

Variant: *NM_000038.6(APC):c.3083G>A (p.Ser1028Asn)*

Version: 2.0

CA16028084 [↗](#)

428186 (ClinVar) [↗](#)

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

Condition: familial adenomatous polyposis 1 ([MONDO:0021056](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 7cb03244-ee57-4d80-9542-a0a5abc44d98

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HGVS expressions

NM_000038.6:c.3083G>A

NM_000038.6(APC):c.3083G>A (p.Ser1028Asn)

NC_000005.10:g.112838677G>A

CM000667.2:g.112838677G>A

NC_000005.9:g.112174374G>A

CM000667.1:g.112174374G>A

NC_000005.8:g.112202273G>A

NG_008481.4:g.151157G>A

ENST00000502371.3:c.2748G>A

ENST00000504915.3:c.3137G>A

ENST00000505350.2:c.*3089G>A

ENST00000507379.6:c.3029G>A

ENST00000509732.6:c.3083G>A

ENST00000512211.7:c.3083G>A

ENST00000257430.9:c.3083G>A

ENST00000257430.8:c.3083G>A

ENST00000502371.2:c.1436G>A

ENST00000507379.5:c.3029G>A

ENST00000508376.6:c.3083G>A

ENST00000508624.5:c.*2405G>A

ENST00000512211.6:c.3083G>A

ENST00000520401.1:c.230+9705G>A

NM_000038.5:c.3083G>A

NM_001127510.2:c.3083G>A

NM_001127511.2:c.3029G>A

NM_001354895.1:c.3083G>A

NM_001354896.1:c.3137G>A

NM_001354897.1:c.3113G>A

NM_001354898.1:c.3008G>A

NM_001354899.1:c.2999G>A

NM_001354900.1:c.2960G>A

NM_001354901.1:c.2906G>A

NM_001354902.1:c.2810G>A

NM_001354903.1:c.2780G>A

NM_001354904.1:c.2705G>A

NM_001354905.1:c.2603G>A

NM_001354906.1:c.2234G>A

NM_001127510.3:c.3083G>A
NM_001127511.3:c.3029G>A
NM_001354895.2:c.3083G>A
NM_001354896.2:c.3137G>A
NM_001354897.2:c.3113G>A
NM_001354898.2:c.3008G>A
NM_001354899.2:c.2999G>A
NM_001354900.2:c.2960G>A
NM_001354901.2:c.2906G>A
NM_001354902.2:c.2810G>A
NM_001354903.2:c.2780G>A
NM_001354904.2:c.2705G>A
NM_001354905.2:c.2603G>A
NM_001354906.2:c.2234G>A

Likely Pathogenic

Met criteria codes 4

PM5_Supporting PS4_Moderate
PM2_Supporting PP1_Moderate

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polypsis VCEP

Criteria Specification Information

Criteria Specification: ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis 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/Polypsis VCEP

The NM_000038.6:c.3083G>A variant in APC is a missense variant predicted to cause the substitution of serine to asparagine at amino acid position 1028 (p.Ser1028Asn). This variant has been reported in 4 probands/families meeting phenotypic criteria, resulting in a total phenotype score of 2 (PS4_Moderate; internal data Ambry Genetics; Labcorp Genetics (formerly Invitae); Peter MacCallum Cancer Centre, Victoria, Australia). The variant has been reported in 3 additional probands with a colorectal cancer/polypsis associated phenotype not meeting phenotypic criteria and one individual with colorectal cancer in the family history (internal data Ambry Genetics; Labcorp Genetics (formerly Invitae); Peter MacCallum Cancer Centre, Victoria, Australia). This variant has been reported to segregate with FAP in 5 meioses in 2 families (PP1_Moderate; internal data Ambry Genetics and Peter MacCallum Cancer Centre, Victoria, Australia). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). Two other missense variants (c.3084T>A and c.3083G>T) in the same codon leading to a different amino acid change at this position (p.Ser1028Arg; p.Ser1028Ile) have been classified as Likely Pathogenic by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis Variant Curation Expert Panel (HCCP VCEP) (PM5_Supporting). 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 PS4_Moderate, PP1_Moderate, PM2_Supporting and PM5_Supporting (VCEP specifications version v2.1.0; date of approval 11/24/2023).

Met criteria codes

PM5_Supporting  

Two other missense variants (c.3084T>A and c.3083G>T) in the same codon leading to a different amino acid change at this position (p.Ser1028Arg; p.Ser1028Ile) have been classified as Likely Pathogenic by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis Variant Curation Expert Panel (HCCP VCEP) (PM5_Supporting).

PS4_Moderate			This variant has been reported in 4 probands/families meeting phenotypic criteria, resulting in a total phenotype score of 2 (PS4_Moderate; internal data Ambry Genetics; Labcorp Genetics (formerly Invitae); Peter MacCallum Cancer Centre, Victoria, Australia). The variant has been reported in 3 additional probands with a colorectal cancer/polypsis associated phenotype not meeting phenotypic criteria and one individual with colorectal cancer in the family history (internal data Ambry Genetics; Labcorp Genetics (formerly Invitae); Peter MacCallum Cancer Centre, Victoria, Australia).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PP1_Moderate			This variant has been reported to segregate with FAP in 5 meioses in 2 families (PP1_Moderate; internal data Ambry Genetics and Peter MacCallum Cancer Centre, Victoria, Australia).

Curation History

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