

Variant: NM_007294.4(BRCA1):c.2155A>G (p.Lys719Glu)

Version: 2.0

CA001442 [↗](#)

37452 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))

Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))

Inheritance Mode: Autosomal dominant inheritance

UID: fd4bcbc3-5cf5-46ae-b827-465fec09e761

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HGVS expressions

NM_007294.4:c.2155A>G

NM_007294.4(BRCA1):c.2155A>G (p.Lys719Glu)

NC_000017.11:g.43093376T>C

CM000679.2:g.43093376T>C

NC_000017.10:g.41245393T>C

CM000679.1:g.41245393T>C

NC_000017.9:g.38498919T>C

NG_005905.2:g.124608A>G

ENST00000354071.8:n.2219A>G

ENST00000461574.2:c.2155A>G

ENST00000470026.6:c.2155A>G

ENST00000473961.6:c.2029A>G

ENST00000476777.6:c.2152A>G

ENST00000477152.6:c.2077A>G

ENST00000478531.6:c.784+1368A>G

ENST00000489037.2:c.2077A>G

ENST00000493919.6:c.646+1368A>G

ENST00000494123.6:c.2155A>G

ENST00000497488.2:c.1267A>G

ENST00000618469.2:c.2155A>G

ENST00000634433.2:c.2032A>G

ENST00000644379.2:c.2155A>G

ENST00000644555.2:c.646+1368A>G

ENST00000652672.2:c.2014A>G

ENST00000484087.6:c.664+1368A>G

ENST00000700182.1:c.706+1368A>G

ENST00000357654.9:c.2155A>G

ENST00000471181.7:c.2155A>G

ENST00000352993.7:c.671-2344A>G

ENST00000354071.7:c.2155A>G

ENST00000357654.7:c.2155A>G

ENST00000461221.5:c.*1938A>G

ENST00000468300.5:c.787+1368A>G

ENST00000471181.6:c.2155A>G

ENST00000478531.5:c.784+1368A>G

ENST00000484087.5:c.409+1368A>G

ENST00000487825.5:c.412+1368A>G

ENST00000491747.6:c.787+1368A>G
ENST00000493795.5:c.2014A>G
ENST00000493919.5:c.646+1368A>G
ENST00000586385.5:c.5-29425A>G
ENST00000591534.5:c.-43-18855A>G
ENST00000591849.5:c.-99+31895A>G
ENST00000634433.1:c.2032A>G
NM_007294.3:c.2155A>G
NM_007297.3:c.2014A>G
NM_007298.3:c.787+1368A>G
NM_007299.3:c.787+1368A>G
NM_007300.3:c.2155A>G
NR_027676.1:n.2291A>G
NM_007297.4:c.2014A>G
NM_007299.4:c.787+1368A>G
NM_007300.4:c.2155A>G
NR_027676.2:n.2332A>G

Benign

Met criteria codes **3**

BP5_Strong BS1 BP1_Strong

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 1.0.0*

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.2155A>G variant in BRCA1 is a missense variant predicted to cause substitution of Lysine by Glutamic acid at amino acid 719 (p.Lys719Glu). The highest non-cancer, non-founder population filter allele frequency in gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥ 20) or gnomAD v3.1 (non-cancer subset, read depth ≥ 20) is 0.0003 in the African/African American population, which is above the ENIGMA BRCA1/2 VCEP threshold (>0.0001) for BS1, and below the BA1 threshold (>0.001) (BS1 met). This missense variant is located outside of a key functional domain and was not predicted to alter mRNA splicing using the SpliceAI predictor (score 0.01, score threshold <0.1) (BP1_Strong met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.0000515 (based on Family History LR= 0.0000515), below the thresholds for very strong benign evidence (LR <0.00285) (BP5_Very strong met; PMID: 31853058). In summary, this variant meets the criteria to be classified as a Benign variant for BRCA1-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (BS1, BP1_Strong, BP5_Very strong).

Met criteria codes

BP5_Strong



Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.0000515 (based on Family History LR= 0.0000515), below the thresholds for very strong benign evidence (LR <0.00285) (BP5_Very strong met; PMID 31131967).

BS1



The highest non-cancer, non-founder population filter allele frequency in gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥ 20) or gnomAD v3.1 (non-cancer subset, read depth ≥ 20) is 0.0003 in the African/African American population, which is above the ENIGMA BRCA1/2 VCEP threshold (>0.0001) for BS1, and below the BA1 threshold (>0.001) (BS1 met).

BP1_Strong



This missense variant is located outside of a key functional domain and was not predicted to alter mRNA splicing using the SpliceAI predictor (score 0.01, score threshold <0.1) (BP1_Strong met).

Curation History [↗](#)

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