CanVar-UK
Cancer Predisposition Gene
Variant Database

BRIP1:c.2392C>T p.(Arg798Ter)

SUMMARY	
Gene	BRIP1
Ensembl transcript	ENST00000259008
RefSeq transcript	NM_032043.2
Chromosome	17
Genomic position (hg19)	59793412
Genomic position (hg38)	61716051
Reference allele	C
Variant allele	T
HGVS cDNA	c.2392C>T
HGVS (protein)	p.Arg798Ter
HGVS (protein, 1-letter)	p.R798X
Alternative notation	exon17
rsID	rs137852986
Exon/Intron	BRIP1exon17of20
Variant location	exon
Variant type	substitution
Variant coding effect	nonsense
cDNA position	2392
Intronic position	0
First/Last 3 bases of exon	
HGMD classification (2015)	DM
DMuDB classification (2015)	
UMD classification (2015)	
ClinVar interpretation	Pathogenic
ClinVar review status	2 STARS
ClinVar last evaluated	2025/04/09 00:00

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IN SILICO

Missense/nonsense predictions

BayesDel (no AF)	0.66
BayesDel (add AF)	0.413976
CADD v1.4 raw score	7.757311
CADD v1.4 scaled score [0-99]	39
CADD v1.6 (CADD-Splice) raw score	7.52745
CADD v1.6 (CADD-Splice) scaled score [0-99]	38
AlignGVGD variation (GV)	0
AlignGVGD deviation (GD)	0
SIFT weight	0
SIFT median	0
MAPP p-value	0
MAPP p-value median	0

Conservation

No. of orthologues in alignment	0
No. of conserved residues in alignment	0
BLOSUM62	0

Splicing predictions

Distance to nearest splice site	13
Nearest splice site	3'
SpliceAI delta score (acceptor gain)	0.0001
SpliceAI delta score (acceptor loss)	0.1672
SpliceAI delta score (donor gain)	0.0000
SpliceAI delta score (donor loss)	0.0000
Wild-type MaxEntScan Score	4.18267
Variant MaxEntScan Score	4.18267
% change MaxEntScan Score	0
Wild-type SSF Score	73.979
Variant SSF Score	73.979
% change SSF Score	0
Wild-type NNS Score	0.084658
Variant NNS Score	0.062467
% change NNS Score	-26.212525691606

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CONTROL FREQUENCY

GNOMAD NON-CANCER POPULATION FREQUENCIES (V2.1.1 - JAN 2019)

	Allele count	Individuals sequenced	WES in dataset
African	0	7357	7451
Latino	2	16785	17130
Ashkenazi Jewish	0	4749	4786
East Asian	0	8518	8846
European (Finnish)	0	10724	10816
European (Non-Finnish)	28	50549	51377
Other	2	2741	2810
South Asian	2	14904	15263
Total	34	116327	118479

UK BIOBANK POPULATION FREQUENCIES (RETRIEVED JAN. 2023)

	Allele count	Individuals sequenced	WES in dataset
White	367	439920	442266
Mixed	3	2672	2695
Asian	0	9032	9081
Black	1	7217	7267
Chinese	0	1446	1452
Other	1	5730	5769
Total	372	466017	468530

CASE FREQUENCY

CanVar-UK does not currently store UK laboratory case counts for *BRIP1*.

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GENETIC EPIDEMIOLOGY

No genetic epidemiology data is currently available for this variant in CanVar-UK.

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FUNCTIONAL/SPLICING ANALYSIS

CanVar-UK does not currently store any gene-specific functional data for *BRIP1*.

CanVar-UK is a repository of data annotations for variants in cancer predisposition genes. Classifications and notes are as provided by members of CanVIG-UK, a national group of UK clinical scientist and genomic clinicians.

Assuming prior probability of a variant being pathogenic is 10%:
Pathogenic (P): >=10 evidence points, >99% posterior probability of being pathogenic
Likely pathogenic (LP): 6-9 points, 90-99% posterior probability of being pathogenic
Variant of uncertain significance (VUS): 0-5 points, 10-90% posterior probability of being pathogenic
Likely benign (LB): (-1) to (-5) points, <10% posterior probability of being pathogenic
Benign (B): <=(-6) points, <0.1% posterior probability of being pathogenic

Points towards pathogenicity
Supporting: LR = 2.1, evidence points (ACMG LLR) = 1
Moderate LR = 4.3, evidence points (ACMG LLR) = 2
Strong: LR = 18.7, evidence points (ACMG LLR) = 4
Very strong: LR = 350.4, evidence points (ACMG LLR) = 8

Points towards benignity
Supporting: LR = 0.48, evidence points (ACMG LLR) = -1
Strong: LR = 0.05, evidence points (ACMG LLR) = -4

Pan-gene resources
PHE data (retrieved from the National Disease Registration Service, July 2023), gnomAD (https://gnomad.broadinstitute.org/), SIFT, MAPP, AlignGVGD, SpliceSiteFinder, MaxEntScan, NNSplice (ANNOVAR, dbnsfp35c database), MutationTaster (http://www.mutationtaster.org/), SuSPect (http://www.sbg.bio.ic.ac.uk/suspect/about.html), CADD (http://cadd.gs.washington.edu/), REVEL (https://sites.google.com/site/revelgenomics/), SpliceAI (https://spliceailookup.broadinstitute.org/), HGMD (Human Gene Mutation Database http://www.biobase-international.com/product/hgmd), DMuDB (http://www.ngrl.org.uk/Manchester/projects/dmudb)

Gene-specific resources
LOVDs (Leiden Open Variation Database; http://chromium.liacs.nl/), BIC (Breast Cancer Information Core; http://research.nhgri.nih.gov/bic/), published literature as per citations. For additional details of thresholds to be applied for *in silico* tools and other resources, see https://www.canvaruk.org/

Functional datasets collated for *BRIP1* variants
No functional assay data are currently stored in CanVar-UK for *BRIP1*; however, some *BRIP1* variants may have been assessed in the splicing dataset from Wai et al. (2020; PMID: 32123317) and/or the overlapping splicing data from the Wessex Clinical Genetics Service. To request the addition of a new functional dataset to CanVar-UK, please email us at CanVIG@icr.ac.uk.