The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000038.6(APC):c.6510del (p.Glu2172fs)

Version: 1.2

CA645509163

438884 (ClinVar)

Gene: APC (HGNC:324)
Condition: familial adenomatous polyposis 1 (MONDO:0021056)
Inheritance Mode: Autosomal dominant inheritance
UUID: d9cf8b9d-53ac-4983-b393-c2e787459b28
Approved on: 2025/5/19
Published on: 2025/5/19

HGVS expressions

NM_000038.6:c.6510del
NM_000038.6(APC):c.6510del (p.Glu2172fs)
NC_000005.10:g.112842104del
CM000667.2:g.112842104del
NC_000005.9:g.112177801del
CM000667.1:g.112177801del
NC_000005.8:g.112205700del
NG_008481.4:g.154584del
ENST00000504915.3:c.6564del
ENST00000505350.2:c.*6516del
ENST00000507379.6:c.6456del
ENST00000509732.6:c.6510del
ENST00000512211.7:c.6510del
ENST00000257430.9:c.6510del
ENST00000257430.8:c.6510del
ENST00000508376.6:c.6510del
ENST00000508624.5:c.*5832del
ENST00000520401.1:c.230+13132del
NM_000038.5:c.6510del
NM_001127510.2:c.6510del
NM_001127511.2:c.6456del
NM_001354895.1:c.6510del
NM_001354896.1:c.6564del
NM_001354897.1:c.6540del
NM_001354898.1:c.6435del
NM_001354899.1:c.6426del
NM_001354900.1:c.6387del
NM_001354901.1:c.6333del
NM_001354902.1:c.6237del
NM_001354903.1:c.6207del
NM_001354904.1:c.6132del
NM_001354905.1:c.6030del
NM_001354906.1:c.5661del
NM_001127510.3:c.6510del
NM_001127511.3:c.6456del
NM_001354895.2:c.6510del
NM_001354896.2:c.6564del

NM_001354897.2:c.6540del
NM_001354898.2:c.6435del
NM_001354899.2:c.6426del
NM_001354900.2:c.6387del
NM_001354901.2:c.6333del
NM_001354902.2:c.6237del
NM_001354903.2:c.6207del
NM_001354904.2:c.6132del
NM_001354905.2:c.6030del
NM_001354906.2:c.5661del

Pathogenic

Met criteria codes 3

PS4_Supporting PVS1 PM2_Supporting

Evidence Links 0

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.6510del (p.Glu2172ArgfsTer10) variant in APC is a frameshift variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 16 in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant has been reported in 2 probands meeting phenotypic criteria, resulting in a total phenotype score of 1 (PS4_Supporting; internal data GeneDx and Ambry Genetics). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). 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 PVS1, PS4_Supporting, and PM2_Supporting applied (VCEP specifications v2.1.0; date of approval 11/24/2023).

Met criteria codes

PS4_Supporting	✔	This variant has been reported in 2 probands meeting phenotypic criteria, resulting in a total phenotype score of 1 (PS4_Supporting; internal data GeneDx and Ambry Genetics).
PVS1	✔	The NM_000038.6(APC):c.6510del (p.Glu2172ArgfsTer10) variant in APC is a frameshift variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 16 in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History

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