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Variant: NM_007294.4(BRCA1):c.32T>G (p.Val11Gly)

Version: 1.0

CA10584577

245973 (ClinVar)

Gene: BRCA1 (HGNC:672)
Condition: BRCA1-related cancer predisposition (MONDO:0700268)
Inheritance Mode: Autosomal dominant inheritance
UUID: 6dc847fe-e269-4810-b80b-319cf023d574
Approved on: 2025/12/3
Published on: 2025/12/2

HGVS expressions

NM_007294.4:c.32T>G
NM_007294.4(BRCA1):c.32T>G (p.Val11Gly)
NC_000017.11:g.43124065A>C
CM000679.2:g.43124065A>C
NC_000017.10:g.41276082A>C
CM000679.1:g.41276082A>C
NC_000017.9:g.38529608A>C
NG_005905.2:g.93919T>G
ENST00000354071.8:n.96T>G
ENST00000461574.2:c.32T>G
ENST00000470026.6:c.32T>G
ENST00000473961.6:c.32T>G
ENST00000476777.6:c.32T>G
ENST00000477152.6:c.32T>G
ENST00000478531.6:c.32T>G
ENST00000489037.2:c.32T>G
ENST00000493919.6:c.-56T>G
ENST00000494123.6:c.32T>G
ENST00000497488.2:c.-219+1206T>G
ENST00000618469.2:c.32T>G
ENST00000634433.2:c.32T>G
ENST00000644379.2:c.32T>G
ENST00000644555.2:c.-255T>G
ENST00000652672.2:c.-229T>G
ENST00000484087.6:c.32T>G
ENST00000700182.1:c.32T>G
ENST00000700183.1:c.32T>G
ENST00000700184.1:n.275T>G
ENST00000700185.1:n.151T>G
ENST00000700186.1:n.151T>G
ENST00000357654.9:c.32T>G
ENST00000471181.7:c.32T>G
ENST00000642945.1:c.32T>G
ENST00000644555.1:c.-255T>G
ENST00000652672.1:c.-229T>G
ENST00000352993.7:c.32T>G
ENST00000354071.7:c.32T>G

ENST00000357654.7:c.32T>G
ENST00000461221.5:c.32T>G
ENST00000461798.5:c.32T>G
ENST00000468300.5:c.32T>G
ENST00000470026.5:c.32T>G
ENST00000471181.6:c.32T>G
ENST00000476777.5:c.32T>G
ENST00000477152.5:c.32T>G
ENST00000478531.5:c.32T>G
ENST00000489037.1:c.32T>G
ENST00000491747.6:c.32T>G
ENST00000492859.5:c.32T>G
ENST00000493795.5:c.-56T>G
ENST00000493919.5:c.-56T>G
ENST00000494123.5:c.32T>G
ENST00000497488.1:c.-219+1206T>G
ENST00000586385.5:c.4+1117T>G
ENST00000591534.5:c.-44+1206T>G
ENST00000591849.5:c.-99+1206T>G
ENST00000618469.1:c.32T>G
ENST00000634433.1:c.32T>G
NM_007294.3:c.32T>G
NM_007297.3:c.-56T>G
NM_007298.3:c.32T>G
NM_007299.3:c.32T>G
NM_007300.3:c.32T>G
NR_027676.1:n.193T>G
NM_007297.4:c.-56T>G
NM_007299.4:c.32T>G
NM_007300.4:c.32T>G
NR_027676.2:n.234T>G

Likely Pathogenic

Met criteria codes 3

PS3 PP3 PM2_Supporting

Not Met criteria codes 2

BP5 PP4

Evidence Links 0

Expert Panel

ENIGMA BRCA1 and BRCA2 VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.32T>G variant in BRCA1 is a missense variant predicted to cause substitution of Valine by Glycine at amino acid 11 (p.(Val11Gly)). 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 2 calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 30209399, 35659930) (PS3 met). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.325, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein

change. A SpliceAI score of 0.05 predicts no impact on splicing (score threshold ≤0.1) (PP3 met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.15 (based on Family History LR=1.15), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058). In summary, this variant meets the criteria to be classified as a Likely pathogenic variant for BRCA1-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 2 calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 30209399, 35659930) (PS3 met).
PP3	✔	This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.325, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.05 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).

Not Met criteria codes

BP5	✖	Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.15 (based on Family History LR=1.15), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058).
PP4	✖	Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.15 (based on Family History LR=1.15), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058).

Curation History

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