Jane Doe
Biological Sex: Female
Date of Birth: 11/13/2018
Sample ID: SM12805
Sample Type: BLOOD
Collection Date: 11/13/2018
Received Date: 11/14/2018

Clinic: The City Clinic
Physician: Jane Smith, M.D.
Phone: 555-555-5555
Fax: 555-555-5555
NPI: 0123456789

Requisition ID:
RQ12345

Report Number:
RP12345

Report Date:
10/29/2024

Scan to learn more

https://myome.com/r/?id=RP12345

A pathogenic variant was identified in the PALB2 gene.

GENE	RESULT	VARIANT	ZYGOSITY
PALB2	Pathogenic	NM_024675.3:c.2167_2168del	Heterozygous

CLINICAL INFORMATION

This testing found that you have a change in a gene called *PALB2*, which is known to increase the risk of developing certain cancers, primarily breast, ovarian, and pancreatic.

Women with a pathogenic variant in *PALB2* have a 33-58% chance of developing breast cancer (PMID 25099575, 31841383), a 5% chance of developing ovarian cancer and a 1-4% chance of developing pancreatic cancer by age 80. Men have a 2-5% chance of developing pancreatic cancer and a 1% chance of developing male breast cancer by age 80 (PMID 31841383).

Variants in the *PALB2* gene associated with cancer predisposition are inherited in an autosomal dominant manner. This means that there is an increased risk for relatives to also have this variant. *PALB2* is also associated with a rare autosomal recessive condition called Fanconi anemia. Individuals need to inherit two variants, one from each parent, to have Fanconi anemia. This result is consistent with being a carrier for Fanconi anemia.

NEXT STEPS

- This is a medically actionable result that should be discussed with your healthcare provider to learn more about potential next steps and management guidelines, which may include screening for breast cancer earlier and more often, risk-reducing surgery, or medication.
- Family members are also at increased risk of having this variant. It is recommended that you share these results with your family members. Genetic testing can help identify who is at increased risk and would benefit from increased screening and management.
- Genetic counseling is recommended to discuss the significance of these results.
- Further information and resources may be available at https://www.facingourrisk.org/

MyOme, Inc.
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

GENES ANALYZED

ABCD1, ACTA2, ACTC1, ACTN2, ACVRL1, APC, APOB, ATM, ATP7B, BAG3, BAP1, BARD1, BMPR1A, BMPR2, BRCA1, BRCA2, BRIP1, BTD, CACNA1C, CACNA1S, CALM1, CALM2, CALM3, CASQ2, CAV1, CDH1, CDK4, CDKN1B, CDKN2A, CHEK2, COL3A1, COL5A1, COL5A2, CRYAB, CSRP3, DES, DICER1, DMD, DSC2, DSG2, DSP, EGFR, EMD, ENG, EPCAM, F2, F5, F9, FBN1, FH, FHL1, FLCN, FLNC, G6PD, GAA, GCH1, GDF2, GLA, GREM1, HAMP, HFE, HJV, HMBS, HNF1A, HNF1B, HOXB13, JUP, KCNE1, KCNH2, KCNJ2, KCNQ1, KIT, LAMP2, LDLR, LDLRAP1, LMNA, LZTR1, MAX, MEFV, MEN1, MET, MITF, MLH1, MSH2, MSH3, MSH6, MUTYH, MYBPC3, MYH11, MYH7, MYL2, MYL3, MYLK, NF1, NF2, NTHL1, OTC, PALB2, PCSK9, PDGFRA, PKP2, PLN, PMS2, POLD1, POLE, POT1, PRKAG2, PRKG1, PROC, PROS1, PTEN, RAD51C, RAD51D, RB1, RBM20, RET, RPE65, RYR1, RYR2, SCN5A, SDHAF2, SDHB, SDHC, SDHD, SERPINA1, SERPINC1, SLC40A1, SMAD3, SMAD4, SMAD9, STK11, TFR2, TGFB2, TGFB3, TGFBR1, TGFBR2, TMEM127, TMEM43, TNNC1, TNNI3, TNNT2, TP53, TPM1, TRDN, TSC1, TSC2, TTN, TTR, VCL, VHL, WT1. See limitations in subsequent page(s).

MyOme, Inc.
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

CLINICAL SUMMARY

A pathogenic variant was identified in the *PALB2* gene.

Clinical Information

The *PALB2* gene encodes a protein that may function in tumor suppression. This protein binds to and colocalizes with the breast cancer 2 early onset protein (BRCA2) in nuclear foci and likely permits the stable intranuclear localization and accumulation of BRCA2. [Source: NCBI]

Inheritance Pattern

Autosomal Dominant

Variant Details

Variant	NM_024675.3:c.2167_2168del
Category	Pathogenic

Evidence

The identified heterozygous deletion (c.2167_2168delAT) lies in exon 5 of the *PALB2* gene and is predicted to cause a frameshift and consequent premature termination of the protein (p.Met723ValfsTer21). Loss of function variants are known to be pathogenic in *PALB2*. This variant has been previously reported in patients affected with breast cancer [PMID 25099575, 24556926, 32339256].

This variant has been reported in the dbSNP database (rs587776416) and in the Genome Aggregation Database (gnomAD) with an allele frequency of 0.005%. In the ClinVar database, the identified variant has been reported as 'pathogenic' (VCV000136132.51) with respect to multiple conditions including hereditary breast ovarian cancer syndrome, familial cancer of breast and hereditary cancer-predisposing syndrome.

References

- Antoniou et al. *Breast-cancer risk in families with mutations in PALB2.* N Engl J Med. 2014; 371(371):497-506. PMID: 25099575.
- Yang et al. *Cancer Risks Associated With Germline PALB2 Pathogenic Variants: An International Study of 524 Families.* J Clin Oncol. 2020; 38(38):674-685. PMID: 31841383.
- Catucci et al. *PALB2 sequencing in Italian familial breast cancer cases reveals a high-risk mutation recurrent in the province of Bergamo.* Genet Med. 2014; 16(16):688-94. PMID: 24556926.
- Zhou et al. *Spectrum of PALB2 germline mutations and characteristics of PALB2-related breast cancer: Screening of 16,501 unselected patients with breast cancer and 5890 controls by next-generation sequencing.* Cancer. 2020; 126(126):3202-3208. PMID: 32339256.

MyOme, Inc.
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

ADDITIONAL INFORMATION

- https://actionability.clinicalgenome.org/ac/Adult/ui/stg2SummaryRpt?version=23115&doc=AC133

TEST METHODS

- Specimen receipt, accessioning, data analysis, and interpretation is performed by MyOme Inc., 1455 Adams Drive, Suite 1150, Menlo Park, CA 94025, CLIA# 05D2203070. Whole Genome Sequencing, excluding data analysis and interpretation, is performed by Broad Clinical Labs LLC, 27 Blue Sky Dr, Burlington, MA 01803, CLIA#22D2055652.
- Genomic DNA obtained from submitted samples was sequenced using Illumina technology. Reads were aligned to the NCBI GRCh37.p13 reference assembly.
- Variants are interpreted and reported based on the standards and guidelines set forth by the American College of Medical Genetics and Genomics (ACMG). Classification categories include pathogenic (P), likely pathogenic (LP), variants of unknown significance (VUS), likely benign (LB) and benign (B). Reported variants only include those which are classified as P or LP. Variants in genes associated with phenotypes inherited in an autosomal recessive fashion need 2 P and/or LP variants to meet the threshold for reporting.
- All reported variants are confirmed by a secondary technology: SNVs are confirmed using Sanger sequencing; CNVs are confirmed using arrays, MLPA or PCR depending on the nature of the copy number variant.

TEST LIMITATIONS

- This test is designed to detect clinically relevant single-nucleotide variants, small insertions and deletions, and copy number variants (CNVs) in the genes listed above. Currently variants cannot be reliably called in certain regions and are not analyzed: PMS2 exons 11-15, BMPR1A exons 12 and 13, TTN exons 173-197, and PTEN exon 9. Additionally, the untranslated region of exon 1 in KCNH2, SMAD3 and STK11 are not analyzed.
- CDK4: analysis is limited to codon 24; EPCAM: analysis is limited to CNV analysis that encompass the 3' end of the gene including exons 8 and 9; F5: analysis is limited to R534Q (i.e. Factor V Leiden); GREM1: analysis is limited to a 40kb duplication overlapping the 5' UTR; HFE: analysis and reporting is limited to p.C282Y homozygotes and p.C282Y/H63D compound heterozygotes; HOXB13: analysis is limited to c.251G>A (p.G84E); MITF: analysis is limited to c.952G>A (p.E318K); POLD1: analysis is limited to the exonuclease domain in exons 6-12; POLE: analysis is limited to c.1270C>G, (p.L424V).
- The sensitivity of this test to detect deletions and duplications may vary depending on the depth of coverage, the size of the variant or other inherent sequence properties. For example, sensitivity to detect all CNVs 50-100 bp in size and duplications < 1kb is reduced.
- This test is not designed to detect aneuploidies or certain types of variation including tandem repeat polymorphisms and low complexity repeats (including BRCA1/2 AluY insertion) and complex structural variants including inversions (including the Boland inversion), translocations, rearrangements, and gene fusions. Sensitivity to detect variants may be reduced in low complexity regions such as homopolymer regions (including MSH2 c.942+3A>T).
- There may be variants in this test that cannot be detected with the current technology.
- A history of stem cell or bone marrow transplantation, or recent blood transfusion may impact the accuracy of the results.
- Like most tests, this test carries a risk of false negative or false positive results, which may be caused by, without limitation, sample contamination from biological or non-biological sources, specimen marking issues, rare genetic variants interfering with analysis, and other technical issues and limitations.

MyOme, Inc.
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502

DISCLAIMERS

This test was developed, and its performance characteristics were determined, by MyOme, Inc., a clinical laboratory certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) to perform high complexity clinical laboratory testing. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test is a screening test for hereditary conditions resulting from mutations in 151 genes. This test provides no information for genomic variants in other genes. Like most tests, this test carries a risk of false negative or false positive results. Testing is unavailable for samples damaged by human error, lost/destroyed due to weather, transit issues or other problems beyond the control of MyOme. Test results should always be interpreted by a clinician in the context of clinical and familial data with the availability of genetic counseling when appropriate. MyOme is not responsible for the content of third-party websites referenced in this report.

REVIEWED BY

Random Person

Random Person

10/29/2024

Date

MyOme, Inc.
1455 Adams Drive, #1150
Menlo Park CA 94025
Email: clinical@myome.com
Phone: +1-628-265-3818

Lab Director:
Brynn Levy M.Sc.(Med)., Ph.D., FACMG
CLIA #05D2203070 CAP #8939502