The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

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
Approved on: 2023/2/18
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HGVS expressions

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

PVS1 PP1_Strong PM2_Supporting PS4

Not Met criteria codes 11

BS2 BS1 BS4 BS3 BP2 BP5 PS2 BA1 PM6 PM1 PM3

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

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).
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).

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
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.

Not Met criteria codes

BS2	✖	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
BP2	✖	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
PS2	✖	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
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

Curation History

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