

Variant: *NM_024675.3(PALB2):c.2074C>T (p.Gln692Ter)*

Version: 2.0

CA294556 [↗](#)

143966 (ClinVar) [↗](#)

Gene: PALB2 ([HGNC:79728](#))

Condition: PALB2-related cancer predisposition ([MONDO:0700272](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: b1afce5b-5094-4d86-9eea-9cd72732a7f7

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HGVS expressions

NM_024675.3(PALB2):c.2074C>T (p.Gln692Ter)

NM_024675.3:c.2074C>T

NC_000016.10:g.23630080G>A

CM000678.2:g.23630080G>A

NC_000016.9:g.23641401G>A

CM000678.1:g.23641401G>A

NC_000016.8:g.23548902G>A

NG_007406.1:g.16278C>T

ENST00000561514.3:c.2080C>T

ENST00000565038.2:c.212-805C>T

ENST00000566069.6:c.2074C>T

ENST00000697377.2:c.2080C>T

ENST00000697379.2:c.2080C>T

ENST00000561514.2:c.1189C>T

ENST00000697374.1:c.1189C>T

ENST00000697375.1:n.3421C>T

ENST00000697376.1:c.1189C>T

ENST00000697377.1:c.1189C>T

ENST00000697378.1:n.2594C>T

ENST00000697379.1:c.1189C>T

ENST00000697380.1:n.1002C>T

ENST00000697381.1:n.769C>T

ENST00000697382.1:c.1189C>T

ENST00000697383.1:c.49-805C>T

ENST00000697384.1:n.2228C>T

ENST00000261584.9:c.2074C>T

ENST00000261584.8:c.2074C>T

ENST00000565038.1:c.87-805C>T

ENST00000568219.5:c.1189C>T

NM_024675.4:c.2074C>T

Likely Pathogenic

Met criteria codes 2

PM5_SupportingPVS1

Not Met criteria codes 2

PP1PM2

Evidence Links 0

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Criteria Specification Information

Criteria Specification: ClinGen Hereditary Breast, Ovarian and Pancreatic Cancer Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PALB2 Version 1.0.0

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.2074C>T (p.Gln692Ter) variant in PALB2 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 5 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism. This alteration results in a termination codon upstream of the most C-terminal pathogenic alteration (PALB2 p.Tyr1183*), as classified by the HBOP VCEP, and is expected to be more deleterious. The highest population minor allele frequency in gnomAD v2.1.1 is 0.000009 in the non-Finnish European population (PM2_Supporting, BS1, and BA1 are not met). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant hereditary breast and ovarian cancer and autosomal recessive FANCN based on the ACMG/AMP criteria applied, as specified by the HBOP VCEP. (PVS1, PM5_Supporting)

Met criteria codes

PM5_Supporting

This alteration results in a termination codon upstream of the most C-terminal pathogenic alteration (PALB2 p.Tyr1183Ter), as classified by the ClinGen Hereditary Breast, Ovarian, and Pancreatic Cancer VCEP, and is expected to be more deleterious (PM5_Supporting).

PVS1

The c.2074C>T (p.Gln692Ter) variant in PALB2 is a nonsense variant predicted to cause a premature stop codon in biologically-relevant-exon 5 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Not Met criteria codes

PP1

This variant has a Bayes factor of 0.9862 based on segregation in one family.

PM2

The highest population minor allele frequency in gnomAD v2.1.1 is 0.000009 (1/113760 alleles) in the non-Finnish European population (PM2_Supporting, BS1, and BA1 are not met).

Curation History

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