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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
Approved on: 2025/5/23
Published on: 2025/5/23

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

PM2 PM5

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.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

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).
PM5	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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