Variant: NM_007294.4(BRCA1):c.5140G>T (p.Val1714Phe)

Version: 1.0

CA10591261

631061 (ClinVar)

Gene: BRCA1 (HGNC:672)
Condition: BRCA1-related cancer predisposition (MONDO:0700268)
Inheritance Mode: Autosomal dominant inheritance
UUID: 0a203129-ae2a-44d4-ac6b-7fb9c767ffbc
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HGVS expressions

NM_007294.4:c.5140G>T
NM_007294.4(BRCA1):c.5140G>T (p.Val1714Phe)
NC_000017.11:g.43063886C>A
CM000679.2:g.43063886C>A
NC_000017.10:g.41215903C>A
CM000679.1:g.41215903C>A
NC_000017.9:g.38469429C>A
NG_005905.2:g.154098G>T
ENST00000461574.2:c.5137G>T
ENST00000470026.6:c.5140G>T
ENST00000473961.6:c.5014G>T
ENST00000476777.6:c.5134G>T
ENST00000477152.6:c.5062G>T
ENST00000478531.6:c.1828G>T
ENST00000489037.2:c.5062G>T
ENST00000493919.6:c.1690G>T
ENST00000494123.6:c.5140G>T
ENST00000497488.2:c.4252G>T
ENST00000618469.2:c.5140G>T
ENST00000634433.2:c.5017G>T
ENST00000644379.2:c.5206G>T
ENST00000644555.2:c.1690G>T
ENST00000652672.2:c.4999G>T
ENST00000484087.6:c.1702G>T
ENST00000357654.9:c.5140G>T
ENST00000471181.7:c.5203G>T
ENST00000644379.1:c.1527G>T
ENST00000352993.7:c.1714G>T
ENST00000357654.7:c.5140G>T
ENST00000461221.5:c.*4923G>T
ENST00000468300.5:c.1828G>T
ENST00000471181.6:c.5203G>T
ENST00000478531.5:c.1828G>T
ENST00000484087.5:c.1453G>T
ENST00000491747.6:c.1828G>T
ENST00000493795.5:c.4999G>T
ENST00000493919.5:c.1690G>T

ENST00000586385.5:c.70G>T
ENST00000591534.5:c.613G>T
ENST00000591849.5:c.-98-13696G>T
NM_007294.3:c.5140G>T
NM_007297.3:c.4999G>T
NM_007298.3:c.1828G>T
NM_007299.3:c.1828G>T
NM_007300.3:c.5203G>T
NR_027676.1:n.5276G>T
NM_007297.4:c.4999G>T
NM_007299.4:c.1828G>T
NM_007300.4:c.5203G>T
NR_027676.2:n.5317G>T

Likely Pathogenic

Met criteria codes 3

PM2_Supporting PS3 PP3

Not Met criteria codes 1

PP1

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.5140G>T variant in BRCA1 is a missense variant predicted to cause substitution of valine by phenylalanine at amino acid 1714 (p.(Val1714Phe)). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.50, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.00 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). Cosegregation analysis of one family carrying this variant has a Bayes Score of 1.85 and provided no evidence (Internal lab contributor). 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). 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 (PP3, PS3, PM2_Supporting).

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).
PS3	✔	Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID: 30209399).
PP3	✔	This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.50, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.00 predicts no impact on splicing (score threshold ≤0.1).

Not Met criteria codes

PP1	✖	Cosegregation analysis of one family carrying this variant has a Bayes Score of 1.85 and provided no evidence (Internal lab contributor).

Curation History

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