

Variant: *NM_007294.4(BRCA1):c.5425G>T (p.Val1809Phe)*

Version: 2.0

CA003588 [↗](#)

55573 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))

Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 92dbefd2-5679-4694-be89-56cf41771cff

Approved on: 2026/1/15

Published on: 2026/1/15

HGVS expressions

NM_007294.4:c.5425G>T

NM_007294.4(BRCA1):c.5425G>T (p.Val1809Phe)

NC_000017.11:g.43047685C>A

CM000679.2:g.43047685C>A

NC_000017.10:g.41199702C>A

CM000679.1:g.41199702C>A

NC_000017.9:g.38453228C>A

NG_005905.2:g.170299G>T

ENST00000461574.2:c.5422G>T

ENST00000470026.6:c.5425G>T

ENST00000473961.6:c.5299G>T

ENST00000476777.6:c.5419G>T

ENST00000477152.6:c.5347G>T

ENST00000478531.6:c.2113G>T

ENST00000489037.2:c.5347G>T

ENST00000493919.6:c.1975G>T

ENST00000494123.6:c.5425G>T

ENST00000497488.2:c.4537G>T

ENST00000618469.2:c.5425G>T

ENST00000634433.2:c.5302G>T

ENST00000644379.2:c.5491G>T

ENST00000644555.2:c.1975G>T

ENST00000652672.2:c.5284G>T

ENST00000484087.6:c.1987G>T

ENST00000700081.1:n.1308G>T

ENST00000700082.1:n.789G>T

ENST00000357654.9:c.5425G>T

ENST00000471181.7:c.5488G>T

ENST00000644379.1:c.1812G>T

ENST00000352993.7:c.1999G>T

ENST00000357654.7:c.5425G>T

ENST00000461221.5:c.*5208G>T

ENST00000468300.5:c.2039G>T

ENST00000471181.6:c.5488G>T

ENST00000491747.6:c.2113G>T

ENST00000493795.5:c.5284G>T

ENST00000586385.5:c.355G>T

ENST00000591534.5:c.898G>T
ENST00000591849.5:c.124G>T
NM_007294.3:c.5425G>T
NM_007297.3:c.5284G>T
NM_007298.3:c.2113G>T
NM_007299.3:c.2039G>T
NM_007300.3:c.5488G>T
NR_027676.1:n.5561G>T
NM_007297.4:c.5284G>T
NM_007299.4:c.2039G>T
NM_007300.4:c.5488G>T
NR_027676.2:n.5602G>T

Likely Pathogenic

Met criteria codes 3

PP1_Strong PM2_Supporting PS3

Not Met criteria codes 6

BP4 BP1 BP5 BP7 PP3 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.5425G>T variant in BRCA1 is a missense variant predicted to cause substitution of Valine by Phenylalanine at amino acid 1809 (p. (Val1809Phe)). 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 two calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:32546644, 38709234) (PS3 met). mRNA experimental analysis indicates no impact on splicing (PMID: 32123317) but is not applied as strong evidence against pathogenicity since missense impact has not been excluded (BP7_Strong (RNA) not met). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of -0.144, below the recommended threshold of 0.15 for no predicted impact on BRCA1 function via protein change. However, the SpliceAI score of 0.14 indicates an unclear predicted impact on splicing (score range 0.10-0.20) (no bioinformatic code is applied). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.8 (Co-occurrence LR=1.18; Family History LR=0.68), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; Internal lab contributor). Cosegregation analysis of 2 families carrying this variant provided evidence towards pathogenicity, and has a Bayes Score of 23.66 (14.17 and 1.67, applied as LR), within the thresholds for strong pathogenic evidence (LR ≥18.7 & <350) (PP1_Strong met; PMID:15689452, Internal lab contributor). 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, PP1_Strong).

Met criteria codes

PP1_Strong



Cosegregation analysis of 2 families carrying this variant provided evidence towards pathogenicity, and has a Bayes Score of 23.66 (14.17 and 1.67, applied as LR), within the thresholds for strong pathogenic evidence (LR ≥18.7 & <350) (PP1_Strong met; PMID:15689452, Internal lab contributor).

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

i

✓

Reported by two calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:32546644, 38709234) (PS3 met).

Not Met criteria codes

- BP4

i

✗

This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of -0.144, below the recommended threshold of 0.15 for no predicted impact on BRCA1 function via protein change. However, the SpliceAI score of 0.14 indicates an unclear predicted impact on splicing (score range 0.10-0.20) (no bioinformatic code is applied).
- BP1

✗

This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of -0.144, below the recommended threshold of 0.15 for no predicted impact on BRCA1 function via protein change. However, the SpliceAI score of 0.14 indicates an unclear predicted impact on splicing (score range 0.10-0.20) (no bioinformatic code is applied).
- BP5

i

✗

Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.8 (Co-occurrence LR=1.18; Family History LR=0.68), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; Internal lab contributor).
- BP7

i

✗

mRNA experimental analysis indicates no impact on splicing (PMID: 32123317) but is not applied as strong evidence against pathogenicity since missense impact has not been excluded (BP7_Strong (RNA) not met).
- PP3

i

✗

This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of -0.144, below the recommended threshold of 0.15 for no predicted impact on BRCA1 function via protein change. However, the SpliceAI score of 0.14 indicates an unclear predicted impact on splicing (score range 0.10-0.20) (no bioinformatic code is applied).
- PP4

i

✗

Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.8 (Co-occurrence LR=1.18; Family History LR=0.68), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; Internal lab contributor).

Curation History [↗](#)

Showing 1 to 2 of 2 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.