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.7967T>A (p.Leu2656Gln)

Version: 1.0

CA16613950

409564 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: dba4db7d-bf0b-4f56-978a-4c3187cfdf29
Approved on: 2025/12/3
Published on: 2025/12/2

HGVS expressions

NM_000059.4:c.7967T>A
NM_000059.4(BRCA2):c.7967T>A (p.Leu2656Gln)
NC_000013.11:g.32362684T>A
CM000675.2:g.32362684T>A
NC_000013.10:g.32936821T>A
CM000675.1:g.32936821T>A
NC_000013.9:g.31834821T>A
NG_012772.3:g.52205T>A
ENST00000470094.2:c.7967T>A
ENST00000528762.2:c.7967T>A
ENST00000530893.7:c.7598T>A
ENST00000665585.2:c.7967T>A
ENST00000666593.2:c.7967T>A
ENST00000700202.2:c.7967T>A
ENST00000700202.1:c.434T>A
ENST00000380152.8:c.7967T>A
ENST00000544455.6:c.7967T>A
ENST00000614259.2:c.7975T>A
ENST00000665585.1:c.532T>A
ENST00000680887.1:c.7967T>A
ENST00000380152.7:c.7967T>A
ENST00000544455.5:c.7967T>A
NM_000059.3:c.7967T>A

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PS3 PP3

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.7967T>A variant in BRCA2 is a missense variant predicted to cause substitution of Leucine by Glutamine at amino acid 2656 (p.(Leu2656Gln)). 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) (PM2_Supporting met). Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 38417439, 39779857, 39779848) (PS3 met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.416, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.03 predicts no impact on splicing (score threshold ≤0.1) (PP3 met). 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 (PM2_Supporting, PS3, PP3).

Met criteria codes

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) (PM2_Supporting met).
PS3 ✔	Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 38417439, 39779857, 39779848) (PS3 met).
PP3 ✔	This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.416, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.03 predicts no impact on splicing (score threshold ≤0.1) (PP3 met).

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.