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.203del (p.Leu68fs)*

Version: 1.0

*CA1139658985*

*934724 (ClinVar)*

**Gene**: APC (HGNC:324)
**Condition**: familial adenomatous polyposis 1 (MONDO:0021056)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** 11e3fbb8-fe19-45e6-a2dc-435180a69a70
**Approved on**: 2025/5/19
**Published on**: 2025/5/19

## *HGVS expressions*

**NM_000038.6:c.203del**
**NM_000038.6(APC):c.203del (p.Leu68fs)**
NC_000005.10:g.112766393del
CM000667.2:g.112766393del
NC_000005.9:g.112102090del
CM000667.1:g.112102090del
NC_000005.8:g.112129989del
NG_008481.4:g.78873del
ENST00000502371.3:c.203del
ENST00000504915.3:c.203del
ENST00000505084.2:n.259del
ENST00000505350.2:c.*209del
ENST00000507379.6:c.233del
ENST00000509732.6:c.203del
ENST00000512211.7:c.203del
ENST00000257430.9:c.203del
ENST00000257430.8:c.203del
ENST00000507379.5:c.233del
ENST00000508376.6:c.203del
ENST00000508624.5:c.203del
ENST00000509732.5:c.203del
ENST00000512211.6:c.203del
NM_000038.5:c.203del
NM_001127510.2:c.203del
NM_001127511.2:c.233del
NM_001354895.1:c.203del
NM_001354896.1:c.203del
NM_001354897.1:c.233del
NM_001354898.1:c.128del
NM_001354899.1:c.203del
NM_001354900.1:c.26del
NM_001354901.1:c.26del
NM_001354902.1:c.233del
NM_001354903.1:c.203del
NM_001354904.1:c.128del
NM_001354905.1:c.26del
NM_001354906.1:c.-833del

NM_001127510.3:c.203del
NM_001127511.3:c.233del
NM_001354895.2:c.203del
NM_001354896.2:c.203del
NM_001354897.2:c.233del
NM_001354898.2:c.128del
NM_001354899.2:c.203del
NM_001354900.2:c.26del
NM_001354901.2:c.26del
NM_001354902.2:c.233del
NM_001354903.2:c.203del
NM_001354904.2:c.128del
NM_001354905.2:c.26del
NM_001354906.2:c.-833del

**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.203del (p.Leu68TyrfsTer2) variant in APC is a nonsense variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 3 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 Invitae, MGZ Medical Genetics Center). 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: criteria PVS1, PS4_Supporting and PM2_Supporting applied (VCEP specifications v2.0.3; date of approval 7/24/2023).**

**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 Invitae, MGZ Medical Genetics Center). |
| **PVS1** | ✔ | The NM_000038.6(APC):c.203del (p.Leu68TyrfsTer2) variant in APC is a nonsense variant located between codon 49 and 2645 and predicted to cause a premature stop codon in exon 3 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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