

Variant: *NM_024675.4(PALB2):c.109C>A (p.Arg37Ser)*

Version: 2.0

CA191059 [↗](#)

185108 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 168d5508-5262-4204-bdd9-e319bb7ff161

Approved on: 2023/4/5

Published on: 2025/9/16

HGVS expressions

NM_024675.4:c.109C>A

NM_024675.4(PALB2):c.109C>A (p.Arg37Ser)

NC_000016.10:g.23637952G>T

CM000678.2:g.23637952G>T

NC_000016.9:g.23649273G>T

CM000678.1:g.23649273G>T

NC_000016.8:g.23556774G>T

NG_007406.1:g.8406C>A

ENST00000561514.3:c.115C>A

ENST00000565038.2:c.109C>A

ENST00000566069.6:c.109C>A

ENST00000697377.2:c.115C>A

ENST00000697379.2:c.115C>A

ENST00000561514.2:c.-777C>A

ENST00000697374.1:c.-777C>A

ENST00000697375.1:n.1456C>A

ENST00000697376.1:c.-777C>A

ENST00000697377.1:c.-777C>A

ENST00000697378.1:n.629C>A

ENST00000697379.1:c.-777C>A

ENST00000697382.1:c.-777C>A

ENST00000697383.1:c.48+3158C>A

ENST00000697384.1:n.263C>A

ENST00000261584.9:c.109C>A

ENST00000261584.8:c.109C>A

ENST00000561514.1:c.115C>A

ENST00000567003.1:n.387C>A

ENST00000568219.5:c.-777C>A

NM_024675.3:c.109C>A

Uncertain Significance

Met criteria codes **1**

BP1

Not Met criteria codes **4**

PM2

BS1

BS3

BA1

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

The c.109C>A variant in PALB2 is a missense variant predicted to cause substitution of arginine by serine at amino acid 37 (p.Arg37Ser). The highest population minor allele frequency in gnomAD v2.1.1 is 0.00012 in the African population (PM2_Supporting, BS1, and BA1 are not met). This variant is functional in multiple different protein assays (PMID: 31636395); however due to a lack of positive missense controls with known clinical impact, these protein assays do not meet the requirements for use by the HBOP VCEP. PALB2, in which the variant was identified, is defined by the HBOP VCEP as a gene for which primarily truncating variants are known to cause disease. In summary, this variant meets the criteria to be classified as a variant of uncertain significance for autosomal dominant hereditary breast and pancreatic cancer and autosomal recessive FANCN based on the ACMG/AMP criteria applied as specified by the HBOP VCEP. (BP1)

Met criteria codes

BP1			PALB2, in which the variant was identified, is defined by the ClinGen HBOP VCEP as a gene for which primarily truncating variants are known to cause disease (BP1).
-----	---	---	---

Not Met criteria codes

PM2			The highest population minor allele frequency in gnomAD v2.1.1 is 0.00012 (2/16254 alleles) in the African population (PM2_Supporting, BS1, and BA1 are not met).
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			This variant is non-functional in multiple different protein assays (31636395); however due to a lack of known positive missense controls with known clinical impact, protein assays do not meet the requirements for use by the ClinGen HBOP VCEP. Table 1: This variant had a 4.5-fold change in a homology directed DNA repair assay which above 2.4, the authors threshold for benign variation (PMID 31636395). This is ascribed moderate (aka 2 supporting) benign evidence PubMed:31636395 
BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline



 ▾

 ▾

Showing 1 to 2 of 2 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.