

Variant: *NM_007294.4(BRCA1):c.591C>T (p.Cys197=)*

Version: 2.0

CA003746 [↗](#)

55642 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 6ac2e36d-f569-4692-b7b4-8dd2fa5615bd

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HGVS expressions

NM_007294.4(BRCA1):c.591C>T (p.Cys197=)

NM_007294.4:c.591C>T

NC_000017.11:g.43097246G>A

CM000679.2:g.43097246G>A

NC_000017.10:g.41249263G>A

CM000679.1:g.41249263G>A

NC_000017.9:g.38502789G>A

NG_005905.2:g.120738C>T

ENST00000354071.8:n.655C>T

ENST00000461574.2:c.591C>T

ENST00000470026.6:c.591C>T

ENST00000473961.6:c.545-2386C>T

ENST00000476777.6:c.588C>T

ENST00000477152.6:c.513C>T

ENST00000478531.6:c.588C>T

ENST00000489037.2:c.513C>T

ENST00000493919.6:c.450C>T

ENST00000494123.6:c.591C>T

ENST00000497488.2:c.-218-2386C>T

ENST00000618469.2:c.591C>T

ENST00000634433.2:c.548-2386C>T

ENST00000644379.2:c.591C>T

ENST00000644555.2:c.450C>T

ENST00000652672.2:c.450C>T

ENST00000484087.6:c.548-2386C>T

ENST00000700182.1:c.510C>T

ENST00000700183.1:c.*599C>T

ENST00000357654.9:c.591C>T

ENST00000471181.7:c.591C>T

ENST00000642945.1:c.*465C>T

ENST00000652672.1:c.450C>T

ENST00000352993.7:c.591C>T

ENST00000354071.7:c.591C>T

ENST00000357654.7:c.591C>T

ENST00000461221.5:c.*374C>T

ENST00000468300.5:c.591C>T

ENST00000470026.5:c.591C>T

	ENST00000471181.6:c.591C>T ENST00000473961.5:c.268-2386C>T ENST00000476777.5:c.588C>T ENST00000477152.5:c.513C>T ENST00000478531.5:c.588C>T ENST00000484087.5:c.293-2386C>T ENST00000487825.5:c.296-2386C>T ENST00000491747.6:c.591C>T ENST00000492859.5:c.*527C>T ENST00000493795.5:c.450C>T ENST00000493919.5:c.450C>T ENST00000494123.5:c.591C>T ENST00000497488.1:c.-218-2386C>T ENST00000586385.5:c.4+27936C>T ENST00000591534.5:c.-43-22725C>T ENST00000591849.5:c.-99+28025C>T ENST00000634433.1:c.548-2386C>T NM_007294.3:c.591C>T NM_007297.3:c.450C>T NM_007298.3:c.591C>T NM_007299.3:c.591C>T NM_007300.3:c.591C>T NR_027676.1:n.727C>T NM_007297.4:c.450C>T NM_007299.4:c.591C>T NM_007300.4:c.591C>T NR_027676.2:n.768C>T
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Benign

Met criteria codes 3

BA1BP7_StrongBP5_Strong

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 1.0.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

ENIGMA BRCA1 and BRCA2 VCEP

The c.591C>T variant in BRCA1 is a synonymous variant (p.Cys197=). The highest non-cancer, non-founder population filter allele frequency in gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥20) or gnomAD v3.1 (non-cancer subset, read depth ≥20) is 0.001402 in the European (non-Finnish) population, which is above the ENIGMA BRCA1/2 VCEP threshold (>0.001) for BA1 (BA1 met). This is a synonymous (silent) variant, and mRNA experimental analysis indicates no impact on splicing or an increase of in-frame naturally occurring splice isoforms with production of wildtype transcripts (PMIDs: 19892845, 22505045, 24607278, 23239986), considered strong evidence against pathogenicity (BP7_Strong (RNA)). Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.33E-16 (based on Pathology LR=1.33E-16), below the threshold for very strong benign evidence (LR

<0.00285) (BP5_Very strong met; ENIGMA internal contributor). In summary, this variant meets the criteria to be classified as a Benign variant for BRCA1-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (BA1, BP7_Strong (RNA), BP5_Very strong).

Met criteria codes

BA1			The highest non-cancer, non-founder population filter allele frequency in gnomAD v2.1 (exomes only, non-cancer subset, read depth ≥20) or gnomAD v3.1 (non-cancer subset, read depth ≥20) is 0.001402 in the European (non-Finnish) population, which is above the ENIGMA BRCA1/2 VCEP threshold (>0.001) for BA1 (BA1 met).
BP7_Strong			This is a synonymous (silent) variant, and mRNA experimental analysis indicates no impact on splicing or an increase of in-frame naturally occurring splice isoforms with production of wildtype transcripts (PMIDs: 19892845, 22505045, 24607278, 23239986), considered strong evidence against pathogenicity (BP7_Strong (RNA)).
BP5_Strong			Multifactorial likelihood ratio analysis using clinically calibrated data produced a combined LR for this variant of 1.33E-16 (based on Pathology LR=1.33E-16), below the threshold for very strong benign evidence (LR <0.00285) (BP5_Very strong met; ENIGMA internal contributor).

Curation History



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