenotype points. In addition, this variant is also reported in 50 probands with FAP not otherwise specified, meeting ≥ 16 phenotype points in total (PS4_VeryStrong; PMIDs 30897307, 20924072, 20685668, 10768871, 9950360, 12901799, 11857735, 26625971, 23159591, Bonn internal data). The variant has been reported to segregate with FAP in 5 meioses from 1 family and in 31 members from 1 large FAP family (PP1_Strong; PMID: 12901799, Bonn internal data). The variant is not reported in gnomAD (PM2_Supporting). In summary, this variant meets the criteria to be classified as Pathogenic for FAP based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation Expert Panel: PVS1, PS4_VeryStrong, PM2_Supporting and PP1_Strong (VCEP specifications version 1; date of approval: 12/12/2022).

Met criteria codes

PP1_Strong



The variant has been reported to segregate with FAP in 5 meioses from 1 family (PMID: 12901799) and the variant was detected in 31 members from 1 large FAP family (PP1_Strong, Internal data Institute of Human Genetics, Bonn, Germany).

PVS1



The c.847C>T (p.Arg283Ter) variant in APC is a variant to cause a premature stop codon in biologically-relevant-exon 8 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

PS4			The variant c.847C>T (p.Arg283Ter) has been reported in at least 15 probands meeting at least 8 phenotype points, there are > 50 probands with FAP but no detailed phenotype information (PS4_VeryStrong); PMIDs 30897307, 20924072,10768871, 9950360, 12901799, Internal data Institute of Human Genetics, Bonn, Germany.
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
Not Met criteria codes			
PM6			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
PM3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline



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