

Sample Report

Hereditary Cancer Test

PATIENT/CLIENT

Jane Doe

DOB: May 25, 1977

ID: 123456

Sex: Female

Requisition #: 123456

ORDERING PHYSICIAN

Dr. Jenny Jones
Sample Medical Group
123 Main St.
Sample, CA

PRIMARY CONTACT

Kelly Peters
Sample Medical Group
123 Main St.
Sample, CA

SPECIMEN

Type: Saliva
Barcode: 223 234234 2343
Collected: Sept 15, 2018
Received: Sept 20, 2018

Report date: October 2, 2018



No mutations were identified.

This means no pathogenic or likely pathogenic variants (also called mutations) associated with an increased risk of hereditary breast, colorectal, melanoma, ovarian, pancreatic, stomach, or uterine cancers were identified in any of the 30 genes analyzed.

This result does not eliminate your risk of developing cancer. Inherited mutations explain some cases of cancer, but many are not inherited and can not be explained by a single cause. Some non-genetic factors that can influence risk include environment and lifestyle, as well as family history without a known genetic link.

GENES ANALYZED

The genes below were analyzed, and no pathogenic or likely pathogenic variants associated with an increased risk of hereditary breast, colorectal, melanoma, ovarian, pancreatic, stomach, or uterine cancers were identified. Please see the test methodology and limitations section for additional information.

APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A (p14ARF), CDKN2A (p16INK4a), CHEK2, EPCAM, GREM1, MITF, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2, POLD1, POLE, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53

REVIEWED BY

Tom Sample, MD, Pathologist

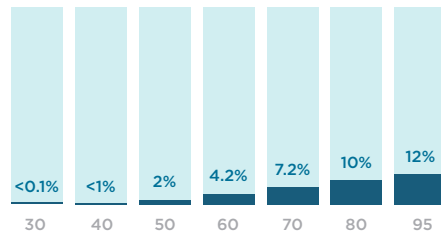
Date

Risk and Family Information

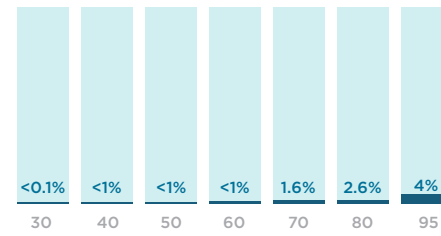
AVERAGE RISK BY AGE AMONG US WOMEN

Average risk among US women to develop specific cancers by different ages in their lives. Breast and colorectal cancers are highlighted because they are more common.

BREAST CANCER



COLORECTAL CANCER



■ Average risk among US women¹

OTHER CANCERS

TYPE	AGE 50	AGE 95
Uterine	< 1%	2.9%
Melanoma	< 1%	1.8%
Ovarian	< 1%	1.3%
Pancreatic	<0.1%	1.5%
Stomach	<0.1%	<1%

FAMILY

Consider sharing your results with relatives who may also benefit from genetic testing. A few key points to remember:

- Your negative result lowers the chance that you have an inherited mutation associated with hereditary cancer.
- It is still possible for your relatives to have a hereditary cancer or a mutation that you did not inherit. They may benefit from their own genetic testing, especially those who have had cancer.
- If any of your relatives has a mutation, there is a 50% chance that their siblings and children also have the same mutation.
- A father and mother are equally likely to pass on a mutation. Sons and daughters are equally likely to inherit a mutation if one of their parents has it.
- If you learn that a relative of yours has a mutation, contact a Color genetic counselor to learn how that information may impact your risk assessment and interpretation of results.

Know your screening guidelines

Below are guidelines for women who have the same cancer risk as the average US woman. Your healthcare provider may use these guidelines to help create a customized screening plan for you.

BREAST CANCER ²

- **Starting at age 25:** Breast awareness - Women should be familiar with their breasts and promptly report changes to their healthcare provider.
- **Between ages 25-39:** Breast exam, risk assessment, and risk reduction counseling by your provider every 1-3 years.
- **Starting at age 40:** Breast exam, risk assessment, and risk reduction counseling by your provider and mammogram every year. Your provider may discuss screening with tomosynthesis (3D mammogram).
- **After age 75:** Your provider may discuss an individualized management plan with you.

COLORECTAL CANCER ³

- **Between ages 50-75:**
 - Colonoscopy every 10 years, or
 - Stool-based testing (high-sensitivity, guaiac-based, or immunochemical-based) every year, or
 - Stool-based FIT-DNA testing every 3 years, or
 - Flexible sigmoidoscopy every 5-10 years, or
 - CT colonography every 5 years.
- **After age 75:** Your provider may discuss an individualized management plan with you.
- These recommendations may change if you have polyps, colon cancer, inflammatory bowel disease (IBD), or family history of colorectal cancer.

UTERINE CANCER ⁴

- **At the time of menopause:** All women should be told about the risks and symptoms of uterine cancer. Women should report any unexpected vaginal bleeding or spotting to their doctors.
- Some women, because of their history, may need to consider having a yearly uterine biopsy. Speak with a healthcare provider about your history.

MELANOMA ⁵

- To reduce the chance of developing melanoma, the American Cancer Society recommends limiting exposure to UV light by avoiding excess sun exposure, wearing a hat, sunglasses and long protective clothing, applying sunscreen with SPF of 30 or higher and avoiding tanning beds and sun lamps.
- Any new, unusual, or changing moles should be reported to your provider or dermatologist.

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PANCREATIC

- Currently, there are no standard screening guidelines for pancreatic cancer. Please discuss any family history of pancreatic cancer with your healthcare provider.

OVARIAN⁶

- Currently, there are no standard screening guidelines for ovarian cancer. Please discuss any family history of ovarian cancer with your healthcare provider.

STOMACH

- Currently, there are no standard screening guidelines for stomach cancer. Please discuss any family history of stomach cancer with your healthcare provider.

**GENERAL
RECOMMENDATIONS
FOR ALL
INDIVIDUALS**⁴

- Avoid all forms of tobacco.
- Get to and stay at a healthy weight.
- Get moving with regular physical activity.
- Eat healthy with plenty of fruits and vegetables.
- Limit how much alcohol you drink (if you drink at all).
- Protect your skin.
- Know yourself, your family history, and your risks.
- Get regular check-ups and cancer screening tests. A cancer-related check-up should include health counseling and, depending on a person's age and gender, exams for cancers of the thyroid, oral cavity, skin, lymph nodes, testes, and ovaries, as well as for some other diseases besides cancer.

Common Questions

GENERAL QUESTIONS

What does a negative test result mean?

A negative result means that no mutations, or genetic changes associated with an increased risk of the most common hereditary cancers were identified in the genes that were analyzed. This result does not eliminate your risk of developing cancer. You may still be at increased risk of cancer due to other factors, mutations not detected by current technology, or mutations in other genes.

Does this result mean I'm not at risk for cancer?

No, the absence of mutations does not mean that you will not develop cancer. Your risk is also influenced by factors such as family history, environment, lifestyle, and random chance. In addition, not all of the genes related to hereditary cancer are known or included on the Color test. You should continue to follow the screening and prevention advice of your healthcare team, or schedule an appointment with a Color genetic counselor if you have questions.

Who will see these test results?

Your results are available to you and the healthcare provider who ordered your test, as well as any additional providers you designated. Your results will not be sent by Color to your insurance company, employer, or any other healthcare provider without consent.

Should I share my results with my healthcare provider?

Color recommends you share your results with your healthcare provider. Sharing your results allows your provider to guide you to appropriate resources and discuss tailored options for screening, prevention, and management.

Are there any protections against discrimination based on these results?

In 2008, a federal law called the Genetic Information Nondiscrimination Act (GINA) was passed to prohibit medical insurance companies and employers from discriminating against individuals on the basis of genetic information, including genetic test results, family cancer history, and even the fact that genetic testing occurred. GINA does not extend to life, disability, or long-term care insurance, which may be governed under state law. Protection against these and other types of discrimination may vary by state. Individuals may consider purchasing these policies prior to undergoing genetic testing. Federal and state laws regarding genetic discrimination change from time to time. We encourage you to keep informed of these important laws and regulations.

*The statements made herein are for informational purposes only and do not constitute legal advice.

What else can cause cancer besides gene mutations?

Most cancers are sporadic, meaning they do not seem to run in the family. Sporadic cancers are likely influenced by a combination of many factors, including age, sex, environment, and even random chance. Some families have more cancer than expected, but without a known genetic mutation or other single explanation. This is called familial cancer. Several risk factors have been associated with familial cancer, including family history, environmental exposures, and lifestyle factors.

GENERAL QUESTIONS*(Continued)***What health history factors may influence my risk of breast cancer?**

All women have some risk of developing breast cancer, even when they do not have a mutation in one of the genes analyzed by this test. There are many factors that can increase risk, including personal and family health history. Your healthcare provider can help determine how your screening plan might be influenced by your health history and other factors.

For breast cancer specifically, some factors known to influence risk include:

- History of cancer
- Family history of breast or ovarian cancer
- Ancestry (where a person is from in the world), including if they are of Ashkenazi Jewish descent
- Age at first period
- Age of first birth, if a woman has given birth
- One or more breast biopsies
- Breast biopsy showing atypical hyperplasia or lobular carcinoma in situ
- History of chest radiation therapy, mastectomy (removal of one's breast or breasts), or oophorectomy (removal of one's ovaries)

FAMILY IMPACT**What do my results mean to my relatives and do any of them need to consider genetic testing?**

Though you do not carry a mutation in any of the genes analyzed, it is possible that your relatives have one that you did not inherit. The only way for them to know whether or not they have such a mutation is for them to undergo genetic testing. Genetic testing can be particularly informative for individuals in the family who have been diagnosed with cancer. Please schedule an appointment with a Color genetic counselor for general recommendations about testing tailored to your family.

Should I talk with my relatives about my result?

You are encouraged to share these results with your relatives. Knowing this information may help them decide whether genetic testing is right for them. Relatives who have had cancer may especially find this information useful. However, keep in mind that not everyone wants to know their genetic status and genetic testing is a personal decision.

TEST METHODOLOGY AND LIMITATIONS

Methodology

Genomic DNA is extracted from the submitted sample, enriched for select regions using a hybridization protocol, and sequenced using Illumina Next Generation Sequencing. Sequence data is aligned to a reference genome, and variants are identified using a suite of bioinformatic tools designed to detect single nucleotide variants, small insertions/deletions, and structural variants such as copy number variants, insertions and inversions. Reported variants may be confirmed by alternate technologies, including Sanger sequencing, MLPA or aCGH. Analysis, variant calling and reporting focus on the complete coding sequence and adjacent intronic sequence of the primary transcript(s), unless otherwise indicated.

Variants are classified according to the standards and guidelines for sequence variant interpretation of the American College of Medical Genetics and Genomics (ACMG). Variant classification categories include pathogenic, likely pathogenic, variant of uncertain significance (VUS), likely benign, and benign. All variants are evaluated by a board certified medical geneticist or pathologist. Identified likely benign and benign variants are not reported. The presence of a VUS is always reported, and the details are available upon request. All VUS and likely pathogenic variants are reviewed bi-annually for updates in the scientific literature. As part of the Color service, we will attempt to recontact the provider and/or the person that was tested if any reported variant's classification changes.

This test was developed and its performance characteristics determined by Color Genomics, a clinical laboratory accredited by the College of American Pathologists (CAP) and certified under the Clinical Laboratory Improvement Amendments (CLIA) to perform high-complexity testing (CAP #8975161 - CLIA #05D2081492). This test has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This test has received the European Conformity (CE) mark in compliance with the EU legislation.

Genes

APC, ATM, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDH1, CDK4, CDKN2A(p14ARF), CDKN2A(p16INK4a), CHEK2, EPCAM*, GREM1*, MITF*, MLH1, MSH2, MSH6, MUTYH, NBN, PALB2, PMS2*, POLD1*, POLE*, PTEN, RAD51C, RAD51D, SMAD4, STK11, TP53*

* These genes are only analyzed at specific locations (see Limitations).

Limitations

This test aims to detect all clinically relevant variants within the genes analyzed (defined above). The majority of these genes are assessed for variants within all coding exons (and adjacent intronic sequence). Exons 12-15 of *PMS2* cannot be reliably assessed with standard target enrichment protocols. For the *CDK4*, *MITF*, *POLD1* and *POLE* genes, the elevated risk of cancer is associated with distinct functional genomic regions; therefore, the complete coding sequences of these genes are not reported, but instead only the following regions: *CDK4* - chr12:g.58145429-58145431 (codon 24), *MITF* - chr3:g.70014091 (including c.952G>A), *POLD1* - chr19:g.50909713 (including c.1433G>A) and *POLE* - chr12:g.133250250 (including c.1270C>G). In *EPCAM*, only large deletions and duplications including the 3' end of the gene are reported since these are the only variants known to silence the *MSH2* gene and therefore increase risk of

**TEST
METHODOLOGY
AND LIMITATIONS***(Continued)*

associated cancer. *GREM1* is only analyzed for duplications in the upstream regulatory region.

This test is not designed to detect chromosomal aneuploidy or complex rearrangements such as translocations. It also does not reliably detect mosaicism. The sensitivity to detect deletions and duplications in the range of 40-250bp, as well as those which deletion/duplication do not overlap more than 250bp of contiguous coding sequence, may be reduced. The presence of a large insertion may interfere with the chemistry used to target the genes of interest, which could decrease the detection sensitivity. In addition, the sequence and identity of a large insertion may not be completely resolved. Inversions including at least one coding exon will be detected only if the breakpoints are covered by the Color test. The sensitivity to detect variants may be reduced in regions of low/high GC content, and in the vicinity of homopolymers and simple sequence repeats.

Color only reports findings within the genes that are on the panel. It is important to understand that there may be variants in those genes that current technology is not able to detect. Additionally, there may be genes associated with hereditary cancer whose clinical association has not yet been definitively established. The test may therefore not detect all variants associated with hereditary cancer. Additionally, in the unlikely event a variant is detected that is associated with a disorder other than hereditary cancer, this information will not be included in the report. Genetic counseling and/or physician consultation may be warranted to ensure complete understanding of your test results.

In very rare cases, such as circulating hematolymphoid neoplasm, allogeneic bone marrow transplant, or recent blood transfusion (within 7 days of testing), the results of germline DNA analysis may be complicated by somatic and/or donor mutations. DNA quality may be affected if a participant has received chemotherapy within the last 120 days.

Disclaimers

Color implements several safeguards to avoid technical errors, such as 2-dimensional barcoding and barcode scanning at several steps throughout the sequencing process. Color is not responsible for errors in specimen collection, transportation, and activation or other errors made prior to receipt at our laboratory. Due to the complexity of genetic testing, diagnostic errors, although rare, may occur due to sample mix-up, DNA contamination, or other laboratory operational errors. In addition, poor sample DNA quality and certain characteristics inherent to specific regions of an individual's genomic DNA may limit the accuracy of results in those regions.

In the absence of an identified pathogenic or likely pathogenic mutation, standard risk models may be employed to determine potential risk of hereditary cancer and guidelines displayed on this report. All risk estimation is approximate, sometimes cannot be specifically calculated, and is based on previously analyzed cohorts. Additionally, risk estimation may be incorrect if inaccurate personal or family history is provided. An elevated risk for hereditary cancer is not a diagnosis and does not guarantee that a person will develop the disease.

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Contact us free of charge at (844) 352-6567 with any questions.

¹ Surveillance, Epidemiology, and End Results (SEER) Program, National Cancer Institute. 2013-2015. DevCan software (<http://surveillance.cancer.gov/devcan>) V 6.7.6. Accessed May 2018.

² National Comprehensive Cancer Network. Breast Cancer Screening and Diagnosis. *NCCN Guidelines Version 2.2018*. Published May 2018. Available at www.nccn.org

³ National Comprehensive Cancer Network. Colorectal Cancer Screening. *NCCN Guidelines Version 1.2018*. Published March 2018. Available at www.nccn.org

⁴ American Cancer Society Guidelines for the Early Detection of Cancer. Updated July 7, 2017. Accessed April 2, 2018. Available at www.cancer.org

⁵ Skin Cancer Prevention and Early Detection. *The American Cancer Society*. Updated March 19, 2017. Accessed April 2, 2018. Available at www.cancer.org

⁶ Ovarian, Fallopian Tube, and Primary Peritoneal Cancer Screening. *National Cancer Institute*. Updated February 2017. Accessed April 2018.

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