

Variant: NM_007294.4(BRCA1):c.5191G>A (p.Glu1731Lys)

Version: 1.0

CA003333 [↗](#)

91641 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))
Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))
Inheritance Mode: Autosomal dominant inheritance
UUID: 5d4daf42-5ef3-49d1-9d6d-a2815a7cdeb4
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HGVS expressions

NM_007294.4:c.5191G>A
NM_007294.4(BRCA1):c.5191G>A (p.Glu1731Lys)
NC_000017.11:g.43063335C>T
CM000679.2:g.43063335C>T
NC_000017.10:g.41215352C>T
CM000679.1:g.41215352C>T
NC_000017.9:g.38468878C>T
NG_005905.2:g.154649G>A
ENST00000461574.2:c.5188G>A
ENST00000470026.6:c.5191G>A
ENST00000473961.6:c.5065G>A
ENST00000476777.6:c.5185G>A
ENST00000477152.6:c.5113G>A
ENST00000478531.6:c.1879G>A
ENST00000489037.2:c.5113G>A
ENST00000493919.6:c.1741G>A
ENST00000494123.6:c.5191G>A
ENST00000497488.2:c.4303G>A
ENST00000618469.2:c.5191G>A
ENST00000634433.2:c.5068G>A
ENST00000644379.2:c.5257G>A
ENST00000644555.2:c.1741G>A
ENST00000652672.2:c.5050G>A
ENST00000484087.6:c.1753G>A
ENST00000357654.9:c.5191G>A
ENST00000471181.7:c.5254G>A
ENST00000644379.1:c.1578G>A
ENST00000352993.7:c.1765G>A
ENST00000357654.7:c.5191G>A
ENST00000461221.5:c.*4974G>A
ENST00000468300.5:c.1879G>A
ENST00000471181.6:c.5254G>A
ENST00000491747.6:c.1879G>A
ENST00000493795.5:c.5050G>A
ENST00000586385.5:c.121G>A
ENST00000591534.5:c.664G>A
ENST00000591849.5:c.-98-13145G>A

NM_007294.3:c.5191G>A
NM_007297.3:c.5050G>A
NM_007298.3:c.1879G>A
NM_007299.3:c.1879G>A
NM_007300.3:c.5254G>A
NR_027676.1:n.5327G>A
NM_007297.4:c.5050G>A
NM_007299.4:c.1879G>A
NM_007300.4:c.5254G>A
NR_027676.2:n.5368G>A

Uncertain Significance

Met criteria codes **3**

BP4 PM2_Supporting PS3

Evidence Links **1**

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.5191G>A variant in BRCA1 is a missense variant predicted to cause substitution of glutamic acid by lysine at amino acid 1731 (p.Glu1731Lys). 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). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.13, which is below the recommended threshold of 0.15 for predicting no impact on BRCA1 via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold ≤ 0.1) This variant is reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID:30209399). 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, BP4, PS3).

Met criteria codes

BP4



This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.13, which is below the recommended threshold of 0.15 for predicting no impact on BRCA1 via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold ≤ 0.1) (BP4 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).

PS3



This variant is reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID:30209399) (PS3 met).

Non Functional PubMed:30209399



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