

Variant: *NM\_000059.4(BRCA2):c.7685T>G (p.Phe2562Cys)*

Version: 1.0

CA025232 [↗](#)

142784 (ClinVar) [↗](#)

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

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

**Inheritance Mode:** Autosomal dominant inheritance

**UUID:** 3d2945e6-7975-4aaf-a101-bf76844675cb

**Approved on:** 2026/1/5

**Published on:** 2026/1/5

## HGVS expressions

**NM\_000059.4(BRCA2):c.7685T>G (p.Phe2562Cys)**

**NM\_000059.4:c.7685T>G**

NC\_000013.11:g.32357809T>G

CM000675.2:g.32357809T>G

NC\_000013.10:g.32931946T>G

CM000675.1:g.32931946T>G

NC\_000013.9:g.31829946T>G

NG\_012772.3:g.47330T>G

ENST00000470094.2:c.7685T>G

ENST00000528762.2:c.7685T>G

ENST00000530893.7:c.7316T>G

ENST00000665585.2:c.7685T>G

ENST00000666593.2:c.7685T>G

ENST00000700202.2:c.7685T>G

ENST00000700202.1:c.152T>G

ENST00000380152.8:c.7685T>G

ENST00000544455.6:c.7685T>G

ENST00000614259.2:c.7685T>G

ENST00000665585.1:c.250T>G

ENST00000680887.1:c.7685T>G

ENST00000380152.7:c.7685T>G

ENST00000544455.5:c.7685T>G

ENST00000614259.1:n.7685T>G

NM\_000059.3:c.7685T>G

**Likely Pathogenic**

**Met criteria codes** 3

PM2\_Supporting PP3 PS3

**Not Met criteria codes** 3

BP5 PP4 PM3

**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**

Evidence submitted by expert panel

**ENIGMA BRCA1 and BRCA2 VCEP**

The c.7685T>G variant in BRCA2 is a missense variant predicted to cause substitution of Phenylalanine by Cysteine at amino acid 2562 (p. (Phe2562Cys)). 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:38417439, 39779857, 39779848) (PS3 met). This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.42, 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 0.98 (based on Family History LR=0.98), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058). This variant has been detected in one individual with phenotype suggestive of BRCA2-Fanconi Anemia (FA). Only one clinical feature of FA (physical features, pathology findings or cancer diagnosis ≤5yr) and unknown chromosome breakage was seen in this individual. They were compound heterozygous for the variant and a pathogenic or likely pathogenic variant confirmed to be in trans. Total points equated to 0 (PM3 not met; internal lab contributor). In summary, this variant meets the criteria to be classified as a Likely pathogenic variant for BRCA2-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**

|                       |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                        |
|-----------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>PM2_Supporting</b> |    |    | 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).                                                                                                                                                                     |
| <b>PP3</b>            |    |    | This BRCA2 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.42, 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). |
| <b>PS3</b>            |  |  | Reported by three calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs:38417439, 39779857, 39779848) (PS3 met).                                                                                                                                                                                |

**Not Met criteria codes**

|            |                                                                                     |                                                                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>BP5</b> |  |  | Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.98 (based on Family History LR=0.98), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058).                                                                                                                                                                        |
| <b>PP4</b> |  |  | Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 0.98 (based on Family History LR=0.98), which is above the ENIGMA BRCA1/2 VCEP threshold for BP5 (>0.48) and below PP4 (<2.08) (BP5 and PP4 not met; PMID: 31853058).                                                                                                                                                                        |
| <b>PM3</b> |  |  | This variant has been detected in one individual with phenotype suggestive of BRCA2-Fanconi Anemia (FA). Only one clinical feature of FA (physical features, pathology findings or cancer diagnosis ≤5yr) and unknown chromosome breakage was seen in this individual. They were compound heterozygous for the variant and a pathogenic or likely pathogenic variant confirmed to be in trans. Total points equated to 0 (PM3 not met; internal lab contributor). |



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