

Variant: NM_007294.4(BRCA1):c.5098A>G (p.Thr1700Ala)

Version: 1.0

CA003238 [↗](#)

55399 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))
Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 01c696bf-081a-4371-b9d8-38ee8cb70adf
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HGVS expressions

NM_007294.4(BRCA1):c.5098A>G (p.Thr1700Ala)
NM_007294.4:c.5098A>G
NC_000017.11:g.43063928T>C
CM000679.2:g.43063928T>C
NC_000017.10:g.41215945T>C
CM000679.1:g.41215945T>C
NC_000017.9:g.38469471T>C
NG_005905.2:g.154056A>G
ENST00000461574.2:c.5095A>G
ENST00000470026.6:c.5098A>G
ENST00000473961.6:c.4972A>G
ENST00000476777.6:c.5092A>G
ENST00000477152.6:c.5020A>G
ENST00000478531.6:c.1786A>G
ENST00000489037.2:c.5020A>G
ENST00000493919.6:c.1648A>G
ENST00000494123.6:c.5098A>G
ENST00000497488.2:c.4210A>G
ENST00000618469.2:c.5098A>G
ENST00000634433.2:c.4975A>G
ENST00000644379.2:c.5164A>G
ENST00000644555.2:c.1648A>G
ENST00000652672.2:c.4957A>G
ENST00000484087.6:c.1660A>G
ENST00000357654.9:c.5098A>G
ENST00000471181.7:c.5161A>G
ENST00000644379.1:c.1485A>G
ENST00000352993.7:c.1672A>G
ENST00000357654.7:c.5098A>G
ENST00000461221.5:c.*4881A>G
ENST00000468300.5:c.1786A>G
ENST00000471181.6:c.5161A>G
ENST00000478531.5:c.1786A>G
ENST00000484087.5:c.1411A>G
ENST00000491747.6:c.1786A>G
ENST00000493795.5:c.4957A>G
ENST00000493919.5:c.1648A>G

ENST00000586385.5:c.28A>G
ENST00000591534.5:c.571A>G
ENST00000591849.5:c.-98-13738A>G
NM_007294.3:c.5098A>G
NM_007297.3:c.4957A>G
NM_007298.3:c.1786A>G
NM_007299.3:c.1786A>G
NM_007300.3:c.5161A>G
NR_027676.1:n.5234A>G
NM_007297.4:c.4957A>G
NM_007299.4:c.1786A>G
NM_007300.4:c.5161A>G
NR_027676.2:n.5275A>G

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PS3 PP3

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.5098A>G variant in BRCA1 is a missense variant predicted to cause substitution of Threonine by Alanine at amino acid 1700 (p. (Thr1700Ala)). 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 to exhibit protein function similar to pathogenic control variants (PMIDs:30209399, 38709234, 35196514) (PS3 met). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.41, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.14 indicates an unclear predicted impact on splicing (score threshold 0.10-0.20) (PP3 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, PS3, PP3).

Met criteria codes

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			Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:30209399, 38709234, 35196514) (PS3 met).
PP3			

This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.41, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.14 indicates an unclear predicted impact on splicing (score threshold 0.10-0.20) (PP3 met).

Curation History [↗](#)

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