

Variant: *NM_000059.4(BRCA2):c.6859A>T (p.Arg2287Ter)*

Version: 1.0

CA387792666 [↗](#)

575178 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 3364ff23-c57d-4025-9a7d-f69cf58a4ac4

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HGVS expressions

NM_000059.4(BRCA2):c.6859A>T (p.Arg2287Ter)

NM_000059.4:c.6859A>T

NC_000013.11:g.32344575A>T

CM000675.2:g.32344575A>T

NC_000013.10:g.32918712A>T

CM000675.1:g.32918712A>T

NC_000013.9:g.31816712A>T

NG_012772.3:g.34096A>T

ENST00000470094.2:c.6859A>T

ENST00000528762.2:c.6859A>T

ENST00000530893.7:c.6490A>T

ENST00000665585.2:c.6859A>T

ENST00000666593.2:c.6859A>T

ENST00000700202.2:c.6859A>T

ENST00000380152.8:c.6859A>T

ENST00000544455.6:c.6859A>T

ENST00000614259.2:c.6859A>T

ENST00000680887.1:c.6859A>T

ENST00000380152.7:c.6859A>T

ENST00000544455.5:c.6859A>T

ENST00000614259.1:n.6859A>T

NM_000059.3:c.6859A>T

Pathogenic

Met criteria codes **2**

PS3

PVS1

Not Met criteria codes **2**

PM5

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.6859A>T variant in BRCA2 is predicted to cause a change in the length of the protein due to the insertion of a terminating codon instead of the usual arginine at amino acid 2287 (p.(Arg2287Ter)). This variant is present in 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). Nonsense of exon 12 variant predicted to cause a premature stop codon in biologically-relevant-exon 12/27 leading to nonsense mediated decay (PVS1 met). Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID:32046981) (PS3 met). In summary, this variant meets the criteria to be classified as a Pathogenic variant for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PVS1, PS3).

Met criteria codes

PS3			Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID:32046981) (PS3 met).
PVS1			Nonsense of exon 12 variant predicted to cause a premature stop codon in biologically-relevant-exon 12/27 leading to nonsense mediated decay (PVS1 met).

Not Met criteria codes

PM5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM2			This variant is present in 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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