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Variant: NM_007294.4(BRCA1):c.5528C>A (p.Ala1843Glu)

Version: 1.0

CA003698

182082 (ClinVar)

Gene: BRCA1 (HGNC:672)
Condition: BRCA1-related cancer predisposition (MONDO:0700268)
Inheritance Mode: Autosomal dominant inheritance
UUID: 33ebf93f-ff2f-4ffc-9e03-d880c84e3fc6
Approved on: 2026/8/28
Published on: 2026/8/27

HGVS expressions

NM_007294.4(BRCA1):c.5528C>A (p.Ala1843Glu)
NM_007294.4:c.5528C>A
NC_000017.11:g.43045742G>T
CM000679.2:g.43045742G>T
NC_000017.10:g.41197759G>T
CM000679.1:g.41197759G>T
NC_000017.9:g.38451285G>T
NG_005905.2:g.172242C>A
ENST00000461574.2:c.5525C>A
ENST00000470026.6:c.5528C>A
ENST00000473961.6:c.5402C>A
ENST00000476777.6:c.5522C>A
ENST00000477152.6:c.5450C>A
ENST00000478531.6:c.2216C>A
ENST00000489037.2:c.5450C>A
ENST00000493919.6:c.2078C>A
ENST00000494123.6:c.5528C>A
ENST00000497488.2:c.4640C>A
ENST00000618469.2:c.5528C>A
ENST00000634433.2:c.5405C>A
ENST00000644379.2:c.5594C>A
ENST00000644555.2:c.2078C>A
ENST00000652672.2:c.5387C>A
ENST00000484087.6:c.2090C>A
ENST00000700081.1:n.1411C>A
ENST00000700082.1:n.892C>A
ENST00000357654.9:c.5528C>A
ENST00000471181.7:c.5591C>A
ENST00000644379.1:c.1915C>A
ENST00000352993.7:c.2102C>A
ENST00000357654.7:c.5528C>A
ENST00000461221.5:c.*5311C>A
ENST00000468300.5:c.*42C>A
ENST00000471181.6:c.5591C>A
ENST00000491747.6:c.2216C>A
ENST00000493795.5:c.5387C>A
ENST00000586385.5:c.458C>A

ENST00000591534.5:c.1001C>A
ENST00000591849.5:c.227C>A
NM_007294.3:c.5528C>A
NM_007297.3:c.5387C>A
NM_007298.3:c.2216C>A
NM_007299.3:c.*42C>A
NM_007300.3:c.5591C>A
NR_027676.1:n.5664C>A
NM_007297.4:c.5387C>A
NM_007299.4:c.*42C>A
NM_007300.4:c.5591C>A
NR_027676.2:n.5705C>A

Likely Pathogenic

Met criteria codes 3

PS3 PP3 PM2_Supporting

Not Met criteria codes 1

BP7

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 1.2*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.5528C>A variant in BRCA1 is a missense variant predicted to cause substitution of Alanine by Glutamic acid at amino acid 1843 (p.(Ala1843Glu)). This variant is absent from gnomAD v4.1 (read depth ≥25x in >90% samples, PM2_Supporting met). Reported by 2 calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 30209399, 35196514) (PS3 met). This BRCA1 missense variant is within a key functional domain and a SpliceAI score of 0 predicts no impact on splicing (score threshold ≤0.1). The computational predictor BayesDel (noAF) gives a score of 0.28, equal to or above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change (PP3 met). In summary, this variant meets the criteria to be classified as a Likely pathogenic variant for BRCA1-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (v1.2) (PS3, PM2_Supporting, PP3).

Met criteria codes

PS3	✔	Reported by 2 calibrated studies to exhibit protein function similar to pathogenic control variants (PMIDs: 30209399, 35196514) (PS3 met).
PP3	✔	This BRCA1 missense variant is within a key functional domain and a SpliceAI score of 0 predicts no impact on splicing (score threshold ≤0.1). The computational predictor BayesDel (noAF) gives a score of 0.28, equal to or above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change (PP3 met).
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (read depth ≥25x in >90% samples, PM2_Supporting met).

Not Met criteria codes

BP7 ✖

This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.2795, indicating impact on BRCA1 function via protein change is unclear (score range 0.15-0.28). A SpliceAI score of 0 predicts no impact on splicing (score threshold ≤0.1) (no bioinformatic code is applied).

Curation History

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