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_000059.4(BRCA2):c.7805+3A>C

Version: 1.0

CA025281

52411 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: 6d965a38-858f-499a-ae39-bc0521500627
Approved on: 2025/8/18
Published on: 2025/8/18

HGVS expressions

NM_000059.4(BRCA2):c.7805+3A>C
NM_000059.4:c.7805+3A>C
NC_000013.11:g.32357932A>C
CM000675.2:g.32357932A>C
NC_000013.10:g.32932069A>C
CM000675.1:g.32932069A>C
NC_000013.9:g.31830069A>C
NG_012772.3:g.47453A>C
ENST00000470094.2:c.7805+3A>C
ENST00000528762.2:c.7805+3A>C
ENST00000530893.7:c.7436+3A>C
ENST00000665585.2:c.7805+3A>C
ENST00000666593.2:c.7805+3A>C
ENST00000700202.2:c.7805+3A>C
ENST00000700202.1:c.272+3A>C
ENST00000380152.8:c.7805+3A>C
ENST00000544455.6:c.7805+3A>C
ENST00000614259.2:c.7805+3A>C
ENST00000665585.1:c.370+3A>C
ENST00000680887.1:c.7805+3A>C
ENST00000380152.7:c.7805+3A>C
ENST00000544455.5:c.7805+3A>C
ENST00000614259.1:n.7805+3A>C
NM_000059.3:c.7805+3A>C

Likely Pathogenic

Met criteria codes 3

PVS1_Strong PS3 PM2_Supporting

Evidence Links 0

Expert Panel

ENIGMA BRCA1 and BRCA2 VCEP

Criteria Specification Information

Criteria Specification: *ClinGen ENIGMA BRCA1 and BRCA2 Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BRCA2 Version 1.1.0*
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.7805+3A>C variant is an intronic variant occurring in intron 16 of the BRCA2 gene. This variant is reported to result in aberrant mRNA splicing. Mini-gene assays demonstrated that the variant impacts splicing by skipping of exon 16 (75.3%), utilization of cryptic donor sites 100 bp upstream in exon 16 (13.3%), and retention of 20 bp from intron 16 (3.8%) resulting in >90% of transcripts leading to a frameshift and generating a premature stop codon (PMID: 29881398). Appropriate code strength was determined by comparison of results to PVS1 decision tree with PVS1 (RNA) downgraded to PVS1_Strong (RNA). Intronic variant, functional data considered only from assays that measure effect via mRNA and protein. Reported by two calibrated studies incorporating mRNA splicing effects to exhibit protein function similar to pathogenic control variants (PMIDs:39779857, 39779848) (PS3 met). This variant is absent from gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥25) and gnomAD v3.1 (non-cancer subset, read depth ≥25). In summary, this variant meets the criteria to be classified as a Likely pathogenic variant for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PVS1_Strong (RNA), PM2_Supporting, PS3).

Met criteria codes

PVS1_Strong	✔	This variant is reported to result in aberrant mRNA splicing. Mini-gene assays demonstrated that the variant impacts splicing by skipping of exon 16 (75.3%), utilization of cryptic donor sites 100 bp upstream in exon 16 (13.3%), and retention of 20 bp from intron 16 (3.8%) resulting in >90% of transcripts leading to a frameshift and generating a premature stop codon (PMID: 29881398). Appropriate code strength was determined by comparison of results to PVS1 decision tree with PVS1 (RNA) downgraded to PVS1_Strong (RNA).
PS3	✔	Intronic variant, functional data considered only from assays that measure effect via mRNA and protein. Reported by two calibrated studies incorporating mRNA splicing effects to exhibit protein function similar to pathogenic control variants (PMIDs:39779857, 39779848) (PS3 met).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥25) and gnomAD v3.1 (non-cancer subset, read depth ≥25).

Curation History

Showing 1 to 1 of 1 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.