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Variant: NM_007294.4(BRCA1):c.5257A>G (p.Arg1753Gly)

Version: 1.0

CA10591040

801086 (ClinVar)

Gene: BRCA1 (HGNC:672)
Condition: BRCA1-related cancer predisposition (MONDO:0700268)
Inheritance Mode: Autosomal dominant inheritance
UUID: c60f30dc-7369-4d49-9cea-6dab70fe4c4f
Approved on: 2025/5/23
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HGVS expressions

NM_007294.4:c.5257A>G
NM_007294.4(BRCA1):c.5257A>G (p.Arg1753Gly)
NC_000017.11:g.43057072T>C
CM000679.2:g.43057072T>C
NC_000017.10:g.41209089T>C
CM000679.1:g.41209089T>C
NC_000017.9:g.38462615T>C
NG_005905.2:g.160912A>G
ENST00000461574.2:c.5254A>G
ENST00000470026.6:c.5257A>G
ENST00000473961.6:c.5131A>G
ENST00000476777.6:c.5251A>G
ENST00000477152.6:c.5179A>G
ENST00000478531.6:c.1945A>G
ENST00000489037.2:c.5179A>G
ENST00000493919.6:c.1807A>G
ENST00000494123.6:c.5257A>G
ENST00000497488.2:c.4369A>G
ENST00000618469.2:c.5257A>G
ENST00000634433.2:c.5134A>G
ENST00000644379.2:c.5323A>G
ENST00000644555.2:c.1807A>G
ENST00000652672.2:c.5116A>G
ENST00000484087.6:c.1819A>G
ENST00000357654.9:c.5257A>G
ENST00000471181.7:c.5320A>G
ENST00000644379.1:c.1644A>G
ENST00000352993.7:c.1831A>G
ENST00000357654.7:c.5257A>G
ENST00000461221.5:c.*5040A>G
ENST00000468300.5:c.1945A>G
ENST00000471181.6:c.5320A>G
ENST00000491747.6:c.1945A>G
ENST00000493795.5:c.5116A>G
ENST00000586385.5:c.187A>G
ENST00000591534.5:c.730A>G
ENST00000591849.5:c.-98-6882A>G

NM_007294.3:c.5257A>G
NM_007297.3:c.5116A>G
NM_007298.3:c.1945A>G
NM_007299.3:c.1945A>G
NM_007300.3:c.5320A>G
NR_027676.1:n.5393A>G
NM_007297.4:c.5116A>G
NM_007299.4:c.1945A>G
NM_007300.4:c.5320A>G
NR_027676.2:n.5434A>G

Likely Pathogenic

Met criteria codes 3

PS3 PP3 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.5257A>G variant in BRCA1 is a missense variant predicted to cause substitution of Arg by Gly at amino acid 1753 (p.(Arg1753Gly)). Reported by two calibrated studies to affect protein function similar to pathogenic control variants (PMIDs:30209399, 38709234) (PS3 met). This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.36, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.0 predicts no impact on splicing (score threshold ≤0.1) (PP3 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). 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, PP3, PM2_supporting).

Met criteria codes

PS3	✔	Reported by two calibrated studies to affect protein function similar to pathogenic control variants (PMIDs:30209399, 38709234) (PS3 met).
PP3	✔	This BRCA1 missense variant is within a key functional domain and the computational predictor BayesDel (noAF) gives a score of 0.36, above the recommended threshold of 0.28 for prediction of impact on BRCA1 function via protein change. A SpliceAI score of 0.0 predicts no impact on splicing (score threshold ≤0.1) (PP3 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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