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

Version: 1.0

CA279764

217924 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: 668e53dc-c465-4363-aaf0-a326f0fc82b1
Approved on: 2025-05-15
Published on: 2025-05-19

HGVS expressions

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

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

Pathogenic

Met criteria codes 4

PM2_Supporting | PS2_Moderate | PS4_Very Strong | PS3_Moderate

Evidence Links 1

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>G variant in APC is an intronic variant which is located at the 3rd nucleotide in intron 10. This variant has been reported in more than 16 cases meeting phenotypic criteria resulting in a total phenotype score of 16 points (internal data Labcorp Genetics [formerly Invitae], Peter MacCallum Cancer Centre, Victoria, Australia, GeneDx, Ambry; PMID: 8381580, 15459959, 20223039, 17489848, 19793053, 20685668) (PS4_Very Strong). This variant has been identified as a de novo occurrence with confirmed parental relationships in one individual with FAP, resulting in a total de novo score of 1 (PS2_Moderate, Ambry internal data). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). RNA studies demonstrated that the variant impacts splicing by causing exon 10 skipping (PMID: 15459959, Ambry internal data) (PS3_Moderate). 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: criteria PS4_Very Strong, PS2_Moderate, PM2_Supporting, PS3_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).
PS2_Moderate	✔	This variant has been identified as a de novo occurrence with confirmed parental relationships in one individual with FAP, resulting in a total de novo score of 1 (PS2_Moderate, Ambry internal data).

PS4_Very Strong		✔	This variant has been reported in more than 16 cases meeting phenotypic criteria resulting in a total phenotype score of 16 points (internal data Labcorp Genetics [formerly Invitae], Peter MacCallum Cancer Centre, Victoria, Australia, GeneDx, Ambry; PMID: 8381580, 15459959, 20223039, 17489848, 19793053, 20685668) (PS4_Very Strong).
PS3_Moderate		✔	RNA studies demonstrated that the variant impacts splicing by causing exon 10 skipping (PMID: 15459959, Ambry internal data) (PS3_Moderate). Variant impacts splicing by causing exon 10 skipping PubMed:15459959

Curation History

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