

Variant: *NM_000038.6(APC):c.2240C>G (p.Ser747Ter)*

Version: 1.0

CA16026241 [↗](#)

411368 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 839c68d0-35e8-47e5-a6ed-3aa906be0c3a

Approved on: 2025/5/19

Published on: 2025/5/19

HGVS expressions

NM_000038.6(APC):c.2240C>G (p.Ser747Ter)

NM_000038.6:c.2240C>G

NC_000005.10:g.112837834C>G

CM000667.2:g.112837834C>G

NC_000005.9:g.112173531C>G

CM000667.1:g.112173531C>G

NC_000005.8:g.112201430C>G

NG_008481.4:g.150314C>G

ENST00000502371.3:c.1905C>G

ENST00000504915.3:c.2294C>G

ENST00000505350.2:c.*2246C>G

ENST00000507379.6:c.2186C>G

ENST00000509732.6:c.2240C>G

ENST00000512211.7:c.2240C>G

ENST00000257430.9:c.2240C>G

ENST00000257430.8:c.2240C>G

ENST00000502371.2:c.593C>G

ENST00000507379.5:c.2186C>G

ENST00000508376.6:c.2240C>G

ENST00000508624.5:c.*1562C>G

ENST00000512211.6:c.2240C>G

ENST00000520401.1:c.230+8862C>G

NM_000038.5:c.2240C>G

NM_001127510.2:c.2240C>G

NM_001127511.2:c.2186C>G

NM_001354895.1:c.2240C>G

NM_001354896.1:c.2294C>G

NM_001354897.1:c.2270C>G

NM_001354898.1:c.2165C>G

NM_001354899.1:c.2156C>G

NM_001354900.1:c.2117C>G

NM_001354901.1:c.2063C>G

NM_001354902.1:c.1967C>G

NM_001354903.1:c.1937C>G

NM_001354904.1:c.1862C>G

NM_001354905.1:c.1760C>G

NM_001354906.1:c.1391C>G

NM_001127510.3:c.2240C>G
NM_001127511.3:c.2186C>G
NM_001354895.2:c.2240C>G
NM_001354896.2:c.2294C>G
NM_001354897.2:c.2270C>G
NM_001354898.2:c.2165C>G
NM_001354899.2:c.2156C>G
NM_001354900.2:c.2117C>G
NM_001354901.2:c.2063C>G
NM_001354902.2:c.1967C>G
NM_001354903.2:c.1937C>G
NM_001354904.2:c.1862C>G
NM_001354905.2:c.1760C>G
NM_001354906.2:c.1391C>G

Pathogenic

Met criteria codes 4

PM6_Supporting PS4_Moderate
PM2_Supporting PVS1

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:c.2240C>G p.(Ser747Ter) variant in APC is a nonsense variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 16 in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been reported in 7 probands meeting phenotypic criteria, resulting in a total phenotype score 3.5 (PS4_Moderate, [PMID: 20223039, PMID: 20685668, PMID: 22135120, internal data Institute of Human Genetics, Bonn]). The variant has been reported in 4 additional probands with a polyposis associated phenotype not meeting phenotypic criteria (PMID: 35189564). This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 1 individual with FAP, resulting in a total de novo score of 0.5 (PM6_Supporting, [PMID: 22135120]). 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: criteria PVS1, PS4_Moderate, PM2_Supporting and PM6_Supporting applied (VCEP specifications version v2.1.0; date of approval 11/24/2023).

Met criteria codes

PM6_Supporting  

This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 1 individual with FAP, resulting in a total de novo score of 0.5 (PM6_Supporting, [PMID: 22135120]).

PS4_Moderate  

This variant has been reported in 7 probands meeting phenotypic criteria, resulting in a total phenotype score 3.5 (PS4_Moderate, [PMID: 20223039, PMID: 20685668, PMID: 22135120, internal data Institute of Human Genetics, Bonn]). The variant has been reported in 4 additional probands with a polyposis associated phenotype not meeting phenotypic criteria (PMID: 35189564).

PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1			The NM_000038.6:c.2240C>G p.(Ser747Ter) variant in APC is a nonsense variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 16 in a gene in which loss-of-function is an established disease mechanism (PVS1).

Curation History

▼

▼

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.