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SAMPLE REPORT

Ordered By	Contact ID:405956	Org ID:249	
Physician:	Sample Doctor, A		
Client:	Sample Organization (00403)		
Additional Authorized Recipient:			
Counselor Sample, Genetic MS, CGC			

Patient Name:	**Last, First**		
Accession #:	**00-332049**	Specimen #:	44-55-66
AP2 Order #:	205725	Specimen:	Blood EDTA (Purple top)
Birthdate:	01/01/1980	Gender:	F
MRN #:	####	Collected:	05/18/2018
Indication:	Diagnostic/Family History	Received:	05/19/2018

BRCA1/2 Analyses with CancerNext®

RESULTS

BRCA2 **Pathogenic Mutation: 5'UTR_EX10del**

SUMMARY

POSITIVE: Pathogenic Mutation Detected

INTERPRETATION

- This individual is heterozygous for the **5'UTR_EX10del** pathogenic mutation in the *BRCA2* gene.
- This result is consistent with a diagnosis of hereditary breast and ovarian cancer (HBOC) syndrome.
- **Risk estimate**: 45-84% lifetime risk of breast cancer and 11-18% lifetime risk of ovarian cancer (females only), at least a 6% lifetime risk of male breast cancer and 15% risk of prostate cancer by age 65 (males only), and increased lifetime pancreatic cancer risk.
- The expression and severity of disease for this individual cannot be predicted.
- Genetic testing for pathogenic mutations in family members can be helpful in identifying at-risk individuals.
- Genetic counseling is a recommended option for all individuals undergoing genetic testing.

No additional pathogenic mutations, variants of unknown significance, or gross deletions or duplications were detected. Genes Analyzed (36 total): ***APC, ATM, AXIN2, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, DICER1, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1, PALB2, PMS2, PTEN, RAD51C, RAD51D, RECQL, SMAD4, SMARCA4, STK11*** **and** ***TP53*** **(sequencing and deletion/duplication);** ***HOXB13, POLD1*** **and** ***POLE*** **(sequencing only);** ***EPCAM*** **and** ***GREM1*** **(deletion/duplication only)**.

BRCA2 **Additional Information**

The **5'UTR_EX10del** gross deletion spans the 5' untranslated region (5'UTR) through coding exon 10 in the *BRCA2* gene; however, the exact breakpoints of the deletion were not determined. This alteration is expected to result in loss of function due to an abnormal transcript, a translational frameshift leading to premature truncation, or nonsense-mediated mRNA decay. As such, this alteration is interpreted as a disease-causing mutation.

The *BRCA2* (OMIM *600185, NM_000059.3) tumor suppressor gene is located at 13q13.1 and encodes the 3418 amino acid BRCA2 protein. BRCA2 is involved in DNA double-strand break repair by homologous recombination. Pathogenic mutations in the *BRCA2* gene are associated with significantly increased lifetime risks for breast and ovarian cancers in women. Early studies estimated a female breast cancer risk of 84% by age 70 for female *BRCA2* mutation carriers; however, more recent studies suggest a risk of 45-49% by age 70. Pathogenic *BRCA2* mutations are also associated with a contralateral female breast cancer risk of 34.6% within 10 years of initial breast cancer diagnosis with no intervention. The risk for ovarian cancer, including primary peritoneal and fallopian tube cancer, by age 70 in women with *BRCA2* mutations is estimated to be 11-18%. Male *BRCA2* mutation carriers have a cumulative breast cancer risk of over 6% by age 70 and prostate cancer risk of approximately 15% by age 65. In addition, both men and women have an increased risk for melanoma and cancers of the pancreas, gall bladder, bile duct and stomach compared to the general population, although the exact risks have not yet been well defined. Biallelic mutations in the *BRCA2* gene are known to cause Fanconi anemia type D1 (FA-D1), a rare autosomal recessive disorder affecting multiple body systems. Parents who each carry a *BRCA2* mutation have a 25% chance for a child with FA-D1 in every pregnancy.

Order Summary: The following products were included in the test order for this individual. Please note: tests on hold and those that have been cancelled (including reflex testing steps cancelled due to a positive result in a preceding test) are excluded. For additional information, please contact Ambry Genetics.

- BRCA1/2 seq and del/dup (Product Code 8838)
- CancerNext® (Product Code 8824)

ASSAY INFORMATION

General Information: Cancer is a complex, multifactorial disease diagnosed in approximately 1 out of every 2 men and 1 out of every 3 women over the course of a lifetime. Mutations in cancer predisposition genes appear to be responsible for between 5-10% of cancer diagnoses.

Methodology: The **CancerNext®** test is a comprehensive screen of 36 genes associated with hereditary cancer predisposition. Genomic deoxyribonucleic acid (gDNA) is isolated from the patient's specimen using standardized methodology and quantified. Sequence enrichment of the targeted coding exons and adjacent intronic nucleotides is carried out by a bait-capture methodology using long biotinylated oligonucleotide probes followed by polymerase chain reaction (PCR) and Next-Generation sequencing. Additional Sanger sequencing is performed for any regions missing or with insufficient read depth coverage for reliable heterozygous variant detection. Variants in regions complicated by pseudogene interference, variant calls not satisfying depth of coverage and variant allele frequency quality thresholds, and potentially homozygous variants are verified by Sanger sequencing. The *BRCA2* Portuguese founder mutation, c.156_157insAlu (also known as 384insAlu), and the *MSH2* coding exons 1-7 inversion are detected by next generation sequencing and confirmed by multiplex ligation-dependent probe amplification (MLPA) or PCR and agarose gel electrophoresis. Gross deletion/duplication analysis for the genes sequenced (excluding *HOXB13*, *POLD1, POLE, PMS2*) is performed using a custom pipeline based on read-depth from NGS data and/or targeted chromosomal microarray with confirmatory MLPA when applicable. Gross deletion/duplication analysis of *PMS2* is performed using MLPA kit P008-B1. If a deletion is detected in exons 13, 14, or 15 of *PMS2*, double stranded sequencing of the appropriate exon(s) of the pseudogene *PMS2CL* will be performed to determine if the deletion is located in the *PMS2* gene or pseudogene. Sequence analysis is based on the following NCBI reference sequences: *APC*- NM_000038.5 & NM_001127511.2, *ATM*- NM_000051.3, *AXIN2*- NM_004655.3, *BARD1*- NM_000465.2, *BMPR1A*- NM_004329.2, *BRCA1*- NM_007294.3, *BRCA2*- NM_000059.3, *BRIP1*- NM_032043.2, *CDH1*- NM_004360.3, *CDK4*- NM_000075.3, *CDKN2A*- NM_000077.4 and NM_058195.3 (p14ARF), *CHEK2*- NM_007194.3, *DICER1*-NM_177438.2, *HOXB13*- NM_006361.5, *MUTYH*- NM_001128425.1, *MLH1*- NM_000249.3, *MSH2*- NM_000251.1, *MSH3*- NM_002439.3, *MSH6*- NM_000179.2, *NBN*- NM_002485.4, *NF1*- NM_000267.3, *NTHL1*- NM_002528.5, *PALB2*- NM_024675.3, *PMS2*- NM_000535.5, *POLD1*-NM_002691.2, *POLE*-NM_006231.2, *PTEN*- NM_000314.4, *RAD51C*- NM_058216.1, *RAD51D*- NM_002878.3, *RECQL*- NM_002907.3, *SMAD4*- NM_005359.5, *SMARCA4*- NM_001128849.1, *STK11*- NM_000455.4, *TP53*- NM_000546.4.

Analytical Range: The **CancerNext®** test targets detection of DNA sequence mutations in the sequenced genes (*APC, ATM, AXIN2, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A, CHEK2, DICER1, HOXB13, MLH1, MSH2, MSH3, MSH6, MUTYH, NBN, NF1, NTHL1*, *PALB2, POLD1, POLE, PMS2, PTEN, RAD51C, RAD51D, RECQL, SMAD4, SMARCA4, STK11,* and *TP53)* by either Next-Generation or Sanger sequencing of all coding domains and well into the flanking 5' and 3' ends of all the introns and untranslated regions. For *HOXB13*, only variants impacting codon 84 are routinely reported. For *POLD1* and *POLE*, only missense variants and in-frame insertions/deletions in the exonuclease domains (codons 311-541 and 269-485, respectively) are routinely reported. For *RECQL*, only missense variants in the helicase and RCQ domains (codons 63-592) and exonic truncating variants are routinely reported. The *MSH3* polyalanine repeat region is excluded from analysis. Gross deletion/duplication analysis determines gene copy number for the covered exons and untranslated regions of sequenced genes (excluding *HOXB13, POLD1,* and *POLE*) as well as *GREM1* and *EPCAM*. For *GREM1,* only the status of the 40kb 5'UTR gross duplication is analyzed and reported. For *EPCAM*, only gross deletions encompassing the 3' end of the gene are reported. For *NTHL1*, only full-gene gross deletions and duplications are detected. For *APC*, all promoter 1B gross deletions as well as single nucleotide substitutions within the promoter 1B YY1 binding motif (NM_001127511 c.-196_-186) are analyzed and reported.

Result Reports: Results reported herein may be of constitutional or somatic origin. This methodology cannot differentiate between these possibilities. In result reports, alterations in the following classifications are always reported, and are based on the following definitions and clinical recommendations:

- **Pathogenic Mutation**: alterations with sufficient evidence to classify as pathogenic (capable of causing disease). Targeted testing of at-risk relatives and appropriate changes in medical management for pathogenic mutation carriers recommended. Previously described pathogenic mutations, including intronic mutations at any position, are always reported when detected.
- **Variant, Likely Pathogenic (VLP)**: alterations with strong evidence in favor of pathogenicity. Targeted testing of at-risk relatives and appropriate changes in medical management for VLP carriers typically recommended. Previously described likely pathogenic variants, including intronic VLPs at any position, are always reported when detected.
- **Variant, Unknown Significance (VUS)**: alterations with limited and/or conflicting evidence regarding pathogenicity. Familial testing via the Family Studies Program recommended. Medical management to be based personal/family clinical histories, not VUS carrier status. Note, intronic VUSs are always reported out to 5 basepairs from the splice junction when detected.

Alterations of unlikely clinical significance (those with strong/very strong evidence to argue against pathogenicity) are not routinely included on results reports. These include findings classified as "likely benign" and "benign" alterations.

Assay Information Continued on Next Page

ASSAY INFORMATION *(Supplement to Test Results - Continued)*

Resources: The following references are used in variant analysis and classification when applicable for observed genetic alterations.

1. The 1000 Genomes Project Consortium. An integrated map of genetic variation from 1092 human genomes. *Nature*. 2012;491:56-65.
2. ACMG Standards and guidelines for the interpretation of sequence variants. *Genet Med.* 2015 May;17(5):405-23.
3. Ambry Genetics Variant Classification Scheme. http://www.ambrygen.com/variant-classification.
4. Berkeley Drosophila Genome Project [Internet]. Reese MG et al. *J Comp Biol.* 1997;4:311-23. http://www.fruitfly.org/seq_tools/splice.html.
5. Database of Single Nucleotide Polymorphisms (dbSNP) [Internet]. Bethesda (MD): National Center for Biotechnology Information, National Library of Medicine (dbSNP Build ID:135) Available from: www.ncbi.nlm.nih.gov/SNP. Accessed Jan 2012).
6. ESEfinder [Internet]. Smith PJ, et al. (2006) *Hum Mol Genet.* 15(16):2490-2508 and Cartegni L, et al. *Nucleic Acid Research.* 2003;31(13):3568-3571. http://rulai.cshl.edu/cgi-bin/tools/ESE3/esefinder.cgi?process=home.
7. Exome Variant Server, NHLBI Exome Sequencing Project (ESP) [Internet], Seattle WA. Available from: evs.gs.washington.edu/EVS.
8. Grantham R. Amino acid difference formula to help explain protein evolution. *Science.* 1974;185(4151):862-864.
9. HGMD® [Internet]: Stenson PD et al. *Genome Med.* 2009;1(1):13. www.hgmd.cf.ac.uk.
10. Landrum MJ et al. ClinVar: public archive of relationships among sequence variation and human phenotype. *Nucleic Acids Res*. 2014 Jan 1;42(1):D980-5. doi: 10.1093/nar/gkt1113. PubMed PMID: 24234437.
11. Online Mendelian Inheritance in Man, OMIM®. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD), Copyright® 1966-2012. World Wide Web URL: http://omim.org.
12. Feng BJ. PERCH: A Unified Framework for Disease Gene Prioritization. *Hum Mutat.* 2017 Mar;38(3):243-251.
13. Exome Aggregation Consortium (ExAC) [Internet], Cambridge, MA. Available from: http://exac.broadinstitute.org.
14. Genome Aggregation Database (gnomAD) [Internet], Cambridge, MA. Available from: http://gnomad.broadinstitute.org.
15. Lek M et al. Analysis of protein-coding genetic variation in 60,706 humans. *Nature*. 2016 Aug 17;536(7616):285-91. PMID: 27535533
16. Mu W et al. *J Mol Diagn*. 2016 Oct 4. PubMed PMID: 27720647

Disclaimer: This test was developed and its performance characteristics were determined by Ambry Genetics Corporation. It has not been cleared or approved by the US Food and Drug Administration. The FDA does not require this test to go through premarket FDA review. It should not be regarded as investigational or for research. This test should be interpreted in context with other clinical findings. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. This test analyzes the following types of mutations: nucleotide substitutions, small deletions (up to 25 bp), small insertions (up to 10 bp), small indels and gross deletions/duplications. Unless otherwise noted in the methodology section above, it is not intended to analyze the following types of alterations: gross rearrangements, deep intronic variations, Alu element insertions, and other unknown abnormalities. The pattern of mutation types varies with the gene tested and this test detects a high but variable percentage of known and unknown mutants of the classes stated. A negative result from the analysis cannot rule out the possibility that the tested individual carries a rare unexamined mutation or mutation in the undetectable group. This test is designed and validated to be capable of detecting ~99% of described mutations in the 36 genes represented on the panel (analytical sensitivity). The clinical sensitivity of this test may vary widely according to the specific clinical and family history. Breast, ovarian and colon cancers are complex clinical disorders. Mutations in other genes or the regions not analyzed by this test can also give rise to clinical conditions similar to breast cancer, ovarian or colon cancer. Although molecular tests are highly accurate, rare diagnostic errors may occur. Possible diagnostic errors include sample mix-up, erroneous paternity identification, technical errors, clerical errors, and genotyping errors. Genotyping errors can result from trace contamination of PCR reactions, from maternal cell contamination in fetal samples, from rare genetic variants that interfere with analysis, low-level mosaicism, presence of pseudogenes, technical difficulties in regions with high GC content or homopolymer tracts, presence of pre-malignant or malignant cells in the sample, or from other sources. Rare variants present in the human genome reference sequence (GRCh37.p5/hg19) or rare misalignment due to presence of pseudogenes can lead to misinterpretation of patient sequence data can lead to misinterpretation of patient sequence data**.** This report does not represent medical advice. Any questions, suggestions, or concerns regarding interpretation of results should be forwarded to a genetic counselor, medical geneticist, or physician skilled in interpretation of the relevant medical literature.

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Clinician Management Resource for *BRCA2*

This overview of clinical management guidelines is based on this patient's positive test result for a *BRCA2* gene mutation. Unless otherwise stated, medical management guidelines used here are limited to those issued by the National Comprehensive Cancer Network® (NCCN®)[1] in the U.S. Please consult the referenced guideline for complete details and further information.

Clinical correlation with the patient's past medical history, treatments, surgeries and family history may lead to changes in clinical management decisions; therefore, other management recommendations may be considered. Genetic testing results and medical society guidelines help inform medical management decisions but do not constitute formal recommendations. Discussions of medical management decisions and individualized treatment plans should be made in consultation between each patient and his or her healthcare provider, and may change over time.

SCREENING/SURGICAL CONSIDERATIONS[1]	AGE TO START	FREQUENCY
Female Breast Cancer		
Breast awareness • Women should be familiar with their breasts and promptly report changes to their healthcare provider.	18 years old	Periodic and consistent
Clinical Breast Exam	25 years old	Every 6-12 months
Breast Screening* • Breast MRI with contrast • Mammography with consideration of tomosynthesis	25-29 years old	Individualized
	30-75 years old	Every 12 months
	>75 years old	Individualized
Consider options for risk reduction agents, such as chemoprevention (i.e. tamoxifen, raloxifene)	Individualized	Individualized
Ovarian Cancer		
Recommend risk-reducing salpingo-oophorectomy (RRSO)**	Typically 35 to 40 years old, and upon completion of child bearing	N/A
If RRSO not elected, transvaginal ultrasound combined with serum CA-125, although of uncertain benefit, may be considered	30-35 years old	Clinician's discretion
Consider investigational imaging and screening studies, when available in the context of a clinical trial	Individualized	Individualized
Consider options for risk reduction agents, such as chemoprevention (i.e. oral contraceptives)	Individualized	Individualized
Male Breast Cancer		
Breast self-exam training and education	35 years old	Periodic and consistent
Clinical breast exam	35 years old	Every 12 months
Prostate Cancer		
Recommend prostate cancer screening	40 years old	Clinician's discretion

* *Women treated for breast cancer, and have not undergone bilateral mastectomy: follow screening as described.*

** *Ovarian cancer onset in patients with BRCA2 mutations is an average of 8-10 years later than in patients with BRCA1 mutations. Therefore, it is reasonable to delay RRSO for management of ovarian cancer risk until age 40-45y in patients with BRCA2 mutations , unless age at diagnosis in the family warrants earlier age for consideration of prophylactic surgery.*

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V1.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed December 26, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Clinician Management Resource for *BRCA2*

SCREENING/SURGICAL CONSIDERATIONS[1]	AGE TO START	FREQUENCY
Melanoma		
General risk management, such as annual full-body skin examination and minimizing UV exposure	Individualized	Annual, or shorter intervals if indicated
Pancreatic Cancer		
For individuals with exocrine pancreatic cancer in >1 first-or second-degree relative on the same side of the family as the identified pathogenic/likely pathogenic germline variant, consider pancreatic cancer screening.^	50 years (or 10 years younger than the earliest exocrine pancreatic cancer diagnosis in the family)	Annually (with consideration of shorter intervals if worrisome abnormalities seen on screening)
Other		
Counsel for risk of autosomal recessive condition in offspring • If both parents have a *BRCA2* mutation, each of their children have a 25% chance to have a condition such as Fanconi anemia	Individualized	N/A

^ For individuals considering pancreatic cancer screening, the Guidelines recommends that screening be performed in experienced high-volume centers, ideally under research conditions. The Guidelines recommends that such screening only take place after an in-depth discussion about the potential limitations to screening, including cost, the high incidence of pancreatic abnormalities, and uncertainties about the potential benefits of pancreatic cancer screening.

The Guidelines recommends that screening be considered using annual contrast-enhanced MRI/MRCP and/or EUS, with consideration of shorter screening intervals for individuals found to have worrisome abnormalities on screening. The Guidelines emphasizes that most small cystic lesions found on screening will not warrant biopsy, surgical resection, or any other intervention.

1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic. V1.2020. © National Comprehensive Cancer Network, Inc. 2019. All rights reserved. Accessed December 26, 2019. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

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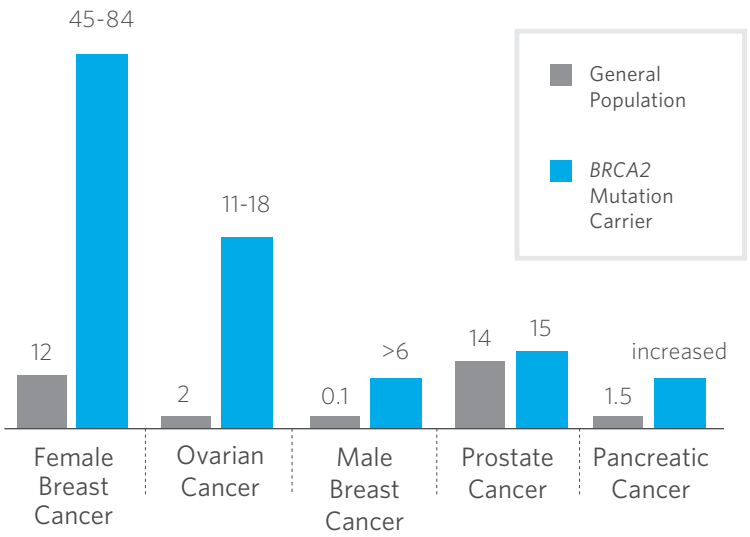
Understanding Your Positive *BRCA2* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

5 Things To Know

1	*BRCA2* mutation	Your testing shows that you have a pathogenic mutation or a variant that is likely pathogenic in the *BRCA2* gene.
2	Hereditary breast and ovarian cancer (HBOC)	People with *BRCA2* mutations have hereditary breast and ovarian cancer (HBOC).
3	Cancer risks	You have an increased chance to develop female or male breast cancer, ovarian cancer, pancreatic cancer, prostate cancer, and possibly other types of cancer.
4	What you can do	There are risk management options to detect cancer early or lower the risk to develop cancer. It is important to discuss these options with your doctor, and decide on a plan that best manages cancer risks.
5	Family	Family members may also be at risk – they can be tested for the *BRCA2* mutation that was identified in you.

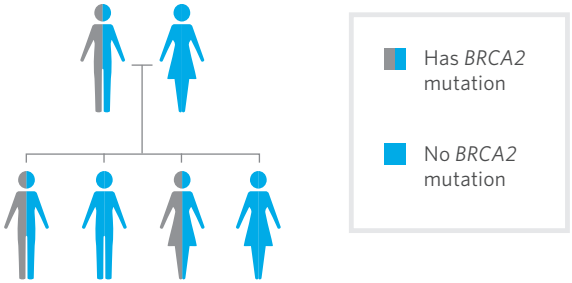
BRCA2 Mutation Lifetime Cancer Risks (%)*



**The above cancer risks represent the typical range for individuals with a mutation in this gene. If available, cancer risks specific to the mutation found in you will be provided in your results report.*

BRCA2 Mutations in the Family

There is a 50/50 random chance to pass on a *BRCA2* mutation to your sons and daughters. The image below shows that both men and women can carry and pass on these mutations.



Understanding Your Positive *BRCA2* Genetic Test Result

INFORMATION FOR PATIENTS WITH A **PATHOGENIC MUTATION** OR **VARIANT, LIKELY PATHOGENIC**

Result	**MUTATION**	Your testing shows that you have a pathogenic mutation (a disease-causing change in the gene, like a spelling mistake) or a variant that is likely pathogenic in the *BRCA2* gene. Both of these results should be considered positive.
Gene	***BRCA2***	Everyone has two copies of the *BRCA2* gene, which we randomly inherit from each of our parents. Mutations in one copy of the *BRCA2* gene can increase the chance for you to develop certain types of cancer in your lifetime.
Condition	**HBOC**	People with *BRCA2* mutations have hereditary breast ovarian cancer (HBOC).
Cancer Risks	**INCREASED**	You have an increased chance to develop female or male breast cancer, ovarian, fallopian tube, or primary peritoneal cancer, pancreatic cancer, prostate cancer, and possibly other types of cancer.
Other Medical Concerns	**MAY BE PRESENT**	Individuals with *BRCA2* mutations may have an increased risk to have a child with Fanconi anemia, but only if their partner also carries a mutation in the *BRCA2* gene. Fanconi anemia is a rare condition that can cause specific physical characteristics, bone marrow failure, and an increased risk of certain cancers.
Management Options	**FOR WOMEN**	Options for early detection and prevention for women may include: breast exam, mammogram, breast MRI, transvaginal ultrasound, a blood test called CA-125, preventive medications, and options for preventive surgery. Talk to your doctor about what options may be right for you.
Management Options	**FOR MEN**	Options for screening and early detection for men may include: breast exam, mammogram, and increased prostate screening. Talk to your doctor about what options may be right for you.
Risk Management	**VARIES**	Risk management decisions are very personal, and the best option depends on many factors. Screening typically begins earlier than the general population and is often more frequently performed. It is important to discuss these options with your doctor.
Family Members	**50/50 CHANCE**	Your close relatives (like your parents, brothers, sisters, children) have a 50/50 random chance of inheriting the *BRCA2* mutation that you carry, and other family members (like your aunts, uncles, cousins) may also inherit it. Your relatives can be tested for this same mutation. Depending on the family history, those who DO NOT have it may not have an increased chance (above the general population) to develop cancer.
Next Steps	**DISCUSS**	It is recommended that you share this information with family members so they can learn more and discuss this with their healthcare providers.
Reach Out	**RESOURCES**	• Ambry's Hereditary Cancer Site for Families patients.ambrygen.com/cancer • Bright Pink brightpink.org • FORCE facingourrisk.org • Sharsheret sharsheret.org • Susan G. Komen Foundation komen.org • Genetic Information Nondiscrimination Act (GINA) ginahelp.org • National Society of Genetic Counselors nsgc.org • Canadian Society of Genetic Counsellors cagc-accg.ca

Please discuss this information with your healthcare provider. The cancer genetics field is continuously evolving, so updates related to your *BRCA2* result, medical recommendations, and/or potential treatments may be available over time. This information is not meant to replace a discussion with a healthcare provider, and should not be considered or interpreted as medical advice.

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PROMPT
Prospective Registry Of MultiPlex Testing

Opportunity to Enroll in Hereditary Cancer Research

Genetic testing can help individuals and families by giving them a clearer idea of their cancer risks. Genetic tests (called multi-gene or multiplex panels) look for changes in several different genes, all in a single test. While all of the genes on these panels have been tied to an increased risk of cancer, we understand the risks associated with some of the genes better than we understand others. One way to help improve our understanding is to enroll people with pathogenic mutations or variants of unknown significance in registries. Registries typically follow people over many years to learn more about these alterations and how they impact their health.

How can I find a research registry?

There are several hereditary cancer research registries that are studying individuals who have had multi-gene panel testing. One registry that is open to individuals nationwide is PROMPT (or Prospective Registry Of MultiPlex Testing). PROMPT is an online registry for patients and families who have had multi-gene testing and have been found to have a genetic variation which may be linked to an increased risk of cancer. PROMPT is a joint effort involving several academic medical centers and commercial laboratories, working together to learn more about the genes that are studied on multi-gene panels. PROMPT will allow researchers to better understand the cancer risks associated with changes in these genes and thus provide a better understanding of the best way to take care of individuals who have such changes.

What is involved in participation?

Participation in the study simply involves completing online surveys. You can take part without providing any personal information to the PROMPT study. But, if you are interested, the PROMPT team will reach out to you to talk about ways that you can get more involved with the research effort. Either way, your participation will help researchers learn more and improve the ability of this genetic testing to help people.

How do I enroll?

You can learn more about or register for PROMPT by going to www.promptstudy.org
or by scanning the QR code to the right.

Thank you again for considering taking part in PROMPT!

If you would like to read more about multi-gene panels, including details about specific genes, please visit our informational website at www.promptstudy.info.

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Opportunity to Enroll in a Family Connection Study

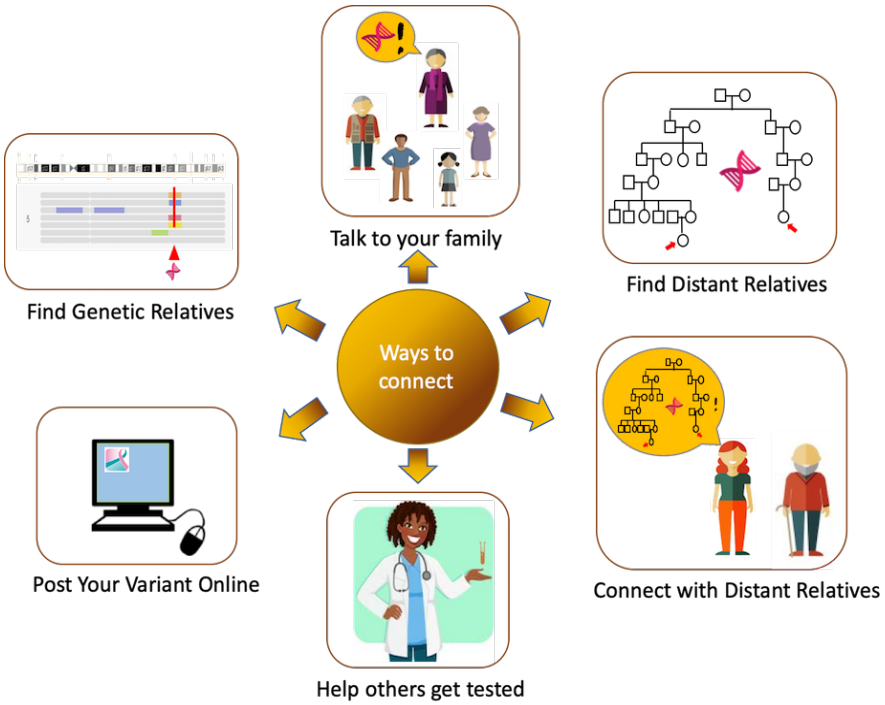
Receiving a positive genetic test for a cancer predisposition gene can feel like an isolating and confusing time for you and your family. Questions such as "Where did this variant come from?" or "What can I do to help others in my family?" are common. That's where researchers at the University of Washington can help with a study called Connect My Variant.

The Connect My Variant study seeks to help study participants talk to their relatives, share important genetic information, expand family trees, identify and connect with distant at-risk relatives, and to help participants guide others to get genetic testing.

"Prevention Through Connection"

Almost all mutations (harmful genetic variants) happened for the first time with a single person in history. That person could be alive today or could have lived hundreds of years ago. Other people with your same genetic variant are probably related to you through the same ancestor. This means that your specific variant is a key to understanding your past. It is also a key that you can use to help many relatives prevent cancer before it happens.

Your close relatives may have your variant; you can talk to them about their possible genetic risk now. Your distant relatives could also share your same genetic variant and may not know about it. These relatives may have had similar experiences with their health and the disease, the same experiences with doctors, and have had to face the same life-planning decisions. Reaching out and helping at-risk relatives get genetic testing may help them prevent cancer and save lives.



You can learn more about this study by visiting http://connectmyvariant.org/ or by contacting us directly by phone (206-598-6807) or email (findmyvariant@uw.edu).