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.8375T>C (p.Leu2792Pro)

Version: 1.0

CA025612

52568 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: 0304cdd3-f9e1-479f-b381-8686696e7430
Approved on: 2025/12/3
Published on: 2025/12/2

HGVS expressions

NM_000059.4:c.8375T>C
NM_000059.4(BRCA2):c.8375T>C (p.Leu2792Pro)
NC_000013.11:g.32370445T>C
CM000675.2:g.32370445T>C
NC_000013.10:g.32944582T>C
CM000675.1:g.32944582T>C
NC_000013.9:g.31842582T>C
NG_012772.3:g.59966T>C
ENST00000470094.2:c.8375T>C
ENST00000528762.2:c.8375T>C
ENST00000530893.7:c.8006T>C
ENST00000665585.2:c.8375T>C
ENST00000666593.2:c.8375T>C
ENST00000700202.2:c.8375T>C
ENST00000700202.1:c.842T>C
ENST00000380152.8:c.8375T>C
ENST00000544455.6:c.8375T>C
ENST00000614259.2:c.8383T>C
ENST00000665585.1:c.940T>C
ENST00000680887.1:c.8375T>C
ENST00000380152.7:c.8375T>C
ENST00000544455.5:c.8375T>C
NM_000059.3:c.8375T>C

Likely Pathogenic

Met criteria codes 3
PP3 PP4 PS3

Not Met criteria codes 3
PM2 BA1 BS1

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.8375T>C variant in BRCA2 is a missense variant predicted to cause substitution of Leucine by Proline at amino acid 2792 (p.(Leu2792Pro)). This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met). Reported by four calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:39779857, 32444794, 38417439, 39779848) (PS3 met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.54, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold <0.10) (PP3 met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 2.65 (based on Co-occurrence LR=1.05; Family History LR=2.53), within the thresholds for supporting evidence towards pathogenicity (LR >2.08 & ≤4.3) (PP4 met; Internal lab contributor). 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 (PS3, PP3, PP4).

Met criteria codes

PP3	✔	This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.54, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold <0.10) (PP3 met).
PP4	✔	Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 2.65 (based on Co-occurrence LR=1.05; Family History LR=2.53), within the thresholds for supporting evidence towards pathogenicity (LR >2.08 & ≤4.3) (PP4 met; Internal lab contributor).
PS3	✔	Reported by four calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:39779857, 32444794, 38417439, 39779848) (PS3 met).

Not Met criteria codes

PM2	✖	This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met).
BA1	✖	This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met).
BS1	✖	This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not 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.