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Your genetic guide to

BREAST CANCER RISK

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Introduction

Human health is a complex interplay between genetics and the environment (lifestyle, diet, activity, stress and other triggers). Your genes and environmental factors play a vital role in your health and well-being.

This is not a medical diagnostic report. Ancestry tests are not clinically certified and not suitable for medical purposes

The health outcomes presented in this report are determined by the number of markers present in your genome raw data, which differs significantly between companies. Genetic Research is an emerging field and the genetic basis of many health conditions is yet to be fully established.

Breast cancer tends to run in certain families, but some family members buck the trend. Unlike a few decades ago, when few remedies were available, today, early detection can significantly reduce and even nearly eliminate the risk.

This report helps you learn about your predisposition and take preventive action.

Cancers that run in families, referred to as, familial or hereditary cancers, are often characterized by variations in certain genes (ie, a high penetrance phenotype). These variations may be transmitted to the progeny from either the father or the mother.

Testing positive for a pathogenic mutation (like in the BRCA1 gene) means your risk of developing breast and ovarian cancer is greater than that of the average woman. However, a higher risk does not imply a diagnosis of cancer. In fact, several individuals with high risk variants will never develop the disease.

Your actual risk of developing breast cancer is dependant on several genetic and non-genetic factors. Carrying a high risk genetic variant merely serves as an alerting mechanism to consult an expert and follow professional guidance to rule out the possibility of cancer.

According to The National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology

(1) serve as a resource for healthcare providers to identify individuals who may benefit from cancer risk assessment and genetic counseling;

(2) provide genetic counselors with an updated tool for the assessment of individual breast and ovarian cancer risk and to guide decisions related to genetic testing;

(3) facilitate a multidisciplinary approach in the management of individuals at increased risk for hereditary breast and/or ovarian cancer.

Some facts about genes and breast cancer-

- **Approximately 10 % of breast cancer patients carry specific gene variations that are associated with an increased risk of developing the disease.**
- **Further, a close family member who also had breast cancer could increase the risk by 20%, even if there are no specific genetic variants.**
- **BRCA1 and BRCA2 are the most common genes known to increase the risk of breast and ovarian cancers. Gene variations in these genes are also known to be associated with an increased risk for other cancers, including fallopian tube cancer, primary peritoneal cancer, pancreatic cancer, melanoma, male breast cancer, and prostate cancer**
- **Multi-gene testing can be used for the simultaneous analysis of multiple oncogenes which have similar clinical phenotypes**
- **In high risk families, multi-gene testing will help in potentially increasing the detection of clinically actionable gene variants.**

People who should consider genetic testing for breast cancer are those who have been diagnosed

- **early onset breast cancer- less than 50 years.**
- **both Breast and ovarian cancer**
- **multiple breast cancers**
- **triple-negative breast cancer**
- **close relatives on the same side of the family with the same (or related) cancers**

People of the Ashkenazi Jewish ancestry are at a higher risk of developing this type of cancer and will also benefit from genetic testing.

Breast cancer drug therapy is also influenced by your gene variations. Understanding your genetic metabolism of various drugs will help you avoid potential adverse events related to ineffectiveness of or hypersensitivity to the therapeutic agent.

In this report, we profile genes that are shown to be associated with an increased risk of breast cancer and your response to various drugs administered for breast cancer.

We hope this report will help you understand your body better and to align suitable multidisciplinary management procedures to lower the risk for cancer and to live a healthy life

Introduction

This report is presented in a user-friendly language and format. The following tips will help you get the best information value out of the report.

- **What are normal and risk variants?**

Genetic variations come in two flavors, common- present among the majority of people (reference) and uncommon- present amont the minority (other than reference). In most cases, the reference version is the normal functioning and alternate version leads to abnormality. If an alternate version is present, it may be a risk causing variant. Someone with a large number of uncommon variants may carry an increased risk profile of that condifiton.

- **What does pathogenic variant mean?**

A pathogenc variant is a genetic variant that has been indicated as being definitively associated with the disease in some cases.

- **What do "Gene markers analyzed" and "Gene markers present in your genome data" indicate?**

There are a large number of genetic variants in our database. Your raw data may not have all the variants in our database and hence we will not be able to assess the risk status of those. We indicate how many variants we are considering. Out of these, how many are present in your raw data and out of these how many are risk variants and how many are pathogenic variants.

- **Where did the information contained in the report come from?**

The genetic markers that are used in this report are based on scientific studies published in international journals.The recommendations were matched with high authority public resources such as FDA, Clinvar, COSMIC, CPIC guidelines and PharmGKB, among several other sources.

YOUR SUMMARY RESULTS

Trait Name	Your Result	Your Outcomes
Hypertension due to Chemotherapy in Breast Cancer (Bevacizumab) Genetic variations influencing hypertension risk when undergoing chemotherapy (Bevacizumab) Learn More	⚠	[illegible]
Rotating Night Shift Work and Breast Cancer Risk Genetic variations influencing breast cancer risk with long-term rotating night-shift work Learn More	✓	[illegible]
Alcohol Consumption and Breast Cancer Risk Genetic variations influencing breast cancer risk with alcohol consumption Learn More	✓	[illegible]

Radiation Exposure and Breast Cancer Risk Genetic variations influencing breast cancer risk with radiation exposure Learn More	✔	
Exercise and Breast Cancer Risk Genetic variations influencing breast cancer risk with low physical activity Learn More	✔	
Smoked Meat Consumption and Breast Cancer Risk Genetic variations influencing breast cancer risk with smoked meat consumption Learn More	⚠	
Menopausal Hormone Therapy Interaction with Breast Cancer Risk Genetic variations influencing breast cancer risk when on menopausal hormonal therapy Learn More	⚠	

Hair Loss due to Chemotherapy in Breast Cancer Genetic variations influencing hair loss (alopecia) risk when undergoing chemotherapy Learn More	⚠	
Age at Menarche and Breast Cancer Risk Genetic variations influencing breast cancer risk with early menarche Learn More	⚠	
Breast Size/Density and Breast Cancer Risk Genetic variations influencing breast cancer risk in people with bigger/denser breasts Learn More	⚠	
Breast Feeding Duration and Breast Cancer risk Genetic variations influencing breast cancer risk with shorter breastfeeding duration Learn More		✔

Overweight and Breast Cancer risk Genetic variations influencing breast cancer risk when overweight Learn More	✔	
Postmenopausal Breast Cancer risk Genetic variations influencing postmenopausal breast cancer risk Learn More	⚠	
Smoking and Breast Cancer Risk Genetic variations influencing smoking-induced breast cancer risk Learn More	⚠	
Estrogen (Estradiol/Estrone) Plasma Levels and Breast Cancer Risk Genetic variations influencing breast cancer risk with high estrogen/estradiol levels Learn More	⚠	

HYPERTENSION DUE TO CHEMOTHERAPY IN BREAST CANCER (BEVACIZUMAB)

Moderate: Likely to have a moderate risk of developing hypertension due to bevacizumab based chemotherapy

Bevacizumab is a medication used to treat several types of cancer. It restricts tumor growth by limiting blood supply to the tumor blood vessels. There are many side effects of using bevacizumab, and one such significant risk is bevacizumab-induced hypertension. The effect

Recommendations:

- Here are some tips to manage your blood pressure when on chemotherapy:
- **Talk to your doctor to understand the risks:** Talk to your doctor to understand the risks associated with bevacizumab. Understand how effective it could be to treat your breast cancer and if the benefits outweigh the risks.

Genes Analyzed: C18ORF34, MAML2, COL21A1, FLJ46010, NPHP3-AS1, EGLN3, CTBS, UBE2E2, LRRK1, MTMR7, ERBB4, AK5, SPATA1, CNTNAP2, FRMD4B, C1ORF129, CRTAP, PARVB, SLC22A23, LOC100652793, PPP1R3A, SCFD2, NELL1, SV2C, GLIS3, SPEG, TTC35, LOC100506713 ALOX12, EGF, ANXA13, MAP1A, MSRA, MMP16, DRG2, FRMD6, EMR1, NONE, DUSP13, TGFBR2, KCNK2, XKR6, LAMB3, OR5AC1, EPHB2, CPB1, LOC100507466, DEFB135, ZSCAN29, SCUBE2, MAX FNTB CHURC1-FNTB, PCDP1, CPNE4, LOC729852, FUCA2, LOC100133047, TBC1D22A, TUBGCP4, ERMAP, HHAT, PCP4, FLJ30838, CPNE5, HDAC9, AGTR1, WNK1, PFKFB3, CCDC33

Number of Gene Markers Found: 243

Number of Gene Markers Analyzed:303

ROTATING NIGHT SHIFT WORK AND BREAST CANCER RISK

Low: Likely to have a low risk of developing breast cancer in long-term rotating night-shift work exposure

Working the night shift is carcinogenic to humans. Several studies show that disruption in the night's sleep can reduce melatonin levels and increase the risk of tumor growth. The risk

Recommendations:

- Night shift work leads to disrupted circadian rhythm, which has been associated with increased risk of obesity and heart diseases, mood changes, gastrointestinal problems, increased risk of several types of cancer, especially breast cancer.
- **Cluster your night shifts together:** It can be helpful to group your shifts together and stick to a night shift sleep schedule even on your off days. This way, your body gets used to

Genes Analyzed: CRY2, MTNR1B, RORB, ARNTL, NPAS2
Number of Gene Markers Found: 6
Number of Gene Markers Analyzed:8

ALCOHOL CONSUMPTION AND BREAST CANCER RISK

Low: Likely to have a low risk of developing breast cancer with alcohol consumption

Alcohol consumption is a risk factor for breast cancer. Compared to non-drinkers, women who have 1 drink a day have a 7-10% increased risk, and women who have 2 or more drinks a day have about 20% increased risk of developing breast cancer. Studies show that alcohol

Recommendations:

- Alcohol consumption, other than increasing your risk for breast cancer, is associated with many long-term health effects. The best thing to do is avoid alcohol consumption. But if you do occasionally indulge in drinking, here are some tips for safe drinking:
- **Moderation is the key:** Moderation refers to not getting you intoxicated (or drunk); this entails drinking no more than 1 drink per day if you are a woman and no more than 2 if you are a man.

Genes Analyzed: CYP2E1, CASP8, ALDH2, CYP19A1, PPARG, GSR, NONE
Number of Gene Markers Found: 7
Number of Gene Markers Analyzed:7

RADIATION EXPOSURE AND BREAST CANCER RISK

Low: Likely to have a low risk for radiation induced breast cancer

Radiation is the transmission of energy through space or a medium. Some radiation is naturally created, while others are artificially made. People who are exposed to a higher dose of radiation have a higher risk of developing breast cancer. Studies show that women under

Recommendations:

- Radiation can damage the DNA in our cells. Exposure to very high levels of radiation can cause acute health effects such as skin burns. Some long-term effects include cancer and cardiovascular disease.

Genes Analyzed: WRN, PRKDC, BRCA1, PTGS2, ERCC2, H19
Number of Gene Markers Found: 8
Number of Gene Markers Analyzed:8

EXERCISE AND BREAST CANCER RISK

Low: Likely to have a low risk of developing breast cancer with high physical activity

Women who exercise regularly have a reduced risk of breast cancer. 150-300 minutes of moderate-intensity exercise or 75-150 minutes of high-intensity exercise per week can help reduce the breast cancer risk in women. Physical activity after breast cancer diagnosis

Recommendations:

- Regular exercising impacts your overall health positively. Besides reducing risk for many types of cancer, including breast cancer, it also improves your heart health, promotes healthy aging, and maintains your bone health.
- **Consider aerobic exercise:** Aerobic exercises like walking, running, cycling, swimming, dancing, etc., are highly beneficial for weight loss, reducing cholesterol levels, increasing

Genes Analyzed: CRHR1, TSC1, ERCC5 (XPG), FGFR2, ERCC4 (XPF), LINC00461, SATB1-AS1, NEAR ESR1, MLLT10, RIT2/SYT4, ZNF362, MLH1, LINC01470, MTRR/LOC729506, PML
Number of Gene Markers Found: 16
Number of Gene Markers Analyzed:18

SMOKED MEAT CONSUMPTION AND BREAST CANCER RISK

Moderate: Likely to have a moderate risk of developing breast cancer on smoked-meat intake

One of the chemicals produced due to burning wood while smoking food is Polycyclic Aromatic Hydrocarbon (PAH). PAHs are carcinogenic (cancer-causing) agents. Excess consumption of smoked meat can increase the risk of developing different kinds of cancer,

Recommendations:

- Excess consumption of smoked meat can increase the risk of developing different kinds of cancer, including breast cancer.
- **Try alternate methods of cooking meat:** Some safe ways to cook meat are pressure

Genes Analyzed: CYP1B1, CYP1A1
Number of Gene Markers Found: 2
Number of Gene Markers Analyzed:3

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Only full genome sequences are exhaustive. All other forms of genetic tests only provide a limited subset of genetic information that has been found to be relevant to specific conditions. Since this report is not generated by conducting a whole genome sequence test, the results reported are limited to a specific set of mutations known to be associated with specific conditions. Genetic information is also subject to revision based on the latest advances in scientific research. Therefore it is possible that the interpretation of results reported herein may vary or be altered subject to ongoing research. Sometimes, the interpretations may vary from company to company based on which studies are being given a higher preference compared to others.

Xcode's role is limited to providing results of genetic test and providing a broad set of general recommendations. More detailed recommendations that may be specific to you are to be made by qualified Professional Practitioners only. General guidelines provided in our report are for information purpose only and are meant to aid your Professional Practitioner to render the relevant professional or medical advice and treatment. While assessing your genetic parameters and providing the report and recommendations, we do not consider your past or existing health conditions and or any medication taken by you (either in the past or currently), even if you may have provided us with such information. Our report and the recommendations therein are to be acted upon in consultation with a medical or other health and wellness professional practitioner.

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