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Variant: NM_000038.6(APC):c.1743G>C (p.Lys581Asn)

Version: 1.1

CA16025124

428153 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: 72670e17-83e8-4b17-88e1-e99c60817349
Approved on: 2025/5/16
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HGVS expressions

NM_000038.6(APC):c.1743G>C (p.Lys581Asn)
NM_000038.6:c.1743G>C
NC_000005.10:g.112828972G>C
CM000667.2:g.112828972G>C
NC_000005.9:g.112164669G>C
CM000667.1:g.112164669G>C
NC_000005.8:g.112192568G>C
NG_008481.4:g.141452G>C
ENST00000502371.3:c.1409-5979G>C
ENST00000504915.3:c.1797G>C
ENST00000505084.2:n.1799G>C
ENST00000505350.2:c.*1749G>C
ENST00000507379.6:c.1689G>C
ENST00000509732.6:c.1743G>C
ENST00000512211.7:c.1743G>C
ENST00000257430.9:c.1743G>C
ENST00000257430.8:c.1743G>C
ENST00000502371.2:c.97-5979G>C
ENST00000504915.2:c.432G>C
ENST00000505084.1:n.230G>C
ENST00000507379.5:c.1689G>C
ENST00000508376.6:c.1743G>C
ENST00000508624.5:c.*1065G>C
ENST00000512211.6:c.1743G>C
ENST00000520401.1:c.230G>C
NM_000038.5:c.1743G>C
NM_001127510.2:c.1743G>C
NM_001127511.2:c.1689G>C
NM_001354895.1:c.1743G>C
NM_001354896.1:c.1797G>C
NM_001354897.1:c.1773G>C
NM_001354898.1:c.1668G>C
NM_001354899.1:c.1659G>C
NM_001354900.1:c.1620G>C
NM_001354901.1:c.1566G>C
NM_001354902.1:c.1470G>C
NM_001354903.1:c.1440G>C

NM_001354904.1:c.1365G>C
NM_001354905.1:c.1263G>C
NM_001354906.1:c.894G>C
NM_001127510.3:c.1743G>C
NM_001127511.3:c.1689G>C
NM_001354895.2:c.1743G>C
NM_001354896.2:c.1797G>C
NM_001354897.2:c.1773G>C
NM_001354898.2:c.1668G>C
NM_001354899.2:c.1659G>C
NM_001354900.2:c.1620G>C
NM_001354901.2:c.1566G>C
NM_001354902.2:c.1470G>C
NM_001354903.2:c.1440G>C
NM_001354904.2:c.1365G>C
NM_001354905.2:c.1263G>C
NM_001354906.2:c.894G>C

Likely Pathogenic

Met criteria codes 3

PVS1_Strong PS4_Supporting PM2_Supporting

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.1743G>C (p.?) variant in APC is a G to non-G change at the last nucleotide of exon 14. It is predicted to cause skipping of exon 14, resulting in an in-frame deletion of an exon with sufficient supportive clinical data (PVS1_Strong). This variant has been reported in 1 family meeting phenotypic criteria, resulting in a total phenotype score of 1 (PS4_Supporting [Ambry Genetics]). The variant has been reported in 5 additional probands with a colorectal cancer/polyposis associated phenotype not meeting phenotypic criteria (internal data Labcorp Genetics [formerly Invitae] and Ambry Genetics) and 1 proband without any clinical information (GeneDX). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal-dominant inherited FAP based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis: criteria PVS1_Strong, PS4_Supporting and PM2_Supporting applied (VCEP specifications v2.0.3; date of approval 7/24/2023).

Met criteria codes

PVS1_Strong	✔	The NM_000038.6(APC):c.1743G>C (p.?) variant in APC is a G to non-G change at the last nucleotide of exon 14. It is predicted to cause skipping of exon 14, resulting in an in-frame deletion of an exon with sufficient supportive clinical

data (PVS1_Strong).

PS4_Supporting	✔	This variant has been reported in 1 family meeting phenotypic criteria, resulting in a total phenotype score of 1 (PS4_Supporting [Ambry Genetics]). The variant has been reported in 5 additional probands with a colorectal cancer/polyposis associated phenotype not meeting phenotypic criteria (internal data Labcorp Genetics [formerly Invitae] and Ambry Genetics) and 1 proband without any clinical information (GeneDX).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History

Showing 1 to 2 of 2 rows

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