

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-4c3187cfd29

Approved on: 2025-12-03

Published on: 2025-12-02

HGVS expressions

NM_000059.4(BRCA2):c.7967T>A (p.Leu2656Gln)

NM_000059.4:c.7967T>A

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**

PS3

PP3

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**

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

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).
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).

Curation History



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