

Variant: NM_000038.6(APC):c.220+2T>A

Version: 1.0

CA007244 [↗](#)

141515 (ClinVar) [↗](#)

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

Condition: classic familial adenomatous polyposis ([MONDO:0021055](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 82e95160-be25-4a02-ae6e-b7ac8f7ebab3

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HGVS expressions

NM_000038.6:c.220+2T>A

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NC_000005.10:g.112766412T>A

CM000667.2:g.112766412T>A

NC_000005.9:g.112102109T>A

CM000667.1:g.112102109T>A

NC_000005.8:g.112130008T>A

NG_008481.4:g.78892T>A

ENST00000502371.3:c.220+2T>A

ENST00000504915.3:c.220+2T>A

ENST00000505084.2:n.276+2T>A

ENST00000505350.2:c.*226+2T>A

ENST00000507379.6:c.250+2T>A

ENST00000509732.6:c.220+2T>A

ENST00000512211.7:c.220+2T>A

ENST00000257430.9:c.220+2T>A

ENST00000257430.8:c.220+2T>A

ENST00000507379.5:c.250+2T>A

ENST00000508376.6:c.220+2T>A

ENST00000508624.5:c.220+2T>A

ENST00000509732.5:c.220+2T>A

ENST00000512211.6:c.220+2T>A

NM_000038.5:c.220+2T>A

NM_001127510.2:c.220+2T>A

NM_001127511.2:c.250+2T>A

NM_001354895.1:c.220+2T>A

NM_001354896.1:c.220+2T>A

NM_001354897.1:c.250+2T>A

NM_001354898.1:c.145+2T>A

NM_001354899.1:c.220+2T>A

NM_001354900.1:c.43+2T>A

NM_001354901.1:c.43+2T>A

NM_001354902.1:c.250+2T>A

NM_001354903.1:c.220+2T>A

NM_001354904.1:c.145+2T>A

NM_001354905.1:c.43+2T>A

NM_001354906.1:c.-816+2T>A

NM_001127510.3:c.220+2T>A
NM_001127511.3:c.250+2T>A
NM_001354895.2:c.220+2T>A
NM_001354896.2:c.220+2T>A
NM_001354897.2:c.250+2T>A
NM_001354898.2:c.145+2T>A
NM_001354899.2:c.220+2T>A
NM_001354900.2:c.43+2T>A
NM_001354901.2:c.43+2T>A
NM_001354902.2:c.250+2T>A
NM_001354903.2:c.220+2T>A
NM_001354904.2:c.145+2T>A
NM_001354905.2:c.43+2T>A
NM_001354906.2:c.-816+2T>A

Pathogenic

Met criteria codes 3

PS4 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(APC):c.220+2T>A variant in APC occurs within the canonical splice donor site (+2) of intron 3. RT-PCR and CaptureSeq of patient cDNA demonstrated that the variant impacts splicing by creating a substantial but incomplete aberrant splice defect that is predicted to cause a premature stop codon (r.220+1_220+15ins15 (p.K73_E74insGRF*)) (PVS1, [internal data from Ambry Genetics, Invitae, Copenhagen University Hospital]). This variant has been reported in 25 probands/families meeting phenotypic criteria, resulting in a total phenotype score of 13.5 points (PS4, [Ambry Genetics, Invitae]). Moreover, the variant has been observed in heterozygous state in 20 additional individuals with a “Colorectal cancer/polypsis associated phenotype,” however, the available phenotype information is not sufficient to assign phenotype points (Invitae). 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: PVS1, PS4, PM2_Supporting (VCEP specifications v2.1.0; date of approval 11/24/2023).

Met criteria codes

PS4



This variant has been reported in 25 probands/families meeting phenotypic criteria, resulting in a total phenotype score of 13.5 points (PS4, [Ambry Genetics, Invitae]). Moreover, the variant has been observed in heterozygous state in 20 additional individuals with a “Colorectal cancer/polypsis associated phenotype,” however, the available phenotype information is not sufficient to assign phenotype points (Invitae).

PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1			The NM_000038.6(APC):c.220+2T>A variant in APC occurs within the canonical splice donor site (+2) of intron 3. RT-PCR and CaptureSeq of patient cDNA demonstrated that the variant impacts splicing by creating a substantial but incomplete aberrant splice defect that is predicted to cause a premature stop codon (r.220+1_220+15ins15 (p.K73_E74insGRF*)) (PVS1, [internal data from Ambry Genetics, Invitae, Copenhagen University Hospital]).

Curation History 

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