

Variant: NM_007294.4(BRCA1):c.4211T>G (p.Leu1404Arg)

Version: 1.0

CA059655 [↗](#)

491071 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))
Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: d18a7e33-2187-4ff7-a147-eadb7ab11b60
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HGVS expressions

NM_007294.4(BRCA1):c.4211T>G (p.Leu1404Arg)
NM_007294.4:c.4211T>G
NC_000017.11:g.43082550A>C
CM000679.2:g.43082550A>C
NC_000017.10:g.41234567A>C
CM000679.1:g.41234567A>C
NC_000017.9:g.38488093A>C
NG_005905.2:g.135434T>G
ENST00000461574.2:c.4211T>G
ENST00000470026.6:c.4211T>G
ENST00000473961.6:c.4085T>G
ENST00000476777.6:c.4205T>G
ENST00000477152.6:c.4133T>G
ENST00000478531.6:c.899T>G
ENST00000489037.2:c.4133T>G
ENST00000493919.6:c.761T>G
ENST00000494123.6:c.4211T>G
ENST00000497488.2:c.3323T>G
ENST00000618469.2:c.4211T>G
ENST00000634433.2:c.4088T>G
ENST00000644379.2:c.4211T>G
ENST00000644555.2:c.761T>G
ENST00000652672.2:c.4070T>G
ENST00000484087.6:c.776T>G
ENST00000700182.1:c.821T>G
ENST00000357654.9:c.4211T>G
ENST00000471181.7:c.4211T>G
ENST00000644379.1:c.532T>G
ENST00000352993.7:c.785T>G
ENST00000357654.7:c.4211T>G
ENST00000461221.5:c.*3994T>G
ENST00000461574.1:c.505T>G
ENST00000468300.5:c.902T>G
ENST00000471181.6:c.4211T>G
ENST00000478531.5:c.899T>G
ENST00000484087.5:c.524T>G
ENST00000487825.5:c.527T>G

ENST00000491747.6:c.902T>G
ENST00000493795.5:c.4070T>G
ENST00000493919.5:c.761T>G
ENST00000586385.5:c.5-18599T>G
ENST00000591534.5:c.-43-8029T>G
ENST00000591849.5:c.-98-32360T>G
ENST00000621897.1:n.105T>G
NM_007294.3:c.4211T>G
NM_007297.3:c.4070T>G
NM_007298.3:c.902T>G
NM_007299.3:c.902T>G
NM_007300.3:c.4211T>G
NR_027676.1:n.4347T>G
NM_007297.4:c.4070T>G
NM_007299.4:c.902T>G
NM_007300.4:c.4211T>G
NR_027676.2:n.4388T>G

Uncertain Significance

Met criteria codes 3

BP4 PM2_Supporting PP1

Not Met criteria codes 1

PP3

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.4211T>G variant in BRCA1 is a missense variant predicted to cause substitution of Leucine by Arginine at amino acid 1404 (p. (Leu1404Arg)). This variant is absent from gnomAD v4.1 (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 0.09, which is below the recommended threshold of 0.15 for predicting no impact on BRCA1 via protein change. A SpliceAI score of 0.02 predicts no impact on splicing (score threshold ≤0.1) (BP4 met). Cosegregation analysis of one family carrying this variant provided evidence towards pathogenicity, and has a Bayes Score of 3.9 (applied as LR), within the thresholds for supporting pathogenic evidence (LR ≥2.08 & <4.3) (PP1 met; Internal lab contributor). 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 (BP4, PM2_Supporting, PP1).

Met criteria codes

BP4



This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.09, which is below the recommended threshold of 0.15 for predicting no impact on BRCA1 via protein change. A SpliceAI score of 0.02 predicts no impact on splicing (score threshold ≤0.1) (BP4 met).

PM2_Supporting



This variant is absent from gnomAD v4.1 (read depth ≥25) (PM2_Supporting met).

PP1			Cosegregation analysis of one family carrying this variant provided evidence towards pathogenicity, and has a Bayes Score of 3.9 (applied as LR), within the thresholds for supporting pathogenic evidence (LR $\geq$ 2.08 & <4.3) (PP1 met; Internal lab contributor).
Not Met criteria codes			
PP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History 			
			  
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