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Variant: NM_000038.6(APC):c.531+5_531+8del

Version: 1.0

CA658760464

537529 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: e349d6a4-8d6f-460f-8090-52728b9e030b
Approved on: 2025-05-15
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HGVS expressions

NM_000038.6:c.531+5_531+8del
NM_000038.6(APC):c.531+5_531+8del
NC_000005.10:g.112775742_112775745del
CM000667.2:g.112775742_112775745del
NC_000005.9:g.112111439_112111442del
CM000667.1:g.112111439_112111442del
NC_000005.8:g.112139338_112139341del
NG_008481.4:g.88222_88225del
ENST00000502371.3:c.531+5_531+8del
ENST00000504915.3:c.531+5_531+8del
ENST00000505084.2:n.587+5_587+8del
ENST00000505350.2:c.*537+5_*537+8del
ENST00000507379.6:c.561+5_561+8del
ENST00000509732.6:c.531+5_531+8del
ENST00000512211.7:c.531+5_531+8del
ENST00000257430.9:c.531+5_531+8del
ENST00000257430.8:c.531+5_531+8del
ENST00000507379.5:c.561+5_561+8del
ENST00000508376.6:c.531+5_531+8del
ENST00000508624.5:c.531+5_531+8del
ENST00000512211.6:c.531+5_531+8del
NM_000038.5:c.531+5_531+8del
NM_001127510.2:c.531+5_531+8del
NM_001127511.2:c.561+5_561+8del
NM_001354895.1:c.531+5_531+8del
NM_001354896.1:c.531+5_531+8del
NM_001354897.1:c.561+5_561+8del
NM_001354898.1:c.456+5_456+8del
NM_001354899.1:c.531+5_531+8del
NM_001354900.1:c.354+5_354+8del
NM_001354901.1:c.354+5_354+8del
NM_001354902.1:c.561+5_561+8del
NM_001354903.1:c.531+5_531+8del
NM_001354904.1:c.456+5_456+8del
NM_001354905.1:c.354+5_354+8del
NM_001354906.1:c.-505+5_-505+8del
NM_001127510.3:c.531+5_531+8del

NM_001127511.3:c.561+5_561+8del
NM_001354895.2:c.531+5_531+8del
NM_001354896.2:c.531+5_531+8del
NM_001354897.2:c.561+5_561+8del
NM_001354898.2:c.456+5_456+8del
NM_001354899.2:c.531+5_531+8del
NM_001354900.2:c.354+5_354+8del
NM_001354901.2:c.354+5_354+8del
NM_001354902.2:c.561+5_561+8del
NM_001354903.2:c.531+5_531+8del
NM_001354904.2:c.456+5_456+8del
NM_001354905.2:c.354+5_354+8del
NM_001354906.2:c.-505+5_-505+8del

Likely Pathogenic

Met criteria codes 4

PS3_Moderate PM2_Supporting PS4_Moderate PP3

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.531+5_531+8del variant is located in intron 5 of the APC gene. RT-PCR demonstrated that this variant impacts splicing by skipping of exon 5 resulting in a premature stop codon (PS3_Moderate, PMID: 15459959). This variant is absent from gnomAD v.2.1.1 (PM2_Supporting). This variant has been reported in 5 probands meeting phenotypic criteria, resulting in a total phenotype score of 3.5 (PS4_Moderate; internal data Labcorp Genetics [formerly Invitae] and Institute of Human Genetics, Bonn, Germany, PMID: 15459959 and 20223039). The results from two in silico splicing predictors (SpliceAI and VarSeak) indicate that this variant may affect splicing by disrupting the donor splice site of intron 5 of APC (PP3). 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 VCEP: PS3_Moderate, PM2_Supporting, PP3, and PS4_Moderate (VCEP specifications version v2.1.0; date of approval 11/24/2023).

Met criteria codes

PS3_Moderate	✔	RT-PCR demonstrated that this variant impacts splicing by skipping of exon 5 resulting in a premature stop codon (PS3_Moderate, PMID: 15459959).
PM2_Supporting	✔	This variant is absent from gnomAD v.2.1.1 (PM2_Supporting).

PS4_Moderate		✔	This variant has been reported in 5 probands meeting phenotypic criteria, resulting in a total phenotype score of 3.5 (PS4_Moderate; internal data Labcorp Genetics [formerly Invitae] and Institute of Human Genetics, Bonn, Germany, PMID: 15459959 and 20223039).
PP3		✔	The results from two in silico splicing predictors (SpliceAI and VarSeak) indicate that this variant may affect splicing by disrupting the donor splice site of intron 5 of APC (PP3).

Curation History

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