

Variant: NM_000038.6(APC):c.2476T>G (p.Leu826Val)

Version: 1.0

CA007509 [↗](#)

142010 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: ffcec97a-2384-47b7-808d-bbdfae08259c

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HGVS expressions

NM_000038.6(APC):c.2476T>G (p.Leu826Val)

NM_000038.6:c.2476T>G

NC_000005.10:g.112838070T>G

CM000667.2:g.112838070T>G

NC_000005.9:g.112173767T>G

CM000667.1:g.112173767T>G

NC_000005.8:g.112201666T>G

NG_008481.4:g.150550T>G

ENST00000502371.3:c.2141T>G

ENST00000504915.3:c.2530T>G

ENST00000505350.2:c.*2482T>G

ENST00000507379.6:c.2422T>G

ENST00000509732.6:c.2476T>G

ENST00000512211.7:c.2476T>G

ENST00000257430.9:c.2476T>G

ENST00000257430.8:c.2476T>G

ENST00000502371.2:c.829T>G

ENST00000507379.5:c.2422T>G

ENST00000508376.6:c.2476T>G

ENST00000508624.5:c.*1798T>G

ENST00000512211.6:c.2476T>G

ENST00000520401.1:c.230+9098T>G

NM_000038.5:c.2476T>G

NM_001127510.2:c.2476T>G

NM_001127511.2:c.2422T>G

NM_001354895.1:c.2476T>G

NM_001354896.1:c.2530T>G

NM_001354897.1:c.2506T>G

NM_001354898.1:c.2401T>G

NM_001354899.1:c.2392T>G

NM_001354900.1:c.2353T>G

NM_001354901.1:c.2299T>G

NM_001354902.1:c.2203T>G

NM_001354903.1:c.2173T>G

NM_001354904.1:c.2098T>G

NM_001354905.1:c.1996T>G

NM_001354906.1:c.1627T>G

NM_001127510.3:c.2476T>G
NM_001127511.3:c.2422T>G
NM_001354895.2:c.2476T>G
NM_001354896.2:c.2530T>G
NM_001354897.2:c.2506T>G
NM_001354898.2:c.2401T>G
NM_001354899.2:c.2392T>G
NM_001354900.2:c.2353T>G
NM_001354901.2:c.2299T>G
NM_001354902.2:c.2203T>G
NM_001354903.2:c.2173T>G
NM_001354904.2:c.2098T>G
NM_001354905.2:c.1996T>G
NM_001354906.2:c.1627T>G

Benign

Met criteria codes 2

BP1 BA1

Not Met criteria codes 4

BS1 BP4 PP3 PM2

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

The c.2476T>G variant in APC is a missense variant predicted to cause a substitution of leucine by valine at amino acid position 826 (p.Leu826Val). The highest population minor allele frequency in gnomAD v2.1.1 is 0.1576% in the non-cancer African/African American population, which is higher than the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation threshold (>0.1%) for BA1, and therefore meets this criterion (BA1). Additionally, APC is defined by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation Expert Panel as a gene for which primarily truncating variants are known to cause disease (BP1). Multiple lines of computational evidence suggest no splicing impact. In summary, this variant meets the criteria to be classified as Benign for FAP. ACMG/AMP criteria applied, as specified by the ClinGen/InSiGHT Hereditary Colorectal Cancer/Polyposis Expert Panel: BA1, BP1 (VCEP specifications version 1; date of approval: 12/12/2022).

Met criteria codes

BP1



APC, in which the variant was identified, is defined by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP as a gene for which primarily truncating variants are known to cause disease (BP1).

BA1



The highest population minor allele frequency in gnomAD v2.1.1 is 0.1576% in African/African American population, which is higher than the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation threshold (>0.1%) for BA1, and therefore meets this criterion (BA1).

Not Met criteria codes

BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP3			Multiple lines of computational evidence suggest no splicing impact (SpliceAI and varSEAK).
PM2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 		
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