

Variant: *NM_000059.4(BRCA2):c.7871A>G (p.Tyr2624Cys)*

Version: 1.0

CA025315 [↗](#)

96860 (ClinVar) [↗](#)

Gene: BRCA2 ([HGNC:675](#))

Condition: BRCA2-related cancer predisposition ([MONDO:0700269](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 199d63ac-88a3-4082-b0c3-514f2191a1a1

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HGVS expressions

NM_000059.4(BRCA2):c.7871A>G (p.Tyr2624Cys)

NM_000059.4:c.7871A>G

NC_000013.11:g.32362588A>G

CM000675.2:g.32362588A>G

NC_000013.10:g.32936725A>G

CM000675.1:g.32936725A>G

NC_000013.9:g.31834725A>G

NG_012772.3:g.52109A>G

ENST00000470094.2:c.7871A>G

ENST00000528762.2:c.7871A>G

ENST00000530893.7:c.7502A>G

ENST00000665585.2:c.7871A>G

ENST00000666593.2:c.7871A>G

ENST00000700202.2:c.7871A>G

ENST00000700202.1:c.338A>G

ENST00000380152.8:c.7871A>G

ENST00000544455.6:c.7871A>G

ENST00000614259.2:c.7879A>G

ENST00000665585.1:c.436A>G

ENST00000680887.1:c.7871A>G

ENST00000380152.7:c.7871A>G

ENST00000544455.5:c.7871A>G

ENST00000614259.1:n.7879A>G

NM_000059.3:c.7871A>G

Uncertain Significance

Met criteria codes **2**

PS3 PP3

Not Met criteria codes **5**

BA1 BS1 BP5 PP4 PM2

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 BRCA2 Version 1.1.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

ENIGMA BRCA1 and BRCA2 VCEP

The c.7871A>G variant in BRCA2 is a missense variant predicted to cause substitution of Tyrosine by Cysteine at amino acid 2624 (p. (Tyr2624Cys)). This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met). Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:33609447, 39779857, 39779848) (PS3 met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.44, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold <0.10) (PP3 met). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.76 (based on Co-occurrence LR=1.1; Family History LR=1.6), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMIDs: 31853058, 31131967). In summary, this variant meets the criteria to be classified as a Variant of uncertain significance for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PS3, PP3).

Met criteria codes

PS3			Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:33609447, 39779857, 39779848) (PS3 met).
PP3			This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.44, above the recommended threshold of 0.30 for prediction of impact on BRCA2 function via protein change. A SpliceAI score of 0.01 predicts no impact on splicing (score threshold <0.10) (PP3 met).

Not Met criteria codes

BA1			This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met).
BS1			This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not met).
BP5			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.76 (based on Co-occurrence LR=1.1; Family History LR=1.6), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMIDs: 31853058, 31131967).
PP4			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.76 (based on Co-occurrence LR=1.1; Family History LR=1.6), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMIDs: 31853058, 31131967).
PM2			This variant is present in gnomAD v2.1 (exomes only, non-cancer subset) or gnomAD v3.1 (non-cancer subset) but is below the ENIGMA BRCA1/2 VCEP threshold >0.00002 for BS1_Supporting (PM2_Supporting, BS1, and BA1 are not

met).

Curation History



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