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Variant: NM_000038.6(APC):c.1312+3A>C

Version: 1.0

CA658655920

486792 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: 651c5675-2a31-4cfc-a9d9-6d2b5b2d2bfe
Approved on: 2025/5/16
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HGVS expressions

NM_000038.6(APC):c.1312+3A>C
NM_000038.6:c.1312+3A>C
NC_000005.10:g.112819347A>C
CM000667.2:g.112819347A>C
NC_000005.9:g.112155044A>C
CM000667.1:g.112155044A>C
NC_000005.8:g.112182943A>C
NG_008481.4:g.131827A>C
ENST00000502371.3:c.1312+3A>C
ENST00000504915.3:c.1312+3A>C
ENST00000505084.2:n.1368+3A>C
ENST00000505350.2:c.*1318+3A>C
ENST00000507379.6:c.1258+3A>C
ENST00000509732.6:c.1312+3A>C
ENST00000512211.7:c.1312+3A>C
ENST00000257430.9:c.1312+3A>C
ENST00000257430.8:c.1312+3A>C
ENST00000507379.5:c.1258+3A>C
ENST00000508376.6:c.1312+3A>C
ENST00000508624.5:c.*634+3A>C
ENST00000512211.6:c.1312+3A>C
NM_000038.5:c.1312+3A>C
NM_001127510.2:c.1312+3A>C
NM_001127511.2:c.1258+3A>C
NM_001354895.1:c.1312+3A>C
NM_001354896.1:c.1312+3A>C
NM_001354897.1:c.1342+3A>C
NM_001354898.1:c.1237+3A>C
NM_001354899.1:c.1228+3A>C
NM_001354900.1:c.1135+3A>C
NM_001354901.1:c.1135+3A>C
NM_001354902.1:c.1039+3A>C
NM_001354903.1:c.1009+3A>C
NM_001354904.1:c.934+3A>C
NM_001354905.1:c.832+3A>C
NM_001354906.1:c.463+3A>C
NM_001127510.3:c.1312+3A>C

NM_001127511.3:c.1258+3A>C
NM_001354895.2:c.1312+3A>C
NM_001354896.2:c.1312+3A>C
NM_001354897.2:c.1342+3A>C
NM_001354898.2:c.1237+3A>C
NM_001354899.2:c.1228+3A>C
NM_001354900.2:c.1135+3A>C
NM_001354901.2:c.1135+3A>C
NM_001354902.2:c.1039+3A>C
NM_001354903.2:c.1009+3A>C
NM_001354904.2:c.934+3A>C
NM_001354905.2:c.832+3A>C
NM_001354906.2:c.463+3A>C

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PP3 PS4_Moderate PS1

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.1312+3A>C variant in APC is an intronic variant, which is located at the 3rd nucleotide in intron 10. This variant has been reported in 2 probands meeting phenotypic criteria, resulting in a total phenotype score of 2 points (PS4_Moderate, Ambry Genetics internal data, Tsukanov et al 2017; Russian Journal of Genetics, 2017, Vol. 53, No. 3, pp. 369–375). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). The results from two in silico splicing predictors (SpliceAI and MaxEntScan) indicate that this variant may affect splicing by disrupting the donor splice site of intron 10 of APC (PP3). Moreover, this variant has similar in silico predictions compared to another noncanonical splicing variant at that same nucleotide position (c.1312+3A>G) (ClinVar ID: 217924), which is classified as pathogenic for FAP by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP (HCCP VCEP) (PS1). 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 HCCP VCEP: criteria PS1, PM2_Supporting, PP3, and PS4_Moderate applied (VCEP specifications version v2.1.0; date of approval 11/24/2023).

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PP3	✔	The results from two in silico splicing predictors (SpliceAI and MaxEntScan) indicate that this variant may affect splicing by disrupting the donor splice site of intron 10 of APC (PP3).

PS4_Moderate		✔	This variant has been reported in 2 probands meeting phenotypic criteria, resulting in a total phenotype score of 2 points (PS4_Moderate, Ambry Genetics internal data, Tsukanov et al 2017; Russian Journal of Genetics, 2017, Vol. 53, No. 3, pp. 369–375).
PS1		✔	This variant has similar in silico predictions compared to another noncanonical splicing variant at that same nucleotide position (c.1312+3A>G) (ClinVar ID: 217924), which is classified as pathogenic for FAP by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP (HCCP VCEP) (PS1).

Curation History

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