

Variant: NM_007294.4(BRCA1):c.5096G>C (p.Arg1699Pro)

Version: 1.0

CA003236 [↗](#)

55397 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))
Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: de958936-79e3-46c2-963c-cc255b445281
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HGVS expressions

NM_007294.4:c.5096G>C
NM_007294.4(BRCA1):c.5096G>C (p.Arg1699Pro)
NC_000017.11:g.43063930C>G
CM000679.2:g.43063930C>G
NC_000017.10:g.41215947C>G
CM000679.1:g.41215947C>G
NC_000017.9:g.38469473C>G
NG_005905.2:g.154054G>C
ENST00000461574.2:c.5093G>C
ENST00000470026.6:c.5096G>C
ENST00000473961.6:c.4970G>C
ENST00000476777.6:c.5090G>C
ENST00000477152.6:c.5018G>C
ENST00000478531.6:c.1784G>C
ENST00000489037.2:c.5018G>C
ENST00000493919.6:c.1646G>C
ENST00000494123.6:c.5096G>C
ENST00000497488.2:c.4208G>C
ENST00000618469.2:c.5096G>C
ENST00000634433.2:c.4973G>C
ENST00000644379.2:c.5162G>C
ENST00000644555.2:c.1646G>C
ENST00000652672.2:c.4955G>C
ENST00000484087.6:c.1658G>C
ENST00000357654.9:c.5096G>C
ENST00000471181.7:c.5159G>C
ENST00000644379.1:c.1483G>C
ENST00000352993.7:c.1670G>C
ENST00000357654.7:c.5096G>C
ENST00000461221.5:c.*4879G>C
ENST00000468300.5:c.1784G>C
ENST00000471181.6:c.5159G>C
ENST00000478531.5:c.1784G>C
ENST00000484087.5:c.1409G>C
ENST00000491747.6:c.1784G>C
ENST00000493795.5:c.4955G>C
ENST00000493919.5:c.1646G>C

ENST00000586385.5:c.26G>C
ENST00000591534.5:c.569G>C
ENST00000591849.5:c.-98-13740G>C
NM_007294.3:c.5096G>C
NM_007297.3:c.4955G>C
NM_007298.3:c.1784G>C
NM_007299.3:c.1784G>C
NM_007300.3:c.5159G>C
NR_027676.1:n.5232G>C
NM_007297.4:c.4955G>C
NM_007299.4:c.1784G>C
NM_007300.4:c.5159G>C
NR_027676.2:n.5273G>C

Uncertain Significance

Met criteria codes 2

PP3 PM2_Supporting

Not Met criteria codes 2

PS3 BS3

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.5096G>C variant in BRCA1 is a missense variant predicted to cause substitution of Arginine by Proline at amino acid 1699 (p. (Arg1699Pro)). 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 three calibrated studies with discordant results. Functional effect similar to benign control variants (PMID:38709234) and to pathogenic control variants (PMID:30209399, 35196514) (PS3 and BS3 not met). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.43, 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 < 0.10) (PP3 met). In summary, this variant meets the criteria to be classified as a Variant of uncertain significance for BRCA1-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PM2_Supporting, PP3).

Met criteria codes

PP3



This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.43, 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 < 0.10) (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

PS3			Reported by three calibrated studies with discordant results. Functional effect similar to benign control variants (PMID:38709234) and to pathogenic control variants (PMID:30209399, 35196514) (PS3 and BS3 not met).
BS3			Reported by three calibrated studies with discordant results. Functional effect similar to benign control variants (PMID:38709234) and to pathogenic control variants (PMID:30209399, 35196514) (PS3 and BS3 not met).

Curation History 			
			    
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