The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_024675.3(PALB2):c.2524_2535delinsTCAGA (p.Ala842fs)

Version: 2.0

CA196418

186990 (ClinVar)

Gene: PALB2 (HGNC:79728)
Condition: PALB2-related cancer predisposition (MONDO:0700272)
Inheritance Mode: Autosomal dominant inheritance
UUID: 2fc9b89e-52aa-42d9-a62b-83460b2bf89b
Approved on: 2023/4/5
Published on: 2025/9/16

HGVS expressions

NM_024675.3:c.2524_2535delinsTCAGA
NM_024675.3(PALB2):c.2524_2535delinsTCAGA (p.Ala842fs)
NC_000016.10:g.23629255_23629266delinsTCTGA
CM000678.2:g.23629255_23629266delinsTCTGA
NC_000016.9:g.23640576_23640587delinsTCTGA
CM000678.1:g.23640576_23640587delinsTCTGA
NC_000016.8:g.23548077_23548088delinsTCTGA
NG_007406.1:g.17092_17103delinsTCAGA
ENST00000561514.3:c.2530_2541delinsTCAGA
ENST00000565038.2:c.*5_*16delinsTCAGA
ENST00000566069.6:c.2524_2535delinsTCAGA
ENST00000697377.2:c.2530_2541delinsTCAGA
ENST00000697379.2:c.2530_2541delinsTCAGA
ENST00000561514.2:c.1639_1650delinsTCAGA
ENST00000697374.1:c.1639_1650delinsTCAGA
ENST00000697375.1:n.3871_3882delinsTCAGA
ENST00000697376.1:c.1639_1650delinsTCAGA
ENST00000697377.1:c.1639_1650delinsTCAGA
ENST00000697378.1:n.3044_3055delinsTCAGA
ENST00000697379.1:c.1639_1650delinsTCAGA
ENST00000697380.1:n.1816_1827delinsTCAGA
ENST00000697381.1:n.1219_1230delinsTCAGA
ENST00000697382.1:c.1639_1650delinsTCAGA
ENST00000697383.1:c.58_69delinsTCAGA
ENST00000697384.1:n.2678_2689delinsTCAGA
ENST00000261584.9:c.2524_2535delinsTCAGA
ENST00000261584.8:c.2524_2535delinsTCAGA
ENST00000565038.1:c.96_107delinsTCAGA
ENST00000568219.5:c.1639_1650delinsTCAGA
NM_024675.4:c.2524_2535delinsTCAGA

Pathogenic

Met criteria codes 3

PM5_Supporting PVS1 PM2_Supporting

Expert Panel

Hereditary Breast, Ovarian and Pancreatic Cancer VCEP

Evidence Links 0

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.2524_2535delinsTCAGA (p.Ala842Serfs*7) variant in PALB2 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon 6 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism. This variant is absent from gnomAD v2.1.1. This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (PALB2 p.Tyr1183*) as classified by the HBOP VCEP, and is expected to be more deleterious. In summary, this variant meets criteria to be classified as pathogenic 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. (PVS1, PM2_Supporting, PM5_Supporting)

Met criteria codes

PM5_Supporting	✔	This alteration results in a termination codon upstream of the most C-terminus pathogenic alteration (PALB2 p.Tyr1183*) as classified by the ClinGen HBOP Variant Curation Expert Panel, and is expected to be more deleterious (PM5_Supporting)
PVS1	✔	The c.2524_2535delinsTCAGA (p.Ala842Serfs*7) variant in PALB2 is a frameshift variant predicted to cause a premature stop codon in biologically-relevant-exon 6/13 leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism.
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1.

Curation History

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