

Variant: NM_007294.4(BRCA1):c.5282T>G (p.Phe1761Cys)

Version: 1.0

CA10590980 [↗](#)

440481 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))
Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 2a4ee740-6b07-456e-8d23-4ba221a5e77d
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HGVS expressions

NM_007294.4:c.5282T>G
NM_007294.4(BRCA1):c.5282T>G (p.Phe1761Cys)
NC_000017.11:g.43051113A>C
CM000679.2:g.43051113A>C
NC_000017.10:g.41203130A>C
CM000679.1:g.41203130A>C
NC_000017.9:g.38456656A>C
NG_005905.2:g.166871T>G
ENST00000461574.2:c.5279T>G
ENST00000470026.6:c.5282T>G
ENST00000473961.6:c.5156T>G
ENST00000476777.6:c.5276T>G
ENST00000477152.6:c.5204T>G
ENST00000478531.6:c.1970T>G
ENST00000489037.2:c.5204T>G
ENST00000493919.6:c.1832T>G
ENST00000494123.6:c.5282T>G
ENST00000497488.2:c.4394T>G
ENST00000618469.2:c.5282T>G
ENST00000634433.2:c.5159T>G
ENST00000644379.2:c.5348T>G
ENST00000644555.2:c.1832T>G
ENST00000652672.2:c.5141T>G
ENST00000484087.6:c.1844T>G
ENST00000357654.9:c.5282T>G
ENST00000471181.7:c.5345T>G
ENST00000644379.1:c.1669T>G
ENST00000352993.7:c.1856T>G
ENST00000357654.7:c.5282T>G
ENST00000461221.5:c.*5065T>G
ENST00000468300.5:c.1970T>G
ENST00000471181.6:c.5345T>G
ENST00000491747.6:c.1970T>G
ENST00000493795.5:c.5141T>G
ENST00000586385.5:c.212T>G
ENST00000591534.5:c.755T>G
ENST00000591849.5:c.-98-923T>G

NM_007294.3:c.5282T>G
NM_007297.3:c.5141T>G
NM_007298.3:c.1970T>G
NM_007299.3:c.1970T>G
NM_007300.3:c.5345T>G
NR_027676.1:n.5418T>G
NM_007297.4:c.5141T>G
NM_007299.4:c.1970T>G
NM_007300.4:c.5345T>G
NR_027676.2:n.5459T>G

Likely Pathogenic

Met criteria codes 3

PP3 PS3 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 BRCA1 Version 1.2.0
- Criteria Specification Approval History
- Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.5282T>G variant in BRCA1 is a missense variant predicted to cause substitution of Phenylalanine by Cysteine at amino acid 1761 (p.(Phe1761Cys)). 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). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.47, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold ≤0.1) (PP3 met). Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID:30209399) (PS3 met). 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; PP3; PS3).

Met criteria codes

PP3			This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.47, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold ≤0.1) (PP3 met).
PS3			Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID:30209399) (PS3 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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