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Variant: NM_000038.6(APC):c.1626G>C (p.Gln542His)

Version: 1.0

CA16024860

649594 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2f983945-ecba-4893-851f-7c47a672f57c
Approved on: 2023/2/19
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HGVS expressions

NM_000038.6(APC):c.1626G>C (p.Gln542His)
NM_000038.6:c.1626G>C
NC_000005.10:g.112828006G>C
CM000667.2:g.112828006G>C
NC_000005.9:g.112163703G>C
CM000667.1:g.112163703G>C
NC_000005.8:g.112191602G>C
NG_008481.4:g.140486G>C
ENST00000502371.3:c.1408+6015G>C
ENST00000504915.3:c.1680G>C
ENST00000505084.2:n.1682G>C
ENST00000505350.2:c.*1632G>C
ENST00000507379.6:c.1572G>C
ENST00000509732.6:c.1626G>C
ENST00000512211.7:c.1626G>C
ENST00000257430.9:c.1626G>C
ENST00000257430.8:c.1626G>C
ENST00000502371.2:c.96+6015G>C
ENST00000504915.2:c.315G>C
ENST00000505084.1:n.113G>C
ENST00000507379.5:c.1572G>C
ENST00000508376.6:c.1626G>C
ENST00000508624.5:c.*948G>C
ENST00000512211.6:c.1626G>C
ENST00000520401.1:c.113G>C
NM_000038.5:c.1626G>C
NM_001127510.2:c.1626G>C
NM_001127511.2:c.1572G>C
NM_001354895.1:c.1626G>C
NM_001354896.1:c.1680G>C
NM_001354897.1:c.1656G>C
NM_001354898.1:c.1551G>C
NM_001354899.1:c.1542G>C
NM_001354900.1:c.1503G>C
NM_001354901.1:c.1449G>C
NM_001354902.1:c.1353G>C
NM_001354903.1:c.1323G>C

NM_001354904.1:c.1248G>C
NM_001354905.1:c.1146G>C
NM_001354906.1:c.777G>C
NM_001127510.3:c.1626G>C
NM_001127511.3:c.1572G>C
NM_001354895.2:c.1626G>C
NM_001354896.2:c.1680G>C
NM_001354897.2:c.1656G>C
NM_001354898.2:c.1551G>C
NM_001354899.2:c.1542G>C
NM_001354900.2:c.1503G>C
NM_001354901.2:c.1449G>C
NM_001354902.2:c.1353G>C
NM_001354903.2:c.1323G>C
NM_001354904.2:c.1248G>C
NM_001354905.2:c.1146G>C
NM_001354906.2:c.777G>C

Likely Pathogenic

Met criteria codes 3

PVS1_Strong PM2_Supporting PS4_Supporting

Not Met criteria codes 1

PS3

Evidence Links 1

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.1626G>C variant in APC is a G to non-G change at the last nucleotide of exon 13. It is predicted to cause skipping of exon 13, resulting in an in-frame deletion of an exon with sufficient supportive clinical data (r.1549_1626del) (p.A517_Q542del) (PVS1_Strong). This prediction is confirmed by RT-PCR analysis (supplanted by PVS1_Strong; PMID 24599579). This variant was detected in one proband and two other family members, the combined phenotypic point is 1 (PS4_Supporting). Finally, this variant is absent from gnomAD v2.1.1 (PM2_Supporting). In summary, this variant is classified as Likely Pathogenic for FAP based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation Expert Panel: PVS1_Strong, PS4_Supporting and PM2_Supporting. (VCEP specifications version 1; date of approval: 12/12/2022).

Met criteria codes

PVS1_Strong	✔	The c.1626G>C variant is the last nucleotide of exon 13. It occurs within the canonical splice donor site of intron 13. It is predicted to cause skipping of biologically-relevant-exon 13, resulting in the loss of amino acids (r.1549_1626del) (p.A517_Q542del) (PVS1_Strong). This prediction is confirmed by RT-PCR analysis (supplanted by PVS1; PMID24599579).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

PS4_Supporting	ℹ	✔	This variant was detected in one proband and two other family members, the combined phenotypic point is 1 (PS4_Supporting).

Not Met criteria codes

PS3	ℹ	✖	RT-PCR evidence used to upgrade PVS1_Str to PVS1. PS3 therefore not applied. The c.1626G>C variant in APC occurs within the canonical splice donor site of intron 13. It is predicted to cause skipping of biologically-relevant-exon 13, resulting in the loss of amino acids (r.1549_1626del) (p.A517_Q542del) without sufficient supportive clinical data (PVS1_Moderate). This prediction is confirmed by RT-PCR analysis (PMID24599579). PubMed:24599579

Curation History

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