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Variant: NM_000059.4(BRCA2):c.9016T>G (p.Tyr3006Asp)

Version: 1.0

CA025928

38202 (ClinVar)

Gene: BRCA2 (HGNC:675)
Condition: BRCA2-related cancer predisposition (MONDO:0700269)
Inheritance Mode: Autosomal dominant inheritance
UUID: c5eb8b58-6c54-4270-81d7-397f186a47e2
Approved on: 2026/1/5
Published on: 2026/1/5

HGVS expressions

NM_000059.4(BRCA2):c.9016T>G (p.Tyr3006Asp)
NM_000059.4:c.9016T>G
NC_000013.11:g.32379812T>G
CM000675.2:g.32379812T>G
NC_000013.10:g.32953949T>G
CM000675.1:g.32953949T>G
NC_000013.9:g.31851949T>G
NG_012772.3:g.69333T>G
ENST00000470094.2:c.9016T>G
ENST00000528762.2:c.*383T>G
ENST00000530893.7:c.8647T>G
ENST00000665585.2:c.*578T>G
ENST00000666593.2:c.9016T>G
ENST00000700202.2:c.8965T>G
ENST00000700202.1:c.1432T>G
ENST00000700203.1:n.1143T>G
ENST00000380152.8:c.9016T>G
ENST00000544455.6:c.9016T>G
ENST00000614259.2:c.9024T>G
ENST00000665585.1:c.1894T>G
ENST00000680887.1:c.9016T>G
ENST00000380152.7:c.9016T>G
ENST00000544455.5:c.9016T>G
NM_000059.3:c.9016T>G

Pathogenic

Met criteria codes 4

PS3 PP3 PP4_Strong 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.9016T>G variant in BRCA2 is a missense variant predicted to cause substitution of Tyrosine by Aspartic Acid at amino acid 3006 (p.(Tyr3006Asp)). 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 four calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:38417439, 32444794, 39779857, 39779848) (PS3 met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.33, 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 26.5 (based on Family History LR=26.5), within the thresholds for strong evidence towards pathogenicity (LR >18.7 & ≤350) (PP4_Strong met; PMID: 31853058). In summary, this variant meets the criteria to be classified as a 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, PP4_Strong).

Met criteria codes

PS3	✔	Reported by four calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:38417439, 32444794, 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 0.33, 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_Strong	✔	Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 26.5 (based on Family History LR=26.5), within the thresholds for strong evidence towards pathogenicity (LR >18.7 & ≤350) (PP4_Strong met; PMID: 31853058).
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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