

Variant: NM_007294.4(BRCA1):c.121C>A (p.His41Asn)

Version: 1.0

CA10601917 [↗](#)

409353 (ClinVar) [↗](#)

Gene: BRCA1 ([HGNC:672](#))

Condition: BRCA1-related cancer predisposition ([MONDO:0700268](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: fe2b2921-7830-4646-8938-b388367d9090

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HGVS expressions

NM_007294.4(BRCA1):c.121C>A (p.His41Asn)

NM_007294.4:c.121C>A

NC_000017.11:g.43115739G>T

CM000679.2:g.43115739G>T

NC_000017.10:g.41267756G>T

CM000679.1:g.41267756G>T

NC_000017.9:g.38521282G>T

NG_005905.2:g.102245C>A

ENST00000354071.8:n.185C>A

ENST00000461574.2:c.121C>A

ENST00000470026.6:c.121C>A

ENST00000473961.6:c.121C>A

ENST00000476777.6:c.121C>A

ENST00000477152.6:c.121C>A

ENST00000478531.6:c.121C>A

ENST00000489037.2:c.121C>A

ENST00000493919.6:c.-8+8278C>A

ENST00000494123.6:c.121C>A

ENST00000497488.2:c.-219+9532C>A

ENST00000618469.2:c.121C>A

ENST00000634433.2:c.121C>A

ENST00000644379.2:c.121C>A

ENST00000644555.2:c.-21C>A

ENST00000652672.2:c.-21C>A

ENST00000484087.6:c.121C>A

ENST00000700182.1:c.121C>A

ENST00000700183.1:c.121C>A

ENST00000700184.1:n.364C>A

ENST00000700185.1:n.240C>A

ENST00000357654.9:c.121C>A

ENST00000471181.7:c.121C>A

ENST00000642945.1:c.121C>A

ENST00000644555.1:c.-21C>A

ENST00000652672.1:c.-21C>A

ENST00000352993.7:c.121C>A

ENST00000354071.7:c.121C>A

ENST00000357654.7:c.121C>A

ENST00000461221.5:c.121C>A
ENST00000468300.5:c.121C>A
ENST00000470026.5:c.121C>A
ENST00000471181.6:c.121C>A
ENST00000476777.5:c.121C>A
ENST00000477152.5:c.121C>A
ENST00000478531.5:c.121C>A
ENST00000489037.1:c.121C>A
ENST00000491747.6:c.121C>A
ENST00000492859.5:c.121C>A
ENST00000493795.5:c.-8+8278C>A
ENST00000493919.5:c.-8+8278C>A
ENST00000494123.5:c.121C>A
ENST00000497488.1:c.-219+9532C>A
ENST00000586385.5:c.4+9443C>A
ENST00000591534.5:c.-44+9532C>A
ENST00000591849.5:c.-99+9532C>A
ENST00000634433.1:c.121C>A
NM_007294.3:c.121C>A
NM_007297.3:c.-8+8278C>A
NM_007298.3:c.121C>A
NM_007299.3:c.121C>A
NM_007300.3:c.121C>A
NR_027676.1:n.282C>A
NM_007297.4:c.-8+8278C>A
NM_007299.4:c.121C>A
NM_007300.4:c.121C>A
NR_027676.2:n.323C>A

Likely Pathogenic

Met criteria codes 3

PP3 PS3 PM2_Supporting

Evidence Links 0

Expert Panel

ENIGMA BRCA1 and BRCA2 VCEP

Criteria Specification Information !

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.121C>A variant in BRCA1 is a missense variant predicted to cause substitution of histidine by asparagine at amino acid 41 (p.His41Asn). Reported by two calibrated studies to affect protein function similar to pathogenic control variants (PMID:30209399, 35659930) (PS3 met). 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). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.32, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.02 predicts no impact on splicing (score threshold ≤0.1) (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 (PS3, PM2_Supporting, PP3).

Met criteria codes

PP3			This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.32, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.02 predicts no impact on splicing (score threshold ≤ 0.1) (PP3 met).
PS3			Reported by two calibrated studies to affect protein function similar to pathogenic control variants (PMID:30209399, 35659930) (PS3 met).
PM2_Supporting			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).

Curation History



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