Variant: NM_000038.6(APC):c.1312+5G>C

Version: 1.0

CA10588378

265372 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: 45e51f78-6174-4da9-8b3b-8149f0e60efb
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HGVS expressions

NM_000038.6:c.1312+5G>C
NM_000038.6(APC):c.1312+5G>C
NC_000005.10:g.112819349G>C
CM000667.2:g.112819349G>C
NC_000005.9:g.112155046G>C
CM000667.1:g.112155046G>C
NC_000005.8:g.112182945G>C
NG_008481.4:g.131829G>C
ENST00000502371.3:c.1312+5G>C
ENST00000504915.3:c.1312+5G>C
ENST00000505084.2:n.1368+5G>C
ENST00000505350.2:c.*1318+5G>C
ENST00000507379.6:c.1258+5G>C
ENST00000509732.6:c.1312+5G>C
ENST00000512211.7:c.1312+5G>C
ENST00000257430.9:c.1312+5G>C
ENST00000257430.8:c.1312+5G>C
ENST00000507379.5:c.1258+5G>C
ENST00000508376.6:c.1312+5G>C
ENST00000508624.5:c.*634+5G>C
ENST00000512211.6:c.1312+5G>C
NM_000038.5:c.1312+5G>C
NM_001127510.2:c.1312+5G>C
NM_001127511.2:c.1258+5G>C
NM_001354895.1:c.1312+5G>C
NM_001354896.1:c.1312+5G>C
NM_001354897.1:c.1342+5G>C
NM_001354898.1:c.1237+5G>C
NM_001354899.1:c.1228+5G>C
NM_001354900.1:c.1135+5G>C
NM_001354901.1:c.1135+5G>C
NM_001354902.1:c.1039+5G>C
NM_001354903.1:c.1009+5G>C
NM_001354904.1:c.934+5G>C
NM_001354905.1:c.832+5G>C
NM_001354906.1:c.463+5G>C
NM_001127510.3:c.1312+5G>C

NM_001127511.3:c.1258+5G>C
NM_001354895.2:c.1312+5G>C
NM_001354896.2:c.1312+5G>C
NM_001354897.2:c.1342+5G>C
NM_001354898.2:c.1237+5G>C
NM_001354899.2:c.1228+5G>C
NM_001354900.2:c.1135+5G>C
NM_001354901.2:c.1135+5G>C
NM_001354902.2:c.1039+5G>C
NM_001354903.2:c.1009+5G>C
NM_001354904.2:c.934+5G>C
NM_001354905.2:c.832+5G>C
NM_001354906.2:c.463+5G>C

Likely Pathogenic

Met criteria codes 4

PP3 PS1_Moderate PS4_Moderate 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.1312+5G>C variant in APC is an intronic variant which is located at the 5th nucleotide in intron 10. This variant has been reported in 3 probands meeting phenotypic criteria, resulting in a total phenotype score of 2.5 points (PS4_Moderate, Ambry Genetics, GeneDx, Invitae internal data). 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 non-canonical splicing variant at that same nucleotide position (c.1312+5G>A) which is classified as Likely Pathogenic for FAP by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP (HCCP VCEP) (PS1_Moderate). In summary, this variant meets the criteria to be classified as Likely Pathogenic for FAP based on the ACMG/AMP criteria applied, as specified by the HCCP VCEP: PP3, PS1_Moderate, PS4_Moderate, PM2_Supporting (VCEP specifications version 2.1.0; date of approval: 11/24/2023).

Met criteria codes

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).
PS1_Moderate	✔	This variant has similar in silico predictions compared to another non-canonical splicing variant at that same nucleotide position (c.1312+5G>A) which is classified as Likely Pathogenic for FAP by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP (HCCP VCEP) (PS1_Moderate).

PS4_Moderate		✔	This variant has been reported in 3 probands meeting phenotypic criteria, resulting in a total phenotype score of 2.5 points (PS4_Moderate, Ambry Genetics, GeneDx, Invitae internal data).
PM2_Supporting		✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History

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