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# *Variant: NM_001354906.2:c.2228A>G*

Version: 1.0

*CA16028071*

*1393312 (ClinVar)*

**Gene**: APC (HGNC:324)
**Condition**: familial adenomatous polyposis 1 (MONDO:0021056)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** d54ea820-f491-4667-9b39-a318d8067e2a
**Approved on**: 2023/2/25
**Published on**: 2023/3/14

## *HGVS expressions*

**NM_001354906.2:c.2228A>G**
NC_000005.10:g.112838671A>G
CM000667.2:g.112838671A>G
NC_000005.9:g.112174368A>G
CM000667.1:g.112174368A>G
NC_000005.8:g.112202267A>G
NG_008481.4:g.151151A>G
ENST00000502371.3:c.2742A>G
ENST00000504915.3:c.3131A>G
ENST00000505350.2:c.*3083A>G
ENST00000507379.6:c.3023A>G
ENST00000509732.6:c.3077A>G
ENST00000512211.7:c.3077A>G
ENST00000257430.9:c.3077A>G
ENST00000257430.8:c.3077A>G
ENST00000502371.2:c.1430A>G
ENST00000507379.5:c.3023A>G
ENST00000508376.6:c.3077A>G
ENST00000508624.5:c.*2399A>G
ENST00000512211.6:c.3077A>G
ENST00000520401.1:c.230+9699A>G
NM_000038.5:c.3077A>G
NM_001127510.2:c.3077A>G
NM_001127511.2:c.3023A>G
NM_001354895.1:c.3077A>G
NM_001354896.1:c.3131A>G
NM_001354897.1:c.3107A>G
NM_001354898.1:c.3002A>G
NM_001354899.1:c.2993A>G
NM_001354900.1:c.2954A>G
NM_001354901.1:c.2900A>G
NM_001354902.1:c.2804A>G
NM_001354903.1:c.2774A>G
NM_001354904.1:c.2699A>G
NM_001354905.1:c.2597A>G
NM_001354906.1:c.2228A>G
NM_000038.6:c.3077A>G

NM_001127510.3:c.3077A>G
NM_001127511.3:c.3023A>G
NM_001354895.2:c.3077A>G
NM_001354896.2:c.3131A>G
NM_001354897.2:c.3107A>G
NM_001354898.2:c.3002A>G
NM_001354899.2:c.2993A>G
NM_001354900.2:c.2954A>G
NM_001354901.2:c.2900A>G
NM_001354902.2:c.2804A>G
NM_001354903.2:c.2774A>G
NM_001354904.2:c.2699A>G
NM_001354905.2:c.2597A>G

**Likely Pathogenic**

**Met criteria codes** 4

PS3_Supporting PP1_Strong PS4_Moderate PM2_Supporting

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.3077A>G variant in APC is a missense variant predicted to cause the substitution of asparagine by serine at amino acid position 1026 (p.Asn1026Ser). This variant has been reported to segregate with FAP in ≥ 7 meioses in 2 families (PP1_strong; PMID 18166348, Barcelona internal data). Increased β-catenin regulated transcription activity and decreased binding to β-catenin by surface plasmon resonance are also demonstrated (PS3_Supporting; PMID18166348). This variant has been reported in 2 families meeting phenotypic criteria, resulting in a total phenotype score of 3.5 points (PS4_Moderate, PMID 18166348, Invitae and Barcelona Internal data). Finally, this variant is absent from gnomAD v2.1.1 (PM2_Supporting). 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 ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Variant Curation Expert Panel: PP1_Strong, PS4_Moderate, PS3_Supporting, and PM2_Supporting (VCEP specifications version 1; date of approval: 12/12/2022).**

**Met criteria codes**

| | | |
|---|---|---|
| **PS3_Supporting** | ✔ | APC-VCEP specific modification of PS3 met (PS3_Supporting); PMID: 18166348: Increased β-catenin regulated transcription activity and/or decreased binding to β-catenin by surface plasmon resonance |
| **PP1_Strong** | ✔ | This variant has been reported to segregate with FAP in 10 meioses in 1 family and in 4 meioses in another family (≥ 7 in total) (PP1_Strong; internal data, Menendez et al. 2008, PMID: 18166348). |
| **PS4_Moderate** | ✔ | This variant has been reported in 2 families meeting phenotypic criteria, resulting in a total phenotype score of 3.5 point (PS4_Moderate, PMID 18166348, Invitae and Barcelona Internal data). |
| **PM2_Supporting** | ✔ | This variant is absent from gnomAD v2.1.1 (PM2_Supporting). |

## Curation History

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