

Variant: *NM_000059.4(BRCA2):c.9925G>T (p.Glu3309Ter)*

Version: 2.0

CA026335 [↗](#)

52919 (ClinVar) [↗](#)

Gene: BRCA2 ([HGNC:675](#))

Condition: BRCA2-related cancer predisposition ([MONDO:0012933](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: c0020d30-3b67-46e8-8a83-90ddcfd98a45

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HGVS expressions

NM_000059.4(BRCA2):c.9925G>T (p.Glu3309Ter)

NM_000059.4:c.9925G>T

NC_000013.11:g.32398438G>T

CM000675.2:g.32398438G>T

NC_000013.10:g.32972575G>T

CM000675.1:g.32972575G>T

NC_000013.9:g.31870575G>T

NG_012772.3:g.87959G>T

ENST00000470094.2:c.*448G>T

ENST00000528762.2:c.*1292G>T

ENST00000530893.7:c.9556G>T

ENST00000665585.2:c.*1487G>T

ENST00000700202.2:c.9874G>T

ENST00000700202.1:c.2341G>T

ENST00000700203.1:n.2052G>T

ENST00000380152.8:c.9925G>T

ENST00000544455.6:c.9925G>T

ENST00000614259.2:c.9933G>T

ENST00000680887.1:c.9925G>T

ENST00000380152.7:c.9925G>T

ENST00000533776.1:n.513G>T

ENST00000544455.5:c.9925G>T

NM_000059.3:c.9925G>T

Uncertain Significance

Met criteria codes **1**

PM2_Supporting

Not Met criteria codes **3**

PS3

BS3

PVS1

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 BRCA2 Version 1.0.0

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

ENIGMA BRCA1 and BRCA2 VCEP

The c.9925G>T variant in BRCA2 is predicted to cause a change in the length of the protein due to the insertion of a terminating codon instead of the usual Glutamic acid at amino acid 3309 (p.Glu3309Ter). 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). Nonsense variant predicted to cause a premature stop codon that is predicted to escape nonsense mediated decay, and lead to truncation of a region with unknown protein function (sequence up to BRCA2:p.Glu3309 is maintained) (PVS1 not met). Reported by two calibrated studies with discordant results. Exhibits protein function similar to benign control variants (PMID: 29988080) and pathogenic control variants (PMID: 18607349) (PS3 and BS3 not met). In summary, this variant meets the criteria to be classified as a Variant of uncertain significance for BRCA2-related cancer predisposition based on the ACMG/AMP criteria applied as specified by the ENIGMA BRCA1/2 VCEP (PM2_Supporting).

Met criteria codes

PM2_Supporting

i

✓

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).

Not Met criteria codes

PS3

i

✗

Reported by two calibrated studies with discordant results. Exhibits protein function similar to benign control variants (PMID: 29988080) and pathogenic control variants (PMID: 18607349) (PS3 and BS3 not met).

BS3

i

✗

Reported by two calibrated studies with discordant results. Exhibits protein function similar to benign control variants (PMID: 29988080) and pathogenic control variants (PMID: 18607349) (PS3 and BS3 not met).

PVS1

i

✗

Nonsense variant predicted to cause a premature stop codon that is predicted to escape nonsense mediated decay, and lead to truncation of a region with unknown protein function (sequence up to BRCA2:p.Glu3309 is maintained) (PVS1 not met).

Curation History

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