

Variant: NM\_007294.4(BRCA1):c.5557T>A (p.Tyr1853Asn)

Version: 1.0

CA10590209 [↗](#)

433738 (ClinVar) [↗](#)

**Gene:** BRCA1 ([HGNC:672](#))  
**Condition:** BRCA1-related cancer predisposition ([MONDO:0700268](#))  
**Inheritance Mode:** Autosomal dominant inheritance  
**UUID:** 0dbcecdb-4f0a-4373-b58e-1cba681281ed  
**Approved on:** 2026-07-15  
**Published on:** 2026-07-15

HGVS expressions

NM\_007294.4:c.5557T>A  
NM\_007294.4(BRCA1):c.5557T>A (p.Tyr1853Asn)  
NC\_000017.11:g.43045713A>T  
CM000679.2:g.43045713A>T  
NC\_000017.10:g.41197730A>T  
CM000679.1:g.41197730A>T  
NC\_000017.9:g.38451256A>T  
NG\_005905.2:g.172271T>A  
ENST00000461574.2:c.5554T>A  
ENST00000470026.6:c.5557T>A  
ENST00000473961.6:c.5431T>A  
ENST00000476777.6:c.5551T>A  
ENST00000477152.6:c.5479T>A  
ENST00000478531.6:c.2245T>A  
ENST00000489037.2:c.5479T>A  
ENST00000493919.6:c.2107T>A  
ENST00000494123.6:c.5557T>A  
ENST00000497488.2:c.4669T>A  
ENST00000618469.2:c.5557T>A  
ENST00000634433.2:c.5434T>A  
ENST00000644379.2:c.5623T>A  
ENST00000644555.2:c.2107T>A  
ENST00000652672.2:c.5416T>A  
ENST00000484087.6:c.2119T>A  
ENST00000700081.1:n.1440T>A  
ENST00000700082.1:n.921T>A  
ENST00000357654.9:c.5557T>A  
ENST00000471181.7:c.5620T>A  
ENST00000644379.1:c.1944T>A  
ENST00000352993.7:c.2131T>A  
ENST00000357654.7:c.5557T>A  
ENST00000461221.5:c.\*5340T>A  
ENST00000468300.5:c.\*71T>A  
ENST00000471181.6:c.5620T>A  
ENST00000491747.6:c.2245T>A  
ENST00000493795.5:c.5416T>A  
ENST00000586385.5:c.487T>A

|  |                                                                                                                                                                                                                                                                                                                   |
|--|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|  | ENST00000591534.5:c.1030T>A<br>ENST00000591849.5:c.256T>A<br>NM_007294.3:c.5557T>A<br>NM_007297.3:c.5416T>A<br>NM_007298.3:c.2245T>A<br>NM_007299.3:c.*71T>A<br>NM_007300.3:c.5620T>A<br>NR_027676.1:n.5693T>A<br>NM_007297.4:c.5416T>A<br>NM_007299.4:c.*71T>A<br>NM_007300.4:c.5620T>A<br>NR_027676.2:n.5734T>A |
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Likely Pathogenic

Met criteria codes 3

PM2\_SupportingPS3PP3

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 1.2.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

| Evidence submitted by expert panel |
|------------------------------------|
|                                    |

ENIGMA BRCA1 and BRCA2 VCEP

The c.5557T>A variant in BRCA1 is a missense variant predicted to cause substitution of Tyrosine by Asparagine at amino acid 1853 (p. (Tyr1853Asn)). This variant is absent from gnomAD v4.1 (read depth  $\geq 25\times$  in >90% samples, PM2\_Supporting met). This BRCA1 missense variant is within a key functional domain and a SpliceAI score of 0 predicts no impact on splicing (score threshold  $\leq 0.1$ ). The computational predictor BayesDel (noAF) gives a score of 0.48, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change (PP3 met). Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID: 30209399) (PS3 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) (PM2\_Supporting, PP3, PS3).

Met criteria codes

|                |                                                                                   |                                                                                   |                                                                                                                                                                                                                                                                                                                                           |
|----------------|-----------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| PM2_Supporting |  |  | This variant is absent from gnomAD v4.1 (read depth $\geq 25\times$ in >90% samples, PM2_Supporting met).                                                                                                                                                                                                                                 |
| PS3            |  |  | Reported by one calibrated study to exhibit protein function similar to pathogenic control variants (PMID: 30209399) (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 $\leq 0.1$ ). The computational predictor BayesDel (noAF) gives a score of 0.48, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change (PP3 met). |

Curation History 



 

 

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